8th International Conference on the Tear Film & Ocular Surface: Basic Science and Clinical Relevance

Conference Program & Abstract Book

Montpellier, France

September 7-10, 2016

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Preface

A significant, international research effort is being directed towards understanding the composition, function and regulation of the preocular tear film. This effort is motivated by the recognition that the tear film plays a critical role in maintaining corneal and conjunctival integrity, protecting against microbial challenge and preserving visual acuity. In addition, research is stimulated by the knowledge that tear film deficiency, which occurs in countless individuals throughout the world, may lead to ocular surface desiccation, corneal ulceration, an increased incidence of infectious disease, and potentially pronounced visual disability.

To promote further progress in this field of vision research, the 8th International Conference on the Tear Film & Ocular Surface: Basic Science and Clinical Relevance will be held at Le Corum in Montpellier, France, from September 7 to 10, 2016. This Conference, which is sponsored by TFOS (www.TearFilm.org), is designed to assess the current knowledge and 'state of the art' research on the structure and function of tear film-producing tissues, tears and the ocular surface in both health and disease. The goal of this Conference is to promote an international exchange of information that will be of value to basic scientists involved in eye research, to clinicians in the eye care community, and to pharmaceutical and diagnostic companies with an interest in tear film or ocular surface disorders.

To help achieve this objective, numerous scientists, clinicians and industry representatives from 41 countries, including Algeria, Argentina, Australia, Austria, Belgium, Brazil, Bulgaria, Canada, China, Czech Republic, Denmark, Finland, France, Germany, Ghana, Greece, Iceland, India, Italy, Japan, Mexico, New Zealand, Norway, Poland, Romania, Russia, Singapore, South Africa, South Korea, Spain, Sweden, Switzerland, Thailand, The Netherlands, United Kingdom, United States, Uruguay and Vietnam have registered as participants in this Conference.

This book contains the scientific program, as well as the abstracts of the oral and poster presentations, of this TFOS Conference.

David A. Sullivan

Acknowledgments

TFOS expresses its appreciation to Sabrina Zappia and CITYNet (www.citynetonline.it), Julie Karimi and JAKA Congressi (www.jaka.it) and Haydée Marangoni and h.design (www.hdesign.biz) for their help with this Conference.

Recognition

TFOS congratulates the following individuals, who were the recipients of the Conference Young Investigator Awards: Laura Downie (Australia), Masaki Fukui (Japan), Laura García-Posadas (USA), Ulrike Hampel (Germany), Takenori Inomata (USA), Yusuke Izuta (Japan), Arsia Jamali (USA), Kai Jin (Japan), Yu Jeong Kim (South Korea), Isobel Massie (Germany), Hamid-Reza Moein (USA), Céline Portal (France), Martin Schicht (Germany), Yuichi Uchino (Japan) and Stephanie Wan (USA).

Thursday, September 8, 2016

Opening Remarks

8:00 Dimitri T. Azar, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL, USA

6th Claes H. Dohlman Conference Address

Chairperson – Dimitri Azar (USA)

8:05 Studying both sexes: a guiding principle for ophthalmology. Janine Clayton, Office of Research on Women's Health, National Institutes of Health, Bethesda, MD, USA

Session I

All Eyes On Sex

Chairpersons - Gerd Geerling (Germany), Laura Downie (Australia), Piera Versura (Italy)

8:35 **Keynote Address:** Glucocorticoids, sex and inflammation. Mahita Kadmiel and John A. Cidlowski, Signal Transduction Laboratory, NIH/NIEHS, Research Triangle Park, North Carolina, USA

9:00 **Keynote Address:** Sex & the eye: A potentially blinding impact. Louis R. Pasquale, Massachusetts Eye & Ear, Channing Division of Network Medicine, Brigham & Women's Hospital and Harvard Medical School, Boston, MA, USA

9:25 **Keynote Address:** Ménage à trois: Sex, sex steroids and dry eye disease. David A. Sullivan, Yang Liu, Juan Ding and Wendy R. Kam, Schepens Eye Research Institute, Massachusetts Eye and Ear and Harvard Medical School, Boston, MA, USA

9:50 **Poster Session I (with Coffee & Tea)**
Chairpersons - José M Benitez del Castillo Sanchez (Spain), Darlene A Dartt (USA)

Mechanobiological Stresses: Pathways To Ocular Surface Epitheliopathy

Chairpersons - Christophe Baudouin (France), Ulrike Hampel (Germany), Shigeto Shimmura (Japan)

10:40 **Keynote Address**: Friction, lubrication and wear: the impact of interacting ocular surfaces in relative motion. Tannin A. Schmidt, Faculty of Kinesiology and Schulich School of Engineering, University of Calgary, Calgary, AB, CANADA

11:05 **Keynote Address**: Blinking from a Tribological Viewpoint. Heiko Pult, Optometry and Vision Research, Weinheim, Germany; Cardiff University, School of Optometry and Vison Sciences.,UK; and Ophthalmic Research Group, Life and Health Sciences, Aston University, Birmingham, UK

11:30 **Keynote Address:** Hyperosmolarity-induced glycodeficient corneal epitheliopathy. Benjamin D. Sullivan, TearLab, Inc., San Diego CA. and Lμbris BioPharma, Boston MA

11:55 **Poster Viewing & Lunch**

Prime Time TFOS Debates 1

Chairpersons - Stefan Schrader (Germany, Choun-Ki Joo (South Korea), Yu Jeong Kim (South Korea)

13:15 **Debate 1:** Is ex vivo expansion of limbal stem cells necessary for the treatment of limbal stem cell deficiency?

Yes – Paolo Rama,[1] Stanislav Matuška,[1] Giorgio Paganoni,[2] Graziella Pellegrini[2] Ophthalmology, San Raffaele Hospital, Milano, Italy;[1] Center for Regenerative Medicine, University of Modena and Reggio Emilia, Italy[2]

No – Virender S. Sangwan, L V Prasad Eye Institutte, Hyderabad, India

13:45 **Debate 2:** Which is the bigger risk factor for dry eye disease: meibomian gland dysfunction (MGD) or contact lens discomfort (CLD)?

MGD – Kelly K. Nichols, University of Alabama at Birmingham School of Optometry, Birmingham, AL, USA

CLD – Jason J. Nichols, University of Alabama at Birmingham School of Optometry, Birmingham, AL, USA

Neuropathic Pain

Chairpersons - Yusuke Izuta (Japan), Deborah S Jacobs (USA), Mark I Rosenblatt (USA)

14:15 **Keynote Address**: Definition and clinical endpoints for chronic neuropathic pain. Elizabeth Felix,[1,2] Constantine D. Sarantopoulos,[1,3] Roy C. Levitt, [1,3,4] and Anat Galor,[1,5] Miami Veterans Administration Medical Center, Miami, Florida;[1] Department of Physical Medicine and Rehabilitation, University of Miami Miller School of Medicine; [2] Department of Anesthesiology, Perioperative Medicine and Pain Management, University of Miami Miller School of Medicine; [3] John T. Macdonald Foundation Department of Human Genetics, and the John P. Hussman Institute of Human Genomics, University of Miami Miller School of Medicine; [4] Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, FL, USA[5]

14:40 **Keynote Address:** Origin of corneal neuropathic pain. Carlos Belmonte, Instituto de Neurociencias, Universidad Miguel Hernandez-CSIC, San Juan de Alicante and Instituto Universitario Fernandez-Vega, Oviedo, Spain

15:05 **Keynote Address**: Diagnosis and management of corneal somatosensory dysfunction Anat Galor,[1,2],Constantine D. Sarantopoulos,[1,3] Roy C. Levitt,[1,3,4] Elizabeth R. Felix,[1,5] [1]Miami Veterans Administration Medical Center, Miami, Florida; [2]Bascom Palmer Eye Institute, University of Miami Miller School of Medicine; [3]Department of Anesthesiology, Perioperative Medicine and Pain Management, University of Miami Miller School of Medicine; [4]John T. Macdonald Foundation Department of Human Genetics, and the John P. Hussman Institute of Human Genomics, University of Miami Miller School of Medicine; [5]Department of Physical Medicine and Rehabilitation, University of Miami Miller School of Medicine

15:30 Poster Session I (with Coffee & Tea)
Chairpersons - José M Benitez del Castillo Sanchez (Spain), Darlene A Dartt (USA)

Unique Challenges And Unmet Needs For The Treatment Of Ocular Surface Disease In Various Regions Of The World

Chairpersons – Stefano Barabino (Italy), Cecilia Marini (Argentina), Hamid-Reza Moein (USA)

16:20 **Keynote Address:** India (South Asia). Geetha Iyer, Sankara Nethralaya, Chennai, India

16:40 **Keynote Address**: Africa. Kovin S. Naidoo, Brien Holden Vision Institute, Sydney, Australia.

17:00 **Keynote Address**: Latin America. Denise de Freitas, Department of Ophthalmology and Visual Sciences, Paulista School of Medicine, Federal University of São Paulo, São Paulo, Brazil

17:20 **Keynote Address**: Oceania. Jennifer P. Craig, Department of Ophthalmology, The University of Auckland, New Zealand

17:40 **Keynote Address**: United States. Dimitri T. Azar, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL, USA

18:00 **Keynote Address**: Europe. Stefano Bonini, Section of Ophthalmology, University of Rome Campus BioMedico, Rome, Italy

TFOS i^2 Innovation Showcase

18:30 **Introduction,** Amy Gallant Sullivan, TFOS Executive Director

18:34 **EyeFocus** (UK; www.eyefocus.com), Tobias Stone, Founder

18:40 **Avizorex Pharma** (Spain; www.avizorex.com), Patrick Tresserras, Chief Executive Officer/Founder

18:46 **Cambium Medical** Technologies (USA; www.cambiumbio.com), Terence A. Walts, President & Chief Executive Officer

18:52 **Mu-Drop** (The Netherlands; www.mu-drop.nl), Frans Lichtenauer, Chief Executive Officer

18:58 **Opia Technologies** (France; www.opiatech.com), Pierre Roy, Chief Executive Officer

19:04 **20/20 Optimeyes** (Canada), Heather Sheardown, Co-Founder

19:10 **Signal Ophthalmic Consulting** (USA), Whitney Hauser, Founder

19:16 **Suricog** (France; www.suricog.fr), Benjamin Samuel, Business Developer

19:22 **TearSolutions** (USA; http://www.tearsolutions.com), Gordon Laurie, Co-Founder

Poster Session I

Chairpersons - José M Benitez del Castillo Sanchez (Spain), Darlene A Dartt (USA)

1 HOW COMMON ARE EYELID DISORDERS ACROSS EUROPE? J.M. Benitez del Castillo[(1)], Z. Zagórski[(2)], J. Palmares[(3)], M. Yağmur[(4)], T. Kaercher[(5)], B. Van Dooren[(6)], Dr S. Doan[(7)], P. Jonckheere[(8)], P. K. Jensen[(9)], 1) Hospital Clinico San Carlos, SPAIN 2) Zagorski Eye Surgery Centre, POLAND 3) Hospital Lusíadas, PORTUGAL 4) Cukurova University, TURKEY 5) Augenarztpraxis, GERMANY 6) Erasmus Medical Center, The NETHERLANDS 7) Hôpital Bichat, FRANCE 8) Oogkliniek Deurne, BELGIUM 9) Copenhagen University, DENMARK

2 MEIBOGRAPHY: INTER-RATER RELIABILITY. Johanna Boström[1], Lovisa Pettersson[2], Dr. Karthikeyan Baskaran[1], Dr. Fredrik Källmark[3], Prof. Peter Gierow[1]. [1]Department of Medicine and Optometry, Linnaeus University, Kalmar, Sweden [2]Unit of Optometry, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden [3]Källmarkskliniken, Stockholm, Sweden.

3 MEIBOMIAN GLAND AND TEAR FILM CHARACTERIZATION IN A HEALTHY UNIVERSITY POPULATION. Carme Serés, Genís Cardona, Cristina Álvarez. School of Optics and Optometry of Terrassa, Universitat Politècnica de Catalunya · BarcelonaTech, Terrassa, Spain.

4 AUTOMATED MEASUREMENT OF TEAR FILM DYNAMICS AND LIPID LAYER THICKNESS FOR ASSESSMENT OF NON-SJÖGREN DRY EYE SYNDROME WITH MEIBOMIAN GLAND DYSFUNCTION Tae-im Kim, MD, PhD[1], Ka Young Lee, MD,[1] Yong Woo Ji, MD,[1] Hun Lee, MD,[1,2] Kyoung Yul Seo,

MD, PhD,[1] [1]Corneal Dystrophy Research Institute & Institue of Vision Research, Department of Ophthalmology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea [2]Department of Ophthalmology, International St. Mary's Hospital, Catholic Kwandong University College of Medicine, Incheon, Korea

5 CAN MEIBOGRAPHY FAIL TO REVEAL FUNCTIONAL GLAND STRUCTURE? Donald R. Korb[1], Caroline A Blackie.[2] Korb Research, Boston MA[1]; TearScience, Inc., Morrisville, NC[2]

6 IS DRY EYE THE WRONG DIAGNOSIS FOR MILLIONS? Donald R. Korb[1], Caroline A. Blackie.[2] Korb Research, Boston MA[1]; TearScience, Inc., Morrisville, NC[2]

7 INCOMPLETE BLINKING AND MEIBOMIAN GLAND FUNCTION IN A GRADUATE STUDENT COHORT. Christen Kenrick,[1] Amy Nau,[1] Andrew McLeod.[2] Korb & Associates,[1] New England College of Optometry,[2] Boston, MA, USA

8 CHARACTERIZATION OF DRY EYE DISEASE AND MEIBOMIAN GLAND DYSFUCNTION AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION. Marilia Menezes Trindade Ferrer[1], Melina Veiga Rodrigues[2], Julia Silvestre Castro[1], Francisco Penteado Aranha[2], Afonso Vigorito[2], Monica Alves[1]. University of Campinas – UNICAMP, [1] Discipline of Ophthalmology, Faculty of Medical Sciences and [2] Hematopoietic Stem Cell Transplantation Unit, Brazil.

9 OCULAR SURFACE AND MEIBOMIAN GLANDS CHANGES AFTER ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION Kyung-Sun Na.[1], Young-Sik Yoo,[2] Hyun Seung Kim,[1] Choun-ki Joo, MD., PhD[3] , Department of Ophthalmology and Visual Science, Yeouido St. Mary's Hospital College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea[1], Laboratory of Visual Science, College of Medicine, The Catholic University of Korea, Seoul, South Korea[2],Department of Ophthalmology and Visual Science, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea[3]

10 RELATIONSHIP BETWEEN CHEMOTHERAPY-INDUCED LACRIMAL DRAINAGE OBSTRUCTION AND OBSTRUCTIVE MEIBOMIAN GLAND DYSFUNCTION. Jong Suk Song, Youngsub Eom, Hyo Myung Kim. Department of Ophthalmology, Korea University College of Medicine, Seoul, South Korea

11 CORRELATION BETWEEN TEAR FILM LIPID LAYER BY INTERFEROMETRY AND SYMPTOMS IN PATIENTS DIABETICS WITH MEIBOMIAN GLAND DYSFUNCTION. Johanna Garzón P.,[1-2] Antonio López-Alemany[2].[1]Optometry-Faculty La Salle´s University, Bogotá Colombia. [2]Ocular Surface, Cornea and Contact Lens Research Group "Miguel F. Refojo", University of Valencia, Valencia- Spain.

12 CLINICAL FEATURES OF MEIBOMIAN GLAND DYSFUNCTION IN PATIENTS WITH DIABETES TYPE 2. Johanna Garzón P,[1-2] Antonio López-Alemany[2].[1] Optometry-Faculty La Salle´s University, Bogotá Colombia. [2] Ocular Surface, Cornea and Contact Lens Research Group "Miguel F. Refojo", University of Valencia, Valencia- Spain.

13 Analysis of Factors Associated with Meibomian Gland Loss and Lipid Layer Thickness in Patients with Dry Eye Syndrome. Yong Woo Ji, MD,[1,2] Ka Young Lee, MD,[1,2] Seonghee Choi, MD,[2] Kyoung Yul Seo, MD, PhD,[1,2] Eung Kweon Kim, MD, PhD,[1,2] Tae-im Kim, MD, PhD[1,2]*I* Corneal Dystrophy Research Institute, Department of Ophthalmology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea [2]Institue of Vision Research, Department of Ophthalmology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

14 DEVELOPMENT OF AN MGD GRADING SCALE FOR USE IN CLINICAL PRACTICE. Emma Gibson[1,2], James Wolffsohn[2], Fiona Stapleton[1], Blanka Golebiowski[1]. [1]UNSW, [2]Aston University

15 ASSESSMENT OF MEIBOMIAN GLANDS AND TEAR FILM IN POST-REFRACTIVE SURGERY PATIENTS. Ji Won Jung,1 Da Ham Cho,2 Jung Yong Kim,1 Kang Won Lee,1 Tae-im Kim,3 Kyoung Yul Seo.3 Inha University School of Medicine1, CHUNCHEON NATIONAL HOSPITAL2, Severance Hospital, Yonsei University College of Medicine3, South Korea.

16 DIFFERENTIAL GENE EXPRESSION OF *RNF182* AND *ITLN1* IN MEIBOMIAN GLAND DYSFUNCTION – A VALIDATION STUDY. Ling Lee,[1,2] Qian Garrett,[2] Subhabrata Chakrabarti,[3] Judith Flanagan,[1,2] Eric Papas.[1,2] Brien Holden Vision Institute,[1] University of New South Wales,[2] Australia, L V Prasad Eye Institute,[3] India

17 CORRELATION OF MEIBOMIAN GLAND DROPOUT WITH DRY EYE EVALUATION IN PRIMARY SJÖGREN'S SYNDROME. Karim Mohamed-Noriega, MD, Dr Med,[1] Fernando Morales-Wong, MD;[1] Yunuen Bages-Rousselon, MD,[1] Janett Riega, MD,[2] Dr Med; Mario Garza, MD, PhD,[2] Jesús Mohamed-Hamsho, MD, Dr. Med.[1] Department Of Ophthalmology, Autonomous University Of Nuevo Leon (UANL), Faculty Of Medicine, University Hospital, Monterrey, Mexico.[1] Department Of Rheumatology, Autonomous University Of Nuevo Leon (UANL), Faculty Of Medicine, University Hospital, Monterrey, Mexico.[2]

18 TEAR CYTOKINE PROFILES IN MEIBOMIAN GLAND DYSFUNCTION (MGD) TREATED WITH INTENSE PULSED LIGHT (IPL). Moonjung Choi, MD,[1] Soo Jung Han, MA, Ka Young Lee, MD,[1] Hun Lee,[2] Kyoung Yul Seo, MD, PhD.[1] [1]Department of Ophthalmology, Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea [2]Department of Ophthalmology, International St. Mary's Hospital, Catholic Kwandong University College of Medicine, Incheon, South Korea

19 EFFECTS AND PROGNOSTIC FACTORS OF KCL 1100® AUTOMATED THERMODYNAMIC SYSTEM FOR MEIBOMIAN GLAND DYSFUNCTION. Tae-Young Chung. Department of Ophthalmology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea (South)

20 ILUX SYSTEM FOR MEIBOMIAN GLAND TREATMENT – REPORT OF SAFETY ASSESSMENT ON HEALTHY VOLUNTEERS. Paul M. Karpecki, OD, FAAO, Kentucky Eye Institute, Lexington, KY; James P. Owen, OD, FAAO, Encinitas Optometry, Encinitas, CA

21 MEIBOMIAN GLAND DYSFUNCTION; ONLINE MANAGEMENT USING EYECALM - A COMMERICAL CLINICAL DECISION SUPPORT SYSYTEM COMPARED TO "USUAL CARE" USING PATIENT RELATED OUTCOME MEASURES. Clearkin L, Wood V, Ross H, Billing A, Taylor D, Pilling S, Jones M Eye Department, Arrowe Park Hospital, Upton, Wirral, CH49 5PE, UK

22 EFFICACY OF A SINGLE LIPIFLOW THERMAL PULSATION TREATMENT ON MEIBOMIAN GLAND DYSFUNCTION IN A DRY EYE COHORT FROM ASIA. Tushar Grover, Natasha Pahuja, Rohit Shetty, Harsha Nagaraj, Narayana Nethralaya Super Speciality Eye Hospital and Postgraduate Institute, Bengaluru, India

23 EVALUATION OF RADIO FREQUENCY THERMISTOR FOR USE IN MGD DRY EYE TREATMENT. David Meadows[1], Ph.D., Mike Christensen[2], OD, Ph.D., Rachel Grant[2], OD, Whitney Hauser[2], OD, Christina Newman[2], OD, Al Kabat[2], OD, Greg Almond[1]. 1 ThermiGen LLC, 2 Southern College of Optometry

24 INTENSE PULSED LIGHT THERAPY FOR MEIBOMIAN GLAND DYSFUNCTION. Tae Hyung Lim[1], MD, PhD, Seok Joon Kong[1], MD, Young Joo Cho[1], MD, Sang Youp Han[2], MD, Jae Lim Chung[3], MD, Kyoung Yul Seo[4], MD, PhD HanGil Eye Hospital, Incheon, Korea[1], Sungmo Eye Hospital, Busan, Korea[2], Myung-Gok Eye Research Institute, Department of Ophthalmology, Kim's Eye Hospital, Konyang University College of Medicine, Seoul, Korea[3], The Institute of Vision Research, Department of Ophthalmology, Yonsei University College of Medicine, Seoul, Korea[4]

25 EVALUATION OF THE SAFETY AND EFFECTIVENESS OF INTENSE PULSED LIGHT IN THE TREATMENT OF MEIBOMIAN GLAND DYSFUNCTION. Lu Huibin1, Jiang Xiaodan1, Zhang Mingzhou1, Liu Yan1, Hu Xiaodan1, Li Xuemin1, Wang Wei1 1Department of Ophthalmology, Peking University Third Hospital, Beijing, China

26 EFFICACY OF INTENSE REGULATED PULSED LIGHT THERAPY IN MEIBOMIAN GLAND DYSFUCTION RELATED DRY EYE. Serge DOAN, Iris VAN HOLLEBECKE, Damien GUINDOLET, Isabelle COCHEREAU, Eric GABISON, Fondation A de Rothschild and Bichat Hospital, Paris, France

27 CONJUNCTIVAL INFLAMMATION AFTER PUNCTAL PLUGGING FOR SEVERE DRY EYE. Serge DOAN[1], Luisa RIANCHO[2], Karima KESSAL[2], Christophe BAUDOUIN[2,3], Françoise BRIGNOLE-BAUDOUIN[2,3] 1 - Fondation A de Rothschild and Bichat Hospital, Paris, France; 2 - UPMC University, Paris 6, Vision Institute, INSERM UMRS968, CNRS UMR7210, Paris, France; 3 - Quinze-Vingts National Ophthalmology Hospital, Paris, France

28 EFFECTS OF MECHANICAL MEIBOMIAN GLAND SQUEEZING ON CLINICAL OUTCOMES AND TEAR FILM LIPID LAYER THICKNESS IN MODERATE AND SEVERE MEIBOMIAN GLAND DYSFUNCTION. Hun Lee[1,2], Yong Woo Ji[2], Ka Young Lee[2], MoonJung Choi[2], Si Yoon Park[2], Eung Kweon Kim[2], Kyoung Yul Seo[2], Tae-im Kim[2] [1]Department of Ophthalmology, International St. Mary's Hospital, Catholic Kwandong University College of Medicine, Incheon, South Korea [2]The Institute of Vision Research, Department of Ophthalmology, Yonsei University College of Medicine, Seoul, South Korea

29 PRACTICAL APPROACH TO MEIBOMIAN GLAND PROBBING; María Noel Suárez, Clínica de Ojos Montevideo, Montevideo, Uruguay

30 SURFACE INTERACTION OF LACRITIN C-TERMINAL SYNTHETIC PEPTIDES WITH HUMAN MEIBUM FILMS. Yana Nencheva,[1] Craig Struble,[2] Gordon W. Laurie,[3] Georgi As. Georgiev[1] [1]Department of Optics and Spectroscopy, Faculty of Physics, St. Kliment Ohridski University of Sofia, Sofia, Bulgaria [2]Covance, Madison WI, USA [3]Department of Cell Biology, University of Virginia School of Medicine, Charlottesville, VA USA

31 SURFACE INTERACTIONS OF DIQUAFOSOL AND CHLOHEXIDINE GLUCONATE WITH HUMAN MEIBUM FILMS. Georgi As. Georgiev,[1] Norihiko Yokoi,[2] Yana Nencheva[1] [1]Department of Optics and Spectroscopy, Faculty of Physics, St. Kliment Ohridski University of Sofia, Sofia, Bulgaria [2]Department of Ophthalmology, Kyoto Prefectural University of Medicine, Kyoto, Japan

32 SURFACE INTERACTIONS OF CATIONIC NANOEMULSIONS WITH HUMAN MEIBUM FILMS. Philippe Daull[1], Norihiko Yokoi[2], Yana Nencheva[3], Georgi As. Georgiev.[3] [1]Santen SAS, Evry, France, [2]Department of Ophthalmology, Kyoto Prefectural University of Medicine, Kyoto, Japan, [3]Faculty of Physics, University of Sofia "St. Kliment Ohridski", Bulgaria

33 TOWARD AN UNDERSTANDING OF THE ROLES OF MEIBUM LIPIDS AND DIETARY FAT IN DRY EYE DISEASES. Jillian Meadows,[1] Jianzhong Chen,[1] Kari Green,[2] Jason Nichols,[1] Kelly Nichols[1] [1]University of Alabama at Birmingham, School of Optometry [2]University of Florida, Department of Chemistry

34 LIPID ORDER, SATURATION AND SURFACE PROPERTIES OF HUMAN MEIBUM. Douglas Borchman,[1] Poonam Mudgil[2], Rahul Bhola.[1] [1]Department of Ophthalmology and Visual Sciences, University of Louisville, Louisville, KY, USA, [2]School of Medicine, University of Western Sydney, Penrith NSW, Australia

35 COMPOSITIONAL ANALYSIS OF ω-HYDROXY FATTY ACID-BASED DIESTERS IN HUMAN MEIBUM. Jianzhong Chen, Kelly Nichols. School of Optometry, University of Alabama at Birmingham, Birmingham, AL, USA

36 CHANGE OF TEAR LIPID LAYER THICKNESS AND MEIBOMIAN GLAND STRUCTURES AFTER CATARACT SURGERY. Si Yoon Park, M.D[1], Yong Woo Ji, M.D[1], Sang Ah Kim, M.D[1], Tae-im Kim, M.D, Ph.D[1,2], [1]The Institute of Vision Research, Department of Ophthalmology, Yonsei University College of Medicine, Seoul, South Korea, [2]Corneal Dystrophy Research Institute, Severance Biomedical Science Institute, and Brain Korea 21 Plus Project for Medical Science, Yonsei University College of Medicine, Seoul, South Korea.

37 DIETARY FACTORS ASSOCIATED WITH MEIBOMIAN GLAND AND TEAR FUNCTIONS IN AN ADULT POPULATION. Nisha Yeotikar,[1] Judith Flanagan,[1] Thomas Naduvilath,[1] Maria Markoulli,[2] Eric Papas.[2] Brien Holden Vision Institute,[1] School of Optometry & Vision Science,[2] University of New South Wales, Sydney, Australia

38 *IN VITRO* EFFECTS OF SEX HORMONES IN HUMAN MEIBOMIAN GLAND EPITHELIAL CELLS. Fabian Garreis[1], Antje Schröder[1], Daniel B. Abrar[1], Ulrike Hampel[1,2], Martin Schicht[1] and Friedrich Paulsen[1].[1]Department of Anatomy II, Friedrich Alexander University Erlangen-Nürnberg (FAU), Erlangen, Germany; [2]Departmenty of Ophthalmology, Gutenberg University Mainz, Germany

39 HUMAN MEIBOMIAN GLAND EPITHELIAL CELLS PROTECT CORNEAL EPITHELIAL CELLS FROM BAK INDUCED TOXICITY. Elham Ghahari E, Medi Eslani M, Gidfar Sanaz, Ali R. Djalilian. University of Illinois Eye and Ear Infirmary, University of Illinois at Chicago, Chicago, IL

40 CELL VIABILITY AND PROTEIN EXPRESSION OF HUMAN AMNIOTIC MEMBRANE IN DIFFERENT PRESERVATION METHODS. Jung Huh, Jea-Chan Kim,. Department of Ophthalmology, Chung-Ang University Hospital.

41 EXPRESSION OF P63 AND CHROMATIN FUNCTIONAL STATES FROM LIMBAL EPITHELIAL CELLS GROWN ON SYNTHETIC VERSUS DENUDED HUMAN AMNIOTIC MEMBRANE. Marcela Aldrovani,[1] Ivan R.M. Padua,[1] Livia P. Coelho,[1] Priscila C. Cristovam,[2] José L. Laus,[1] José A.P. Gomes.[2] Department of Small Animal Medicine and Surgery, Faculty of Agrarian and Veterinary Sciences, UNESP Jaboticabal, SP, Brazil,[1] Ocular Surface Advanced Center, Federal University of São Paulo, UNIFESP São Paulo, SP, Brazil.[2]

42 COLLAGEN FIBER ORIENTATION AND THICKNESS IN THE HUMAN AMNIOTIC STROMA BEFORE AND AFTER CELL CULTURE. Marcela Aldrovani,[1] Gisele P. Valdetaro,[1] Livia P. Coelho,[1] Priscila C. Cristovam,[2] José L. Laus,[1] José A.P. Gomes.[2] Department of Small Animal Medicine and Surgery, Faculty of Agrarian and Veterinary Sciences, UNESP Jaboticabal, SP, Brazil,[1] Ocular Surface Advanced Center, Federal University of São Paulo, UNIFESP São Paulo, SP, Brazil.[2]

43 CONCANAVALIN A-POSITIVE GLYCOPROTEINS IN THE NUCLEI OF CORNEAL LIMBAL EPITHELIAL CELLS. Marcela Aldrovani,[1] Karina K. Kobashigawa,[1] Livia P. Coelho,[1] Priscila C. Cristovam,[2] José L. Laus,[1] José A.P. Gomes.[2] Department of Small Animal Medicine and Surgery, Faculty of Agrarian and Veterinary Sciences, UNESP Jaboticabal, SP, Brazil,[1] Ocular Surface Advanced Center, Federal University of São Paulo, UNIFESP São Paulo, SP, Brazil.[2]

44 RECONSTRUCTION OF OCULAR SURFACE BY THE TRANSPLANTATION OF LIMBAL EPITHELIAL CELLS CULTURED IN TRIDIMENSIONAL SYSTEM (SANDWHICH METHOD). Karina K. Kobashigawa,[1] Marcela Aldrovani,[1] Alexandre A.F. Barros Sobrinho,[1] Livia P. Coelho,[1] Paloma E.S. Silva,[1] Paulo F. Marcusso,[2] Fausto A. Marinho Neto,[2] Priscila C. Cristovam,[3] José A.P. Gomes,[3] José L. Laus.[1] Department of Small Animal Medicine and Surgery, Faculty of Agrarian and Veterinary Sciences, UNESP Jaboticabal, SP, Brazil,[1] Department of Veterinary Clinical Medicine and Surgery, UNESP Jaboticabal, SP, Brazil,[2] Ocular Surface Advanced Center, Federal University of São Paulo, UNIFESP São Paulo, SP, Brazil.[2]

45 TRANSPLANTATION OF SUBSTRATE-FREE CULTURED ORAL MUCOSAL EPITHELIAL CELL SHEETS (COMECS) IN TREATMENT OF LIMBAL STEM CELL DEFICIENCY. Yu Jeong Kim,[1,2] Jaeyoung Kim,[1,2] Hyun Ju Lee,[2] Jin Suk Ryu,[2] Yun Hee Kim[3], Saewha Jeon[3], Mee Kum Kim,[1,2] Won Ryang Wee.[1,2] Department of Ophthalmology, Seoul National University College of Medicine, Seoul, Korea[1] Laboratory of Ocular Regenerative Medicine and Immunology, Seoul National University Hospital Biomedical Research Institute, Seoul. Korea[2] Cutigen Research Institute, Tego Science Inc., Seoul, Korea[3]

46 LONG-TERM HOMEOSTASIS IN AN *IN VITRO* EPITHELIAL STEM CELL NICHE MODEL. Shigeto Shimmura, Hideyuki Miyashita, Hiroko Niwano, Satoru Yoshida, Shin Hatou, Emi Inagaki, and Kazuo Tsubota, Department of Opthalmology, Keio University School of Medicine

47 EFFECTS OF INTERMITTENT SHEAR STRESS ON CORNEAL EPITHELIAL CELLS USING AN IN VITRO FLOW CULTURE MODEL. Ulrike Hampel[1,2], Fabian Burgemeister[2], Nicole Eßel[2], Friedrich Paulsen[2]. [1] Department of Ophthalmology, University Medical Center of the Johannes Gutenberg University Mainz, Mainz, Germany, [2] Department of Anatomy II, Friedrich-Alexander University, Erlangen, Germany

48 EXPRESSION OF K^+ CHANNELS BY HUMAN CORNEAL LIMBAL EPITHELIAL CELLS.. John L. Ubels[1], Mark P. Schotanus[1], Peter M. Boersma[1,2], Loren D. Haarsma[2]. Departments of Biology[1] and Physics[2], Calvin College, Grand Rapids, MI, USA

49 COMPARISON OF CYTOTOXICITY AND WOUND HEALING OF DIQUAFOSOL TETRASODIUM AND HYALURONIC ADIS ON HUMAN CORNEAL EPITHELIAL CELLS. Jieun Lee,[1,2] Jonghun Lee,[1,2] Jongsoo Lee.[1,2] Department of Ophthalmology, School of Medicine, Pusan National University, Pusan, Korea,[1] Research Institute for Convergence of Biomedical Science and Technology, Pusan National University Yangsan Hospital, Yangsan, Korea[2]

50 IMPACT OF HYALURONIC ACID CONTAINING ARTIFICIAL TEAR PRODUCTS ON RE-EPITHELIALIZATION IN AN *IN VIVO* CORNEAL WOUND MODEL. Abayomi Ogundele[1], Winston W.Y. Kao[2], Eric Carlson[1] Alcon Research Ltd., Fort Worth, Texas, USA[1]; Department of Ophthalmology, College of Medicine at the University of Cincinnati, Ohio, USA[2]

51 CLINICAL OUTCOMES FOLLOWING USE OF THE DUAL POLYMER HYDROXYPROPYL GUAR/HYALURONIC ACID-BASED LUBRICANT EYE DROPS IN PATIENTS WITH DRY EYE. Christophe Baudouin,[1] Stefanie Schmickler,[2] David Galarreta,[3] Florence Malet,[4] Abayomi Ogundele,[5] Christine Rosko,[5] Guillon Michel,[6] Marc Labetoulle.[7] Quinze-Vingts National Ophthalmology Hospital, Paris, France, [2]Augen-Zentrum-Nordwest Augenpraxis Ahaus, Germany, [3]Hospital Clinico Universitario de Valladolid, Valladolid, Spain; [4]Centre PointVision Bordeaux, France,[5] Alcon Research Ltd., Fort Worth, Texas, US, [6]Ocular Technology Group, London, UK, [7]Ophtalmologie Hôpital Bicêtre, South Paris Université, Kremlin-Bicêtre, France

52 Enhanced Wound Healing in Human Corneal Epithelium in Response to Histatin-1 Application. Dhara Shah1; Marwan Ali1; Vinay K. Aakalu11 Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL, USA

53 CONJUNCTIVAL EPITHELIAL CELLS CHANGES AFTER THE TREATMENT WITH 0.2% XANTHAN GUM EYE DROPS IN MODERATE DRY EYE. Pasquale Aragona,[1] Elisa Postorino,[1] Laura Rania,[1] Rosaria Spinella,[1] Emanuela Aragona,[1] Domenico Puzzolo,[1] Anna Maria Livia Mazza,[2] Vincenzo Papa.[2] Dept. of Biomedical Sciences,[1] University of Messina, Italy, Medical Affairs,[2] SIFI S.p.A., Catania, Italy.

54 AN INFLAMMATORY GENE PROFILE OF HUMAN CONJUNCTIVAL EPITHELIAL CELLS IN DRY EYE DISEASE Suzanne Hagan[1], Boatemaa Omotayo[1], Katherine Oliver[1], Michael Doughty[1], Claire Walshe[2]. [1]Vision Sciences, Glasgow Caledonian University, Glasgow; [2]Topivert Pharma Ltd, Imperial Bioincubator, London, UK.

55 EUPHRASIA PROTECTS HUMAN CONJUNCTIVAL CELLS FROM ULTRAVIOLET LIGHT-INDUCED CELL DAMAGE. Andrea Heidinger, Otto Schmut, Dieter Rabensteiner, Marianne Nitsche-Resch, Ingrid Boldin, Jutta Horwath-Winter, Andreas Wedrich. Department of Ophthalmology, Medical University of Graz, Austria.

56 ROLE OF mTOR SIGNALING IN PTERYGIUM FIBROBLASTS Sunwoong Kim[1], Hyein Kim[2], Keunwook Lee[2] [1]Department of ophthalmology, Yonsei University Wonju Collge of Medicine, Wonju, Korea [2]Depatrment of Biomedical Science, Hallym University, Chuncheon, Korea

57 THE EFFECT OF TOPICAL DIQUAFOSOL TETRASODIUM 3% ON TEAR FILM AND CONJUNCTIVAL GOBLET CELLS AFTER CATARACT SURGERY IN PATIENTS WITH DRY EYE DISEASE. Lian Cui[1,2], Hyo Seok Lee[1], Ying Li[1,2], Kyung Chul Yoon[1,2] [1]Department of Ophthalmology, Chonnam National University Medical School and hospital, Gwangju, South Korea [2]Department of Biomedical Sciences and Center for Creative Biomedical Scientists at Chonnam National University, Gwangju, South Korea

58 STAPHYLOCOCCUS AUREUS-INDUCED MUCIN SECRETION BY CONJUNCTIVAL GOBLET CELLS: DEPENDENCY ON NLRP3 INFLAMMASOME ACTIVATION AND RELEASE OF MATURE IL-1β Darlene Dartt, Dayu Li, Marit Lippestad, Robin Hodges, Michael Gilmore, and Meredith Gregory-Ksander. Schepens Eye Research Institute/Massachusetts Eye and Ear, and Department of Ophthalmology, Harvard Medical School, Boston, MA, School of Dental Medicine and School of Medicine, University of Oslo, Oslo Norway

59 CONJUNCTIVAL GOBLET CELL REGULATION BY ALLERGIC MEDIATORS. Laura García-Posadas,[1,2] Yolanda Diebold,[3] Darlene A. Dartt.[1,2] Schepens Eye Research Institute/MEEI, Boston, MA, USA,[1] Department of Ophthalmology, Harvard Medical School, Boston, MA, USA,[2] IOBA-University of Valladolid, Valladolid, Spain.[3]

60 PRECLINICAL MOUSE MODEL TO MONITOR LIVE CONJUNCTIVAL GOBLET CELL DIFFERENTIATION UNDER PHARMACOLOGICAL TREATMENTS. Portal C[1], Gouyer V[1], Gottrand F[1], Desseyn JL[1]. [1]LIRIC UMR995; Inserm/Université de Lille; CHU de Lille, Lille, France

61 UPPER AND LOWER CONJUNCTIVAL FORNIX DEPTH IN HEALTHY WHITE CAUCASIAN EYES: A METHOD OF OBJECTIVE ASSESSMENT. Valerie Saw,[1,2] David Carpenter,[1] Scott Hau, [1] Debbie Booth, [1] Haneen Jasim, [1] Gurjeet Jutley.[1] Moorfields Eye Hospital,[1] UCL Institute of Ophthalmology,[2] London, UK

62 EYE DISEASE FROM DIAGNOSIS TO TREATMENT: A SURVEY OF PATIENTS WITH AND WITHOUT SJÖGREN'S SYNDROME IN EUROPE. Francisco C. Figueiredo,[1] Marc Labetoulle,[2] Maurizio Rolando,[3] Gysbert van Setten,[4] Elisabeth M. Messmer.[5] Dept. of Ophthalmology, Royal Victoria Infirmary and Newcastle University, Newcastle upon Tyne, UK,[1] Ophthalmology Dept. Bicêtre Hospital, APHP, South Paris University, France,[2] University of Genoa, Genoa, Italy,[3] St Eriks Eye Hospital, Stockholm, Sweden,[4] Dept. of Ophthalmology, Ludwig-Maximilians University, Munich, Germany[5]

63 COMPARISON OF LONG TERM CLINICAL RESULTS OF LIMBAL CONJUNCTIVAL AUTOGRAFT VERSUS AMNIOTIC MEMBRANE TRANSPLANTATION IN PRIMARY PTERYGIUM SURGERY. Hyung Joon Kim[1], Suk Jin Hwang.[1] Department of Ophthalmology[1], Daegu Catholic University Hospital, Daegu, Korea

64 OCULAR SURFACE AND TEAR FILM FUNCTION FOLLOWING MODIFIED HUGHES TARSOCONJUNCTIVAL FLAP PROCEDURE. Rabensteiner DF[1], Boldin I[1], Klein-Theyer A[1], Heidinger A[1], Riedl R[2], Horwath-Winter J[1]. Department of Ophthalmology[1], Institute for Medical Informatics, Statistics and Documentation[2], Medical University of Graz, Austria

65 INTERPLAY BETWEEN EYE MICROBIOME AND DRY EYE DISEASE IN INDIAN PATIENTS. Noopur Gupta,[1] Amit Sharma,[2] Vanathi M, [1] Jyoti Chibber,[2] Radhika Tandon, [1] [1]Dr. Rajendra Prasad Centre for Ophthalmic Sciences, AIIMS, New Delhi, India, [2] International Centre for Genetic Engineering and Biotechnology, New Delhi, India

66 CHANGING PATTERNS OF MICROBIAL KERATITIS. Sanjay Marasini[1], Simon Swift[2], Simon J. Dean[1], Sue Ormonde[1], Jennifer P. Craig.[1] [1]Department of Ophthalmology, and [2]Department of Molecular Medicine and Pathology, University of Auckland, New Zealand

67 LOW POWER NARROWBAND UVC EFFECTIVELY INHIBITS BACTERIAL PROLIFERATION IN A GEL-LIKE MEDIUM. Sanjay Marasini[1], Simon Swift[2], Simon J. Dean[1], Jennifer P. Craig.[1] [1]Department of Ophthalmology, [2]Department of Molecular Medicine and Pathology, University of Auckland, New Zealand

68 OCULAR SURFACE MICROBIOME IN PATIENTS WITH DRY EYE CAUSED BY CHRONIC GRAFT-VERSUS-HOST DISEASE (CGVHD). Eisuke Shimizu, Yoko Ogawa, Yumiko Saijo, Mio Yamane, Shin Mukai, Miki Uchino, Mizuka Kamoi, Masaki Fukui, Kazuo Tsubota Department of Ophthalmology Keio University School of Medicine

69 IL-1R CONTRIBUTES TO THE ABSENCE OF A MICROBIOME AT THE MOUSE CORNEAL SURFACE. Stephanie Wan[1], Aaron Sullivan[1], Peyton Shieh[2], Carolyn Bertozzi[3], David Evans[1,4], Suzanne Fleiszig[1] 1. Optometry, UC Berkeley, 2. Chemistry, UC Berkeley 3. Chemistry, Stanford University, 4. College of Pharmacy, Touro University

70 THE BACTERIAL PROFILES AMONG MGD, ADDE AND HEALTHY CONTROLS. Jiang Xiaodan, Lu Huibin, Zhou Peng, Wen Yiting, Li Xuemin. Department of Ophthalmology, Peking University Third Hospital, Beijing, China

71 COMMENSAL OCULAR MICROFLORA AND TEAR PARAMETERS IN A NORMAL POPULATION. Judith Flanagan[1,2], Nisha Yeotikar[1], Hua Zhu[1,2] 1. Brien Holden Vision Institute, Sydney, Australia 2. School of Optometry and Vision Sciences, UNSW, Sydney, Australia.

72 COMPARISON OF CLINICAL FEATURES, ANTIBIOTICS SUSCEPTIBILITY, AND TREATMENT OUTCOME ACCORDING TO METHICILLIN SENSITIVITY IN *STAPHYLOCOCCUS AUREUS* KERATITIS. Sang-Bumm Lee, Janghwan Ahn. Department of Ophthalmology, Yeungnam University College of Medicine, Daegu, Korea

73 MUTATIONS IN THE QUORUM SENSING GENE LASR ARE ASSOCIATED WITH WORSE CLINICAL OUTCOMES IN *PSEUDOMONAS AERUGINOSA* KERATITIS. Zegans M, Hammond J, Hebert W, Ray K, Naimie A1, Lalitha P, Srinivasan M, Acharya NR, Toutain-Kidd C, Lietman TM, DiGiandomenico A, Hogan D. Dartmouth Geisel School of Medicine, Lebanon, NH, USA

74 UNRAVELING LACRIMAL GLAND STEM CELL DYNAMICS BY LINEAGE TRACING. Natalie Tanke[1], Geraint Parfitt[2], Takeshi Umazume[1], Pamela Segura[1], Ivo Kalajzic[3] James V. Jester[2], Darlene A. Dartt[4] and Helen P. Makarenkova[1] [1]The Scripps research institute, Department of Cell and Molecular Biology, La Jolla, CA, USA; [2]University of California, Gavin Herbert Eye Institute, Irvine, CA, USA, [3]Center for Regenerative Medicine and Skeletal Development, School of Dental Medicine Department of Reconstructive Sciences University of Connecticut Health Center, Farmington, USA [4]Schepens Eye Research Institute/Massachusetts Eye and Ear, Department of Ophthalmology, Harvard Medical School, Boston, MA, USA.

75 LACRIMAL GLAND EPITHELIAL CELL METABOLIC ACTIVITY AND FUNCTION ON A DECELLULARISED SCAFFOLD IS INCREASED USING A DYNAMIC CULTURE FORMAT. Isobel Massie,[1] Kristina Spaniol,[2] Gerd Geerling,[2] Marco Metzger,[3] Stefan Schrader,[1,2]. Laboratory of Experimental Ophthalmology,[1] Eye Clinic,[2] UKD, Düsseldorf, Dept of Tissue Engineering and Regenerative Medicine, UKW, Würzburg,[3] Germany

76 IN VIVO VISUALIZATION OF Ca^{2+} DYNAMICS OF MYOEPITHELIAL CELLS IN LACRIMAL GLAND. Kai Jin[1], Toshihiro Imada[1], Yusuke Izuta[1], Shigeru Nakamura[1], Takahiro Adachi[2], Kazuo Tsubota[1] Department of Ophthalmology, Keio University, Tokyo, Japan[1] Department of Immunology, Tokyo Medical and Dental University, Tokyo, Japan[2]

77 RNASEQ PROFILING OF REGENERATING LACRIMAL GLAND IDENTIFIES MYOEPITHELIAL CELLS AS POTENTIAL PLAYERS IN TISSUE REPAIR. Dillon Hawley[1], Claire Kublin[1], Audrey Michel[1], Lisa Clapisson[1], Jian Ding[2], Michael Mingueneau[2], Driss Zoukhri[1] [1]Tufts University School of Dental Medicine, Boston, MA 02111 [2]Biogen, 225 Binney Street, Cambridge, MA 02142

78 MECHANISMS AND MOLECULAR REGULATION OF LACRIMAL GLAND MORPHOGENESIS AND MAINTENANCE Alison Kuony and Frederic Michon, University of Helsinki, Helsinki, Finland.

79 CENTRAL CONNECTIONS OF THE LACRIMAL FUNCTIONAL UNIT. Catherine Willshire[1], Roger Buckley[1] and Anthony Bron[1,2]. [1]Vision and Eye Research Unit, Anglia Ruskin University, Cambridge, UK, [2]Nuffield Department of Clinical Neurosciences and Nuffield Laboratory of Ophthalmology, University of Oxford, UK.

80 SAFETY AND EFFICACY OF EXCISION OF THE HORISONTAL CANALICULUS IN SEVERE AQUEOUS DEFICIENT DRY EYE. Seika Den,[1] Daisuke Tomida,[1] Hirohiko Kakizaki,[2] Jun Shimazaki.[1] Department of Ophthalmology, Tokyo Dental College Ichikawa General Hospital, Chiba, Japan.[1] Department of Oculoplastic, Orbital & Lacrimal Surgery, Aichi Medical University Hospital, Aichi, Japan.[2]

81 THE EFFECTS OF INTRANASAL NEUROSTIMULATION ON TEAR PRODUCTION AND CLEARANCE AND CONJUNCTIVAL GOBLET CELL SECRETION. Koray Gumus, M.D., FEBOphth,[1, 2] Karri L. Schuetzle, AAS, COA, CCRP,[1] Stephen C. Pflugfelder, M.D.[1] Michael Ackerman, Ph.D.[3] Cullen Eye Institute, Baylor College of Medicine, Houston, Texas, USA,[1] Erciyes University School of Medicine, Department of Ophthalmology, Kayseri, Turkey, [2] and Allergan (Oculeve), South San Francisco, CA, United States[3]

82 OCULAR SURFACE CHANGES IN PROFESSIONAL MOTORSPORT ATHLETES. Stefano Barabino. Clinica Oculistica, University of Genoa, Italy

Friday, September 9, 2016

Session II

Surface Barriers To Inflammation

Chairpersons - Penny Asbell (USA), Ali Djalilian (USA), Arsia Jamali (USA)

8:00 **Keynote Address:** Endothelial barrier (Vascular endothelium: It's more than just a monolayer). Francis W. Luscinskas, Center for Excellence in Vascular Biology, Department of Pathology, Brigham and Women's Hospital, and Harvard Medical School, Boston, MA, USA

8:20 **Keynote Address:** Epithelial barrier (Endocrine regulation of mucosal barrier protection in the human female reproductive tract). Charles R. Wira, Marta Rodriguez-Garcia and Mickey V. Patel, Department of Microbiology and Immunology, Geisel School of Medicine at Dartmouth, Lebanon, NH, USA

8:40 **Keynote Address:** Tear film barrier. Alison M. McDermott The Ocular Surface Institute, University of Houston College of Optometry, Houston, TX, USA

9:00 **Keynote Address:** Ocular surface glycocalyx barrier. Pablo Argüeso. Schepens Eye Research Institute and Massachusetts Eye and Ear, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, USA

9:20 **Keynote Address:** Corneal barrier. Victor L. Perez, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, USA

9:40 **Poster Session II (with Coffee & Tea)**
Chairpersons - Eduardo Rocha (Brazil), Kyung-Sun Na (South Korea)

Ocular Inflammatory Insults: Advances In Understanding Their Mechanism(s) And Treatment

Chairpersons - Esen K Akpek (USA), Takenori Inomata (USA), Bhaskar Srinivasan (India)

10:30 **Keynote Address:** Dynamic instability – a pathway for nuclear transport of adenovirus. Jaya Rajaiya, Department of Ophthalmology, Howe Laboratory, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, MA, USA

10:50 **Keynote Address:** Vernal keratoconjunctivitis – Therapeutic advances of an enigmatic disease. Avi Solomon, Department of Ophthalmology, Hadassah Medical Center, Jerusalem, Israel

11:10 **Keynote Address:** Graft-versus-host disease. Yoko Ogawa, Department of Ophthalmology, Keio University School of Medicine, Tokyo, Japan

11:30 **Keynote Address:** Building an evidence basis for management of ocular Stevens-Johnson syndrome/toxic epidermal necrolysis. James Chodosh, Department of Ophthalmology, Howe Laboratory, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, MA, USA

11:50 **Keynote Address:** Sjögren syndrome and commensal microbiota. Zaheer, M[1]; Bian[1], F; Swennes, AG[2], Britton, RA[3], Pflugfelder, SC[1], De Paiva, CS[1] [1]Ocular Surface Center, Dept. of Ophthalmology, Baylor College of Medicine; [2]Center for Comparative Medicine, Dept. of Molecular Virology and Microbiology, Baylor College of Medicine; [3]Center for Metagenomics and Microbiome Research, Dept. of Molecular Virology and Microbiology, Baylor College of Medicine, Houston, TX, USA

12:10 **Poster Viewing & Lunch**

Did You Know?

Chairpersons - Serge Doan (France), Sihem Lazreg (Algeria), Martin Schicht (Germany)

13:30 **Keynote Address**: Metabolomic fingerprints exist in dry eye disease. Jelle Vehof,[1,2] Department of Twin Research & Genetic Epidemiology, King's College London, St Thomas' Hospital, London, United Kingdom[1]; Department of Ophthalmology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands[2]

13:45 **Keynote Address**: Blood, sweat and tears: human social chemosignaling in health and disease. Noam Sobel, Weizmann Institute of Science, Rehovot, Israel

14:00 **Keynote Address**: Impact of microbiota on resistance to ocular *Pseudomonas aeruginosa*–induced keratitis. Mihaela Gadjeva, Department of Medicine, Division of Infectious Diseases, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

14:15 **Keynote Address**: The pediatric ocular surface is a peculiar system, with peculiar diseases and peculiar management challenges. Edoardo Villani, Department of Clinical Science and Community Health, University of Milan. Eye Clinic San Giuseppe Hospital, Milan, Italy

14:30 **Keynote Address**: Happiness and dry eye. Motoko Kawashima, Keio University School of Medicine, Tokyo, Japan

Ocular Surface Microbiome

Chairpersons - David Evans (USA), Stephanie Wan (USA), Michael Zegans (USA)

14:45 **Keynote Address:** Ocular surface microbiome in the post-genomics era. Val Shestopalov. Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, FL, USA

15:10 **Keynote Address:** Impact of microbiota on adaptive immune effectors on the ocular surface. Gerald B. Pier, Tanweer Zaidi, Abirami Kugadas, Mihaela Gadjeva. Department of Medicine, Brigham & Women's Hospital, Harvard Medical School, Boston, MA, USA

15:35 **Keynote Address:** Is anybody there? Suzanne M.J. Fleiszig,[1] Stephanie J. Wan,[1] Aaron B. Sullivan,[1] Matteo M.E. Metruccio,[1] David J. Evans.[1,2] UC Berkeley,[1],Touro University College of Pharmacy,[2] CA, USA

16:00 **Poster Session II (with Coffee & Tea)**

Chairpersons - Eduardo Rocha (Brazil), Kyung-Sun Na (South Korea)

Ocular Surface Repair And Regeneration

Chairpersons - Kung Chul Yoon (Korea), Kazuo Tsubota (Japan), Yuichi Uchino (Japan)

16:50 **Keynote Address:** Limbal stem cells. Sophie X. Deng, Jules Stein Eye Institute, University of California, Los Angeles, CA, USA

17:10 **Keynote Address:** Restoration of corneal transparency by mesenchymal stem cells. Sunil Chauhan, Schepens Eye Research Institute, Massachusetts Eye and Ear, Harvard Medical School, Boston, MA, USA

17:30 **Keynote Address:** Human induced pluripotent stem cells. Heli Skottman, BioMediTech, University of Tampere, Finland

17:50 **Keynote Address:** Bioengineered cornea. May Griffith, Department of Clinical and Experimental Medicine, Linkoping University, Sweden; Maisonneuve-Rosemont Hospital Research Center and Université de Montréal, Montreal, Canada; Tej Kholi Cornea Institute/LV Prasad Eye Institute, Hyderabad, India

18:10 **Keynote Address:** Recent Innovations in ocular surface surgery. Jod S Mehta, Singapore National Eye Centre, Singapore Eye Research Institute, Duke-NUS Graduate Medical School, School of Material Science & Engineering and School of Mechanical and Aerospace Engineering, Nanyang Technological University, Singapore

Poster Session II

Chairpersons - Eduardo Rocha (Brazil), Kyung-Sun Na (South Korea)

1 THE UTILITY OF A NORMAL TEAR OSMOLARITY TEST IN SYMPTOMATIC PATIENTS. Ashley R. Brissette[1]; Kelley J. Bohm[1]; Christopher E. Starr[1]. [1]Weill Cornell Medical College

2 VARIATION OF TEAR OSMOLARITY AND ASSOCIATION WITH OCULAR SURFACE MEASUREMENTS IN PATIENTS WITH DRY EYE SYNDROME. Priya M. Mathews MD,MPH[1,2], Sezen Karakus MD[1], Pradeep Y. Ramulu MD,PhD[1], Esen K. Akpek MD[1] [1]The Wilmer Eye Institute, Johns Hopkins University School of Medicine [2]Harkness Eye Institute, Columbia University, College of Physicians and Surgeons

3 THE NORWEGIAN OSMOLARITY PROJECT. Olaug Skrøppa for the Interoptik Project Team, Interoptik AS, Oslo, Norway

4 DOES HYPEROSMOLARITY CAUSE AN IRREVERSIBLE PROCESS LEADING TO HUMAN CORNEAL EPITHELIAL CELL DEATH? Wendy R. Kam,1 David A. Sullivan,1 Manoj Venkiteshwar2 and Benjamin D. Sullivan.2 1Schepens Eye Research Institute, Massachusetts Eye and Ear, Harvard Medical School, Boston, MA; 2TearLab Corp., San Diego, CA, USA

5 THE BLOCKADE OF IL-6 COUNTERPARTS THE OSMOLAR STRESS-INDUCED APOPTOTIC CHANGE AND JUNCTIONAL INSTABILITY IN HUMAN CONJUNCTIVAL EPITHELIAL CELLS. Hee-Jung Ju[1], Yong-Soo Byun[1,2], Jee-Won Mok[1], Choun-Ki Joo[1,2] Catholic Institute of Visual Science,[1] Department of Ophthalmology and Visual Science, Catholic University of Korea,[2] Seoul, South Korea

6 TEAR CYTOKINE ANALYSIS AND IN VIVO CONFOCAL MICROSCOPY IN POST-LASIK ECTASIA. Shruti Kochar, [1] Natasha Pahuja, [1] Rohit Shetty, [1] Rashmi Deshmukh, [1] Anupam Sharma, [2] Swaminathan Sethu, [2] Arkasubhra Ghosh. [2] Refractive Services, Narayana Nethralaya, Bangalore, India, [1] GROW Research Laboratory, Narayana Nethralaya Foundation, Bangalore, India. [2]

7 ANALYSIS OF TH17-ASSOCIATED CYTOKINES AND CLINICAL CORRELATIONS IN PATIENTS WITH DRY EYE DISEASE. Hong Qi[1], Rong-jun Liu[1], Cai-feng Gao [1, 2], Hui-jin Chen[1], Ying Jin[1], Ya-xin Li[1] [1]Department of Ophthalmology, Peking University Third Hospital, Beijing, 100191 China; Key laboratory of vision loss and restoration, Ministry of Education [2]Guangdong Women and Children Hospital, Guangzhou, 511442 China

8 ANALYSIS OF TEAR CYTOKINE LEVEL ALTERATIONS AND CLINICAL CORNEAL FINDINGS FOLLOWING PENETRATING KERATOPLASTY. Daisuke Tomida[1], Takefumi Yamaguchi[1], Hiroyuki Yazu[1,2], Mamoru Ogawa[1,2], Murat Dogru[1,2], Seika Shimazaki-Den[1], Yoshiyuki Satake[1], Jun Shimazaki[1] Department of Ophthalmology, Ichikawa General Hospital, Tokyo Dental College, Chiba, Japan[1] Department of Ophthalmology, Keio University School of Medicine, Tokyo, Japan[2]

9 TEAR CYTOKINES OF STEVENS-JOHNSON SYNDROME IN THE CHRONIC STAGE Mayumi Ueta[1], Hiromi Nishigaki[1], Chie Sotozono[2], Shigeru Kinoshita[1] [1] Department of Frontier Medical Science and Technology for Ophthalmology, Kyoto Prefectural University of Medicine, Kyoto, Japan [2] Department of Ophthalmology, Kyoto Prefectural University of Medicine, Kyoto, Japan

10 DIAGNOSTIC PERFORMANCE OF TEAR PROTEINS FOR primary Sjögren's syndrome [1]P. Versura, [2]G. Vukatana, [1]G. Giannaccare, [2]M. Fresina, [1]N. Malavolta, [1]E. Campos. [1]Ophthamology Unit, DIMES, UNIBO and [2]Rheumatology Unit S.Orsola-Malpighi Teaching Hospital, Bologna, Italy.

11 TEAR PROTEINS IN YOUNG HEALTHY ADULTS. DIFFERENCES BETWEEN MALES AND FEMALES IN TWO MENSTRUAL CYCLE PHASE [1]P. Versura, [2]M. Piazzi, [1]G. Giannaccare, [1]M. Fresina, [2]L. Cocco, [1]E Campos [1]Ophthalmology Unit, DIMEC UNIBO and S.Orsola-Malpighi Teaching Hospital, [2]Cell Signaling Lab, DIBINEM UNIBO, Bologna, Italy

12 ANALYSING THE PROCESS OF LYSOZYME TRANSFER INTO TEAR FILM LIPID LAYER. Alicja Wizert[1], D. Robert Iskander[1], Lukasz Cwiklik.[2] Wroclaw University of Science and Technology, Wroclaw, Poland[1], Academy of Sciences of the Czech Republic, Prague, Czech Republic.[2]

13 ASSOCIATIONS BETWEEN CLINICAL MEASURES OF OCULAR SURFACE DISEASE AND TEAR FILM DERIVED NEUROPEPTIDE CONCENTRATIONS. Stephanie M. Cox[1] and Jason J. Nichols.[1] University of Alabama at Birmingham, School of Optometry[1]

14 PHARMACOGENETIC MANIPULATION OF NEURONAL ACTIVITY REVEAL A ROLE OF BRAIN SPINAL TRIGEMINAL NUCLEUS IN REFLEX TEARING. Yusuke Izuta[1,] Michiko Shibuya[1], Erina Onishi[1], Toshihiro Imada[1], Shigeru Nakamura[1], Ayano Katagiri[3], Akihiro Yamanaka[2], Kazuo Tsubota[1] Keio University School of Medicine Department of Ophthalmology, Tokyo, Japan[1] Nagoya University Research Institute of Environmental Medicine, Department of Neuroscience II, Nagoya, Japan[2] Nihon University School of Dentistry, Department of Physiology, Tokyo, Japan[3]

15 OCULAR SURFACE, TEAR FILM AND NEURO-MARKERS IN SUBJECTS WITH OCULAR ITCHINESS. Sailesh Kolanu[1], Blanka Golebiowski[1], Mark Willcox[1], Arthur Ho[1, 2], Isabelle Jalbert[1], [1]School of Optometry and Vision Science, UNSW Australia, [2]Brien Holden Vision Institute, Australia

16 TEAR FILM MMP-9 AND TIMP-1 IN TOPICAL FLUOROQUINOLONE USE. Maria Markoulli,[1] Amy Moreland,[1] Joanna Liang,[1] Benjamin Ashby, [1,2] School of Optometry and Vision Science, University of New South Wales,[1] Specsavers Ltd.[2]

17 TEAR BIOMARKER ANALYSIS AS A DIAGNOSTIC TOOL FOR DRY EYE DISEASE. Eilidh Martin[1], Katherine M. Oliver[1], E. Ian Pearce[1], Suzanne Hagan[1]. [1]Vision Sciences, Glasgow Caledonian University, Glasgow, UK.

18 OPTIMIZATION OF TEAR BIOMARKERS QUANTITATION BY CUSTOMIZED MULTIPLEXED MICROARRAYS. Javier Soria[1], Arantxa Acera[1], Tatiana Suarez[1]. Bioftalmik, [1] Derio, Spain.

19 ANALYSIS OF OXIDATIVE STRESS MARKERS IN TEARS OF THYROID-ASSOCIATED OPHTHALMOPATHY ACCORDING TO DISEASE ACTIVITY. Kyung Chul Yoon,[1] In Cheon You,[2] Hyo Seok Lee,[1] Yeon Soo Kang,[1] Won Choi.[1] Department of Ophthalmology, Chonnam National University Medical School and Hospital, Gwangju, Korea,[1] Department of Ophthalmology, Chonbuk National University Medical School and Hospital, Jeonju, Korea[2]

20 PLASMA GELSOLIN IS PART OF THE HUMAN TEAR FILM AND PROMOTES RE-EPITHELIALIZATION OF CORNEAL WOUNDS. Schicht M,[1] Wittmann J,[1] Dieckow J,[2] Schroeder H,[1] Jacobi C,[3] Hsieh LC,[4] Pulli B,[4] Chen JW,[4] Braeuer L,[1] Schob S,[5] Paulsen F,[1] Department of Anatomy II[1] and Clinic of Ophthalmology[3] at Friedrich-Alexander-University Erlangen-Nürnberg, Germany; Department of Ophthalmology[2] and Department of Neuroradiology[5] at University of Leipzig, Germany; Center for Systems Biology,[4] Boston, MA, USA

21 NANOSCALE ORGANIZATION OF TEAR FILM WAX ESTERS: A VIEW FROM MOLECULAR DYNAMICS SIMULATIONS. Riku O. Paananen,[1] Matti Javanainen,[2] Ilpo Vattulainen,[2] Juha M. Holopainen.[1] Helsinki Eye Lab, Ophthalmology, University of Helsinki and Helsinki University Hospital,[1] Department of Physics, University of Helsinki,[2] FINLAND

22 A LIQUID CHROMATOGRAPHY MASS SPECTROMETRY METHOD FOR DETECTION OF LIPID MEDIATORS OF INFLAMMATION IN THE HUMAN TEAR FILM. Shyam Panthi,[1] Alireza Arabshahi,[2] Stephen Barnes,[2] Jason J. Nichols.[1] School of Optometry, University of Alabama at Birmingham, Birmingham, Alabama,[1] Targeted Metabolomics and Proteomics Laboratory, School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama[2]

23 SHORT-TERM REPRODUCIBILITY OF TEAR FLUID COLLECTION USING A MUC5AC MUCIN ASSAY Woodward AM,1 Senchyna M,2 Franke M,2 Baba S,2 Argüeso P1 1Schepens Eye Research Institute, Boston, MA; 2 Allergan, Irvine, CA.

24 CONCENTRATION OF MUC16 AND MUC5AC USING THREE TEAR COLLECTION METHODS. Anna F. Ablamowicz[1] and Jason J. Nichols.[1] University of Alabama at Birmingham, School of Optometry[1]

25 ASSESSMENT OF THE IMPACT OF SACCADE ON MUCOAQUEOUS SUBPHASE. Zhenghao Yang[1,2], Norihiko Yokoi[1], Hiroaki Kato[1], Aoi Komuro[1], Yukiko Sonomura[1], Chie Sotozono[1], Noriko Koizumi[1,2,] [1]Department of Ophthalmology, Kyoto Prefectural University of Medicine, Kyoto, Japan. [2]Department of Biomedical Engineering, Faculty of Life and Medical Sciences, Doshisha University, Kyotanabe, Japan.

26 CORRELATION BETWEEN TEAR PROSTAGLANDIN E2 LEVELS AND SEVERITY OF DRY EYE. Kaevalin Lekhanont,[1] Kanchalika Sathianvichitr,[1] Kitipong Soontrapa,[2] Umaporn Udomsubpayakul[3]. Department of Ophthalmology, Ramathibodi Hospital[1], Department of Pharmacology, Siriraj Hospital[2], Clinical Epidemiology and Biostatistics Unit, Ramathibodi Hospital[3], Mahidol University, Bangkok, Thailand

27 DROP VOLUME OF ARTIFICIAL TEAR SOLUTIONS: PHARMACOECONOMIC STUDY. Alexandre Xavier da Costa[1], Robson Miranda da Gama[2], Silvia Prado Smit Kitadai[3], Eric Pinheiro de Andrade[3], Gabriela Boia Rocha Ferro[1], José Álvaro Pereira Gomes[1] 1. Department of Ophthalmology, Paulista School of Medicine, Federal University of São Paulo, São Paulo, SP, Brazil. 2. Department of Pharmacy, University of Santo Amaro, São Paulo, SP, Brazil. 3. Department of Ophthalmology, University of Santo Amaro, São Paulo, SP, Brazil.

28 GOBLET CELLS DENSITY AFTER USE OF TOPICAL IMMUNOMODULATOR IN THE TREATMENT OF PATIENTS WITH DRY EYE DISEASE. Rossen M.Hazarbassanov[1],Jose Arthur P. Milhomens[1], Nicolle Queiroz-Hazarbassanov[2], Jose Alvaro P. Gomes[1].[1]Department of Ophthalmology & Visual Sciences, Federal University of Sao Paulo; [2]Department of Pathology ,School of Veterinary Medicine, University of Sao Paulo; Sao Paulo, SP, Brazil.

29 SUPRATARSAL INJECTION OF TRIAMCINOLONE FOR SEVERE VERNAL KERATOCONJUNCTIVITIS. Alexandre Xavier da Costa[1], Leonardo Guedes Candido Marculino[1], Vera Lucia Liendo[1], Telma Pereira Barreiro[1], José Álvaro Pereira Gomes[2], Myrna Serapião dos Santos[1]. 1.Assistant Physician, Corneal and External Diseases, Department of Ophthalmology, Federal University of São Paulo (UNIFESP). 2. Associated Professor and Director of Advanced Ocular Surface Center, Department of Ophthalmology, Federal University of São Paulo (UNIFESP).

30 COMPARISON OF THREE GEL BASED TOPICAL LUBRICANTS ON TEAR FILM THICKNESS IN MODERATE AND SEVERE DRY EYE. Doreen Schmidl[1,2], Katarzyna Witkowska[1,2], Rene Werkmeister[2], Piotr Wozniak[1], Ahmed Bata[1], Klemens Fondi[1], Carina Baar[1], Gerhard Garhöfer[1], Leopold Schmetterer[1,2]. [1]Department of Clinical Pharmacology, [2]Center for Medical Physics and Biomedical Engineering. Medical University of Vienna, Vienna, Austria

31 TEAR VOLUME CHANGES OVER THE INTERBLINK PERIOD. Michel Guillon,[1,2] Kathy Dumbleton,[1] Kishan Patel,[1] Ruchi Gupta,[1] Paris Pariza.[1] OCULAR TECHNOLOGY GROUP International,[1] School of Life and Health Sciences,[2] Aston University, Aston, UK

32 THE ANALYSIS OF POST-BLINK TEAR FILM SURFACE QUALITY TOWARDS UNDERSTANDING THE EATIOLOGIES OF OCULAR SURFACE DISEASE. Dorota H. Szczesna-Iskander,[1] D. Robert Iskander.[2] Department of Optics and Photonics,[1] Department of Biomedical Engineering,[2] Wroclaw University of Science and Technology, Wroclaw, Poland

33 RELATIONSHIP BETWEEN OCULAR SURFACE EPITHELIAL DAMAGE, TEAR ABNORMALITIES, AND BLINK IN DRY-EYE PATIENTS. Hiroaki Kato[1], Norihiko Yokoi[1], Aoi Komuro[1], Yukiko Sonomura[1], Akihide Watanabe[1], Chie Sotozono[1] and Shigeru Kinoshita[2], Department of Ophthalmology[1] and Department of Frontier Medical Science and Technology for Ophthalmology[2], Kyoto Prefectural University of Medicine, Kyoto, Japan

34 A FRACTAL DIMENSION APPROACH TO TEAR FILM DYNAMICS CHARACTERIZATION IN HIGH SPEED VIDEOKERATOSCOPY. Clara Llorens-Quintana[1], D. Robert Iskander[1]. Wroclaw University of Science and Technology, Wroclaw, Poland[1].

35 Factors Impacting the Post-Lens Tear Film Mixing. Pult Heiko[1, 2, 3]& Riede-Pult Britta Helen[1] [1]Optometry and Vision Research, Weinheim, Germany [2]Cardiff University, School of Optometry and Vison Sciences, UK [3]Ophthalmic Research Group, Life and Health Sciences, Aston University, Birmingham, UK

36 COMPARISON OF KERATOGRAPH 5M® TEAR MENISCUS HEIGHT WITH DRY EYE EVALUATION IN PRIMARY SJÖGREN'S SYNDROME. Karim Mohamed-Noriega, MD, Dr Med,[1] Fernando Morales-Wong, MD;[1] Yunuen Bages-Rousselon, MD,[1] Janett Riega, MD,[2] Dr Med; Mario Garza, MD, PhD,[2] Jesús Mohamed-Hamsho, MD, Dr. Med.[1] Department Of Ophthalmology, Autonomous University Of Nuevo Leon (UANL), Faculty Of Medicine, University Hospital, Monterrey, Mexico.[1] Department Of Rheumatology, Autonomous University Of Nuevo Leon (UANL), Faculty Of Medicine, University Hospital, Monterrey, Mexico.[2]

37 TEAR DYNAMICS EVALUATION WITH FLUORESCEIN PROFILOMETER AND OPTICAL COHERENCE TOMOGRAPHY Izabela K. Garaszczuk[1], D. Robert Iskander[2]. [1]University of Valencia, Valencia, Spain [2], Wroclaw University of Science and Technology, Wroclaw, Poland

38 NEWER CLASSIFICATION OF TEAR FILM BREAK PATTERN; CLINICAL AND PATHOPHYSIOLOGICAL ANALYSIS. Hong Kyun Kim1,2, Myung Jun Kim1,2 Jong-Sup Bae3, Man-Il Huh2 1. Department of Ophthalmology, Kyungpook National University School of Medicine 2. . Biomedical Research Institute, Kyungpook National University Hospital. 3. College of Pharmacy, CMRI, Research Institute of Pharmaceutical Sciences, BK21 Plus KNU Multi-Omics based Creative Drug Research Team, Kyungpook National University.

39 RELIABILITY OF A NEW NON-INVASIVE TEAR FILM BREAK-UP TIME MEASUREMENT USING A KERATOGRAPH. Sang-Bumm Lee, Seongyong Jeong. Department of Ophthalmology, Yeungnam University College of Medicine, Daegu, Korea

40 DEVELOPMENT OF AN AUTOMATIZED METHOD FOR ANALYZING TEAR FILM LIPID LAYER THICKNESS AND CORRELATION ANALYSIS AMONG CLINICAL FINDINGS OF DRY EYE DISEASE. Sang-Mok Lee,[1] Eun Chul Kim,[2] Man Soo Kim,[3] Tae Hyung Lim,[4] Ho Sik Hwang.[1] Department of Ophthalmology, Hallym University College of Medicine, Chuncheon,[1] Department of Ophthalmology, Bucheon St Mary's Hospital, The Catholic University of Korea, Bucheon,[2] Department of Ophthalmology, Seoul St Mary's Hospital, Seoul,[3] HanGil Eye Hospital, Incheon,[4] Korea

41 THE EVALUATION OF ANATOMIC STRUCTURE AND TEAR MENISCUS CHANGING AFTER CONJUNCTIVOCHALASIS CAUTERIZATION BY VISANTE OPTICAL COHERENCE TOMOGRAPHY. Lu Huibin, Jiang Xiaodan, Zhang Mingzhou, Xu Ting, Huang Chen, Li Xuemin, Department of Ophthalmology, Peking University Third Hospital, Beijing, China

42 EVALUATION OF THE EFFECT OF CONJUNCTIVOCHALASIS CAUTERIZATION ON TEAR STABILITY AND CONTRAST SENSITIVITY. Lu Huibin, Jiang Xiaodan, Weiqiang Qiu, Zhang Mingzhou, Li Xuemin, Wang Wei, Department of Ophthalmology, Peking University Third Hospital, Beijing, China

43 TEAR MENISCUS VOLUME AFTER CONJUNCTIVOCHALASIS SURGERY USING FOURIER-DOMAIN AS-OCT Woo Chan Park 1, Young Ook Kim1, Jeong Bum Bae2 Dong-A University, College of Medicine, Busan, Korea1, Lee Eye Clinic, Busan, Republic of Korea2

44 CORNEAL SENSITIVITY AND TEAR COMPONENTS IN KERATOCONUS. Preeji Mandathara,[1] Fiona Stapleton,[1] Jim Kokkinakis,[1,2] Mark Willcox[1] School of Optometry and Vision Science,University of New South Wales,Australia; The Eye Practice, Australia.[2]

45 THE EFFECTS OF 3% DIQUAFOSOL SODIUM EYE DROPS ON TEAR FUNCTIONS AND OCULAR SURFACE IN SOD-1 KNOCK OUT MICE TREATED WITH ANTI-GLAUCOMA EYE MEDICATIONS. Yukari Yaguchi, Murat Dogru , Kazunari Higa, Terumasa Suzuki, Junko Higuchi, Ayako Igarashi, Takefumi Yamaguchi, Takahiko Shimizu,Jun Shimazaki, Kazuo Tsubota, Keio University School of Medicine, Tokyo, Japan

46 THE EFFECT OF TOPICAL DIQUAFOSOL TETRASODIUM 3% ON DRY EYE AFTER CATARACT SURGERY. Sung Kun Chung[1], Jiwon Baek[2] and Sang Hee Doh[1]1 Department of Ophthalmology and Visual Science, St. Paul's Hospital, College of Medicine, The Catholic University of Korea 2 Department of Ophthalmology and Visual Science, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea

47 ANTI-INFLAMMATORY EFFECTS OF REBAMIPIDE EYE DROPS ON SUPERIOR LIMBIC KERATOCONJUNTIVITIS Marini, Cecilia[1], Tosi, Jorge[2], Corvino, Viviana[3], Brunzini Ricardo[3]. [1]Hospital El Cruce, Buenos Aires, Argentina.[2] Cosultorio Dr Jorge Tosi, Buenos Aires, Argentina; [3]Consultorio Dr Ricardo Brunzini, Buenos Aires, Argentina.

48 EFFECT OF REBAMIPIDE ON TRANSMEMBRANE MUCIN BIOSYNTHESIS IN STRATIFIED OCULAR SURFACE EPITHELIAL CELLS. Yuichi Uchino, Ashley Woodward and Pablo Argüeso, Schepens Eye Research Institute and Massachusetts Eye and Ear, Department of Ophthalmology, Harvard Medical School, Boston, MA, USA

49 CYCLOSPORINE A LOADED LIPOSOMES FOR DRY EYE DISEASE TREATMENT. M. Caballo-González[1], M. Vicario-de-la-Torre[1], M. Gómez-Ballesteros[1,5], D. Acar[1], E. Rodríguez-Álvaro[2], E. González-Alonso[2], M. Guzmán[3], J.M. Benítez-del-Castillo[4,5], R. Herrero-Vanrell[1,5], I.T. Molina-Martinez[1,5]. [1] Department of Pharmacy and Pharmaceutical Technology, Complutense University of Madrid, Spain, [2] Department of Medicine and Animal Surgery, Complutense University of Madrid, Spain, [3] Department of Pharmacy and Pharmaceutical Technology, University of Alcala de Henares, Spain, [4] Surface Unit and Ocular Inflammation (USIO), San Carlos Clinical Hospital, Complutense University of Madrid, Spain, [5] Pharmaceutical Innovation in Ophthalmology Research Group, Sanitary Research Institute of the San Carlos Clinical Hospital (IdISSC) and the Ocular Pathology National Net (OFTARED) of the Institute of Health Carlos III. Madrid, Spain

50 CYCLOSPORINE A APPLICATIONS BEYOND DRY EYE DISEASE. Alex Hui, OD, PhD, FAAO. School of Optometry and Vision Science, UNSW Australia, Sydney, New South Wales, Australia

51 EFFECTS OF TOPICAL CYCLOSPORINE 0.05% AFTER CATARACT SURGERY IN PATIENTS WITH DRY EYE. Young Min Park,[1] Jong Soo Lee,[2] Department of Ophthalmology, Gyeongsang National University Changwon Hospital, 11, Samjeongja-ro, Seongsan-gu, Changwon-si, Gyeongsangnam-do, 51472, South Korea,[1] Department of Ophthalmology, School of Medicine, Pusan National University and Medical Research Institute, Pusan National University Hospital, Pusan, South Korea,[2]

52 SAFETY AND EFFICACY OF 0.1% (1 MG/ML) CYCLOSPORINE CATIONIC EMULSION (CsA CE) IN PATIENTS WITH DRY EYE DISEASE AND SJÖGREN'S SYNDROME: EXPERIENCE FROM THE FRENCH EARLY ACCESS PROGRAM. Serge Doan[1], Béatrice Cochener[2], Mourad Amrane[3], Jean-Sébastien Garrigue[3], Dahlia Ismail[3], Pierre-Jean Pisella[4,5], Dominique Bremond-Gignac[6] [1]Bichat Hospital and Fondation A. de Rothschild, Paris, France [2]Brest University Medical School, Morvan Hospital, Brest, France [3]Santen SAS, Evry, France [4]University François Rabelais, Tours, France [5]Bretonneau Hospital, Tours, France [6]University Hospital Necker-Enfants Malades, APHP, Paris V Descartes University, Paris, France

53 OVERVIEW OF CLINICAL EFFICACY AND SAFETY OF LIFITEGRAST OPHTHALMIC SOLUTION 5.0% FOR TREATMENT OF DRY EYE DISEASE. Amir Shojaei,[1] Joseph Tauber,[2] Kelly K. Nichols,[3] Aparna Raychaudhuri,[1] Monica Roy.[1] Shire,[1] Tauber Eye Center,[2] University of Alabama at Birmingham,[3] USA

54 TREATMENT FAILURES WITH PROSTHETIC REPLACEMENT OF THE OCULAR SURFACE ECOSYSTEM [PROSE] DEVICE USE. Matthew Schear,[1] Kirolos Ibrahim,[2] Jules Winokur,[1] Corina Busiouc,[1] Ira Udell,[1] Anne Steiner.[1] Northwell Health Department of Ophthalmology,[1] Great Neck, NY, USA. Stony Brook School of Medicine,[2] Stony Brook, NY, USA.

55 TOPICAL LOW-DOSE PRESERVATIVE FREE DEXAMETHASONE (PFD) FOR CHRONIC OCULAR SURFACE DISEASE REFRACTORY TO CONVENTIONAL THERAPY. Adnan Mallick[1], Bennett Hong[1], Carolyn Shih[1], Ira Udell[1], Annie Steiner.[1] [1]Hofrstra-Northwell School of Medicine, Department of Ophthalmology, Great Neck, NY.

56 THE EFFICIENCY OF 0.01% DEXAMETHAZONE SOLUTION IN COMPLEX THERAPY FOR PATIENTS WITH DRY EYE DISEASE OF DIFFERENT ETIOLOGY. Brzheskiy V.V.1, Popov V. Yu.1, Kalinina I.V.2 1Saint Petersburg State Medical Pediatric University, Russia 2 Mariinsky Hospital, Russia

57 CLINICAL SAFETY AND TOLERABILITY OF A MANUKA HONEY-BASED PRODUCT DESIGNED TO PROMOTE EYELID HEALTH. Jennifer P. Craig,[1] Isabella Cheung,[1] Chee S. Loh,[1] Leah Te Weehi,[1] Ilva D. Rupenthal,[1] Simon Swift,[2] Grant Watters.[1] Department of Ophthalmology,[1] Department of Molecular Medicine,[2] The University of Auckland, New Zealand

58 HA-SULFADIAZINE CONJUGATE FOR THE TREATMENT OF DRY EYE DISEASE. Frances Lasowski[1], Ben Muirhead[1], Jafar Mazumder[2], Heather Sheardown[1]. [1]McMaster University, Hamilton, Ontario, Canada; [2]King Fahd University of Petroleum and Minerals, Saudi Arabia.

59 TITLE: NOVEL MICRORNA THERAPEUTICS IN SJÖGREN'S SYNDROME DRY EYE DISEASE. Connolly, Sinéad[1, 2]; Pilson, Qistina[1, 2]; Cryan, Sally-Ann[4]; Ní Gabhann, Joan[1,2] and Murphy, Conor C.[1, 3] [1] Department of Ophthalmology, Royal College of Surgeons in Ireland, Dublin, Ireland, [2] Molecular and Cellular Therapeutics, RCSI, Dublin, Ireland, [3] Department of Ophthalmology, Royal Victoria Eye and Ear Hospital, Dublin, Ireland, [4] RCSI School of Pharmacy, RCSI, Dublin, Ireland.

60 NOVATEARS® AS NEW THERAPY IN DRY EYE – RESULTS FROM THREE PROSPECTIVE, MULTICENTER, NON-INTERVENTIONAL STUDIES IN DIFFERENT PATIENT POPULATIONS. Thomas Kaercher[1], Philipp Steven[2], Elisabeth M. Messmer[3], Michael Beckert[4], Sonja Krösser[5]. Ophthalmology Clinics Heidelberg[1], Dept. of Ophthalmology, University of Cologne[2], Dept. of Ophthalmology, LMU Munich[3], CaRACS, Berlin[4], Novaliq GmbH, Heidelberg[5], Germany

61 TOPICAL, NON-INVASIVE TREATMENT FOR DRY EYE IN CONTROLLED HUMAN AND ANIMAL STUDIES. Wei-wei Chang,[1] Kenneth I. Sawyer.[1] GLIA LLC,[1] Boston, MA, USA

62 PRECLINICAL CANDIDATE WITH A NEW MECHANISM OF ACTION AGAINST OCULAR SURFACE DISEASES. Jurgen Joossens [1,2], Cedric Joossen[1,3], Adrienn Baan[1,4], Hannah Ceuleers[5], Anne-Marie Lambeir[1,6], Benedicte De Winter[5], Carina Koppen[7], Filip Kiekens[1,4], Paul Cos[1,3], Koen Augustyns[1,2]. Antwerp Drug Discovery Network[1], Laboratory of Medicinal Chemistry[2], Laboratory of Microbiology, Parasitology, and Hygiene [3], Laboratory of Pharmaceutical Technology and Biopharmacy[4], Laboratory of Experimental Medicine and Pediatrics[5], Laboratory of Medical Biochemistry[6], University of Antwerp, Antwerp, Belgium and Department of Ophthalmology[7], Antwerp University Hospital, Antwerp, Belgium

63 A RANDOMISED, DOUBLE-MASKED, PLACEBO-CONTROLLED CLINICAL TRIAL OF TWO FORMS OF OMEGA-3 SUPPLEMENTS FOR TREATING DRY EYE DISEASE. Laura E Downie, Laura A Deinema, Holly R Chinnery, Algis J Vingrys. Department of Optometry & Vision Sciences, University of Melbourne, Victoria, Australia.

64 EFFECTS OF HYALURONIC ACID WITH DIFFERENT MOLECULAR WEIGHT ON REPAIR OF MECHANICAL DAMAGE OR UV - INDUCED INJURY FOR HUMAN CORNEAL EPITHELIAL CELLS. Xueping Guo, Xiaoou Zhang, Dejie Li, Bloomage Freda Biopharm Co., Ltd. Jinan, Shandong, China.

65 PHYSIOCHEMICAL PROPERTIES OF HYALURONIC ACID-BASED EYE DROPS. Peter A Simmons[1], Pasquale Aragona[2], Hongpeng Wang[1], Tao Wang[1] [1]Allergan plc, Irvine, California, USA; [2]University of Messina, Messina, Italy

66 ABOUT THE INFLUENCE OF THE VEGETATIVE ACTIVITY ON DRY EYE SYNDROMES. Johannes Nepp[(1,4)], Nikolaus Hocke[(2)], Magdalena Wirth[(3)] , H.Nissel[(4)], K.Stockert[(4)], Manfred Bijak[(2)]. Department of Ophthalmology[(1)] Center for Medical Physics and Biomedical Engineering[(2)] Medical University Vienna, Austria, Ophtalmological department, Triemli Clinic Zurich[(3)], J Bischko Institute of Acupuncture, Vienna[(4)]

67 EFFECTS OF SUBCONJUNCTIVAL ADMINISTRATION OF ANTI-HIGH MOBILITY GROUP BOX 1(HMGB1) ON DRY EYES IN A MOUSE MODEL OF SJÖGREN SYNDROME. Jaeyoung Kim,[1,2] Yu Jeong Kim,[1,2] Kyeong Hwan Kim,[2,3] Dong Hyun Kim,[2,4] Hyun Jeong Jeong,[2] Jin Suk Ryu,[2] Joo Youn Oh,[1,2] Mee Kum Kim,[1,2] Won Ryang Wee.[1,2] Department of Ophthalmology, Seoul National University College of Medicine, Seoul,[1] Laboratory of Corneal Regenerative Medicine and Ocular Immunology, Seoul National University Hospital Biomedical Research Institute, Seoul,[2] Ophthalmology, Haeundae Paik Hospital; Ophthalmology, Inje University College of Medicine, Busan,[3] Ophthalmology, Gachon University, Incheon,[4] Korea

68 LACRITIN C-TERMINAL PROMOTION OF OCULAR SURFACE HEALTH, CORNEAL NERVE ACTIVATION AND TEARING. Jeffrey Romano,[1] Harumitsu Hirata,[2] Nancy McNamara,[3] Sarah M. Knox,[4] Robert L. McKown,[5] Gordon W. Laurie,[1] [1]Department of Cell Biology, University of Virginia School of Medicine, Charlottesville, VA USA [2]Department of Ophthalmology, Weill Cornell Medical College, New York, NY [3]Department of Anatomy, UCSF School of Medicine, San Francisco, CA [4]Department of Cell and Tissue Biology, UCSF School of Dentistry, San Francisco, CA[5]Department of Integrated Science and Technology, James Madison University, Harrisonburg VA

69 EFFICIENCY AND SAFETY OF SUBCONJUNCTIVAL INJECTION OF ANTI-VEGF AGENT – BEVACIZUMAB – IN TREATING DRY EYE. Jiang Xiaodan, Lu Huibin, Qiu Weiqiang, Liu Ziyuan, Li Xuemin, Wang Wei 1Department of Ophthalmology, Peking University Third Hospital, Beijing, China

70 EFFECTIVENESS OF DIFFERENT THERAPIES FOR DRY EYE DISEASE MANAGEMENT. James S Wolffsohn[1], Mike S Berg[2], Venkiteshwar S Manoj[2]. School of Life and Health Sciences, Aston University, Birmingham, UK[1], TearLab Corporation, San Diego[2]

71 THE EFFECT OF ORAL ZANTHOXYLUM SCHINIFOLIUM SEED OIL IN INDIVIDUALS WITH DRY EYE DISEASE. In-Cheon You,[1,2] Jin-Woo Park,[1,2] Mun-Yhung Jung,[3] Wan-Suk Kang,[1,2] Soo-Wan Chae,[1,2] Eun-Ock Park,[1] Nam-Chun Cho,[1,2] Chonbuk National University Hospital,[1] Chonbuk National University Medical School,[2] College of Food Science, Woosuk University,[3] Jeonju, Jeonbuk, South Korea

72 EFFECTS OF AUTOLOGOUS SERUM EYE DROPS FOR THE TREATMENT OF DRY EYE SYDROME AND ASSOCIATED OCULAR SURFACE DISEASES. Quiñones X[1], Valenzuela F[1], Cintron H[1], Davis K[1], Donaldson K[1], Perez VL.[1] Ocular Surface Center, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine[1]

73 USE OF AUTOLOGOUS SERUM IN ADVANCED SURFACE ABLATION CORNEAL REFRACTIVE SURGERY. María J. González-García,[1,2] Giovanna Murillo,[1] José Pinto-Fraga,[1,2] Noelia García-Sánchez,[1] Margarita Calonge,[1,2] Miguel J. Maldonado.[3] Ocular Surface Group, IOBA, University of Valladolid, Valladolid,[1] CIBER-BBN,[2] Refractive Surgery and Visual Rehabilitation Group, IOBA, University of Valladolid, Valladolid,[3] Spain.

74 THE EFFECT OF A NEW OCULAR SURFACE MODULATOR IN CONTROLLING INFLAMMATION IN AN IN VITRO MODEL OF DRY EYE.Stefano Barabino,[1] Barbara De Servi,[2] Marisa Meloni[2 1] Clinica Oculistica, DiNOGMI, Azienda Ospedaliera Universitaria San Marino-IST, Genoa, Italy; [2] in Vitro Research Laboratories, VitroScreen, Milan, Italy; [2] in Vitro Research Laboratories, VitroScreen, Milan, Italy

75 THE INFLUENCE OF EYE CLOSURE ON DRY EYE SYNDROME SYMPTOMS. Charles McMonnies DSc and Nicholas Young BOptom PhD, Adjunct Professor School of Optometry and Vision Science UNSW and Dry Eye Centre, Heathmont Victoria.

76 EXPERIENCE OF THE FIRST OCULAR SURFACE-DRY EYE SERVICE IN ATHENS. George Dalianis, Chryssa Terzidou, Alexandra Trivli, Ophthalmological Clinic, Konstantopouleio-Patission Gen Hptl, N.Ionia, Athens Greece.

77 PHENYLBORONIC ACID BASED POLYMERIC MICELLES FOR MUCOADHESIVE OCULAR DRUG DELIVERY. Ben Muirhead, Heather Sheardown. Department of Biomedical Engineering, McMaster University, Hamilton, ON, Canada

78 INFLUENCE OF A NATURAL EYE DROP EMULSION ON NON-IMMUNE MEDIATED ALLERGIC REACTION. F. Giuliano, T. Tornetta, G. De Pasquale, M. G. Mazzone. S.I.F.I. S.p.A., Aci S. Antonio (CT), Italy.

79 A NOVEL METHOD USED TO MEASURE THE CONTACT ANGLE OF DRY EYE DROP SOLUTIONS. Rebecca Wilcox,[1] Christine Purslow,[2] Falko Drijfhout.[1] School of Physical & Geographical Sciences,[1] School of Optometry & Vision Sciences, Cardiff University,[2] Keele University, UK

80 EASE OF USE OF TWO PRESERVATIVE FREE BOTTLE SYSTEMS FOR DRY EYE DROPS. Rebecca Wilcox,[1] Falko Drijfhout,[1] Christine Purslow.[2] School of Physical & Geographical Sciences,[1] School of Optometry & Vision Sciences, Cardiff University,[2] Keele University, UK

81 EFFECT OF MATRIX REGENERATION THERAPY ON CORNEAL EPITHELIAL HEALING FOLLOWING EPI-OFF CROSS-LINKING IN PATIENTS WITH KERATOCONUS. Ahmed Bata[1], Katarzyna J. Witkowska[1,2], Piotr A. Wozniak[1], Klemens Fondi[1], Gerald Schmidinger[3], Niklas Pircher[3], Stephan Szegedi[1], René M. Werkmeister[2], Gerhard Garhofer[1], Leopold Schmetterer[1,2], Doreen Schmidl[1,2]. [1]Department of Clinical Pharmacology, [2]Center for Medical Physics and Biomedical Engineering, [3]Department of Ophthalmology and Optometry, Medical University of Vienna, Austria

82 LAST OPTION!!ROLE OF KERATOPROSTHESIS IN CHEMICAL INJURY. Bhaskar Srinivasan, Agarwal Shweta, Iyer Geetha, G Sitalakshmi clinic for ocular surface disorders ,CJ Shah cornea services, Sankara Nethralaya, Chennai, India

83 ROLE OF ALLOSLET IN ACUTE CHEMICAL INJURY. Dr Bhaskar Srinivasan, Dr Shweta Agarwal,Dr Geetha Iyer, G Sitalakshmi clinic for ocular surface disorders ,CJ Shah cornea services, Sankara Nethralaya , Chennai , India

84 MUCOUS MEMBRANE GRAFTS IN OCULAR CICATRICIAL PEMPHIGOID: SCHIRMER'S TEST AND LONG TERM FORNIX DEPTH OUTCOMES. Arturo Arturo Grau,1 Gurjeet Jutley,1 John Dart, 1,2 Richard Collin, 1,2 David Verity, 1 Valerie Saw.1,2 Moorfields Eye Hospital,1 UCL Institute of Ophthalmology,2 London, UK

85 PROFILE, TREATMENT AND OUTCOMES OF OCULAR SURFACE SQUAMOUS NEOPLASIA (OSSN) IN A RURAL POPULATION OF CENTRAL INDIA. Charudutt Kalamkar[1], Nishant Radke[1,] Geeta Behera [2] ,Amrita Mukherjee[1], Snehal Radke[1] , Shri ganesh Vinayak Eye Hospital,Raipur,India,[1] IGGGH, Puducherry, India[2]

86 MMC INJECTION-ASSISTED PTERYGIUM EXCISION- A NOVEL TECHNIQUE. Chryssa Terzidou, Alexandra Trivli, Ophthalmological Clinic Konstantopouleio-Patission Gen Hptl, Nea Ionia, Athens, Greece.

87 PREVALENCE OF DRY EYE SYNDROME IN SÃO PAULO – BRAZIL Leonardo Guedes C. Marculino[1], Flávio Hirai[2], Rossen Hazarbassanov[3], Tais Wakamatsu[4], Ruth Santo[6], José Alvaro P. Gomes[5]

88 OCULAR SURFACE CYTOKINE RESPONSE TO MUCUS MEMBRANE GRAFTING FOR LID MARGIN KERATINIZATION IN STEVENS JOHNSON SYNDROME. *Geetha Iyer[2], Srividya Gurumurthy[1], Bhaskar Srinivasan[2], Shweta Agarwal[2], N Angayarkanni[1] [1] Vision Research Foundation,[2] Medical Research Foundation, Sankara Nethralaya, Chennai

Saturday, September 10, 2016

Session III

Innovative Technology

Chairpersons - Gordon Laurie (USA), Kaevalin Lekhanont (Thailand), Isobel Massie (Germany)

8:00 **Keynote Address:** CRISPR/Cas9: Editing the mammalian genome *in vivo*. Fei Ann Ran, The Broad Institute, Cambridge, MA, USA

8:20 **Keynote Address:** Smart glasses: Future uses & limitations for healthcare. Peter Evans, Pristine Inc., Austin, TX, USA

8:40 **Keynote Address:** Translating an idea into a therapy: Escaping the ocular stress trap. Sandeep Jain, Corneal Neurobiology Laboratory, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL, USA

9:00 **Keynote Address:** New developments in ocular surface imaging. Rudolf F. Guthoff, University Eye Department Rostock, Germany

9:20 **Keynote Address:** Organ regeneration of lacrimal gland as a next-generation of regenerative medicine. Masatoshi Hirayama[1], Kazuo Tsubota[1], Takashi Tsuji[2] Department of Ophthalmology, School of Medicine, Keio University, Tokyo;[1] Laboratory for Organ Regeneration, Center for Developmental Biology, RIKEN, Kobe, Japan[2]

9:40 **Poster Session III (with Coffee & Tea)**
Chairpersons - Murat Dogru (Japan), Driss Zoukhri (USA)

Contact Lens Discomfort: Update

Chairpersons - Laura García-Posadas (USA), Kathryn Richdale (USA), Ulrike Stahl (Canada)

10:30 **Keynote Address:** New advances in the understanding of the definition, classification and epidemiology of contact lens discomfort. Rachel Redfern, The University of Houston, College of Optometry, The Ocular Surface Institute, Houston, TX, USA

10:47 **Keynote Address:** New advances in the understanding of the role of contact lens materials and care systems in contact lens discomfort. Lakshman N. Subbaraman, Centre for Contact Lens Research, School of Optometry and Vision Science, University of Waterloo, Waterloo, Canada

11:04 **Keynote Address:** New advances in the understanding of the neurobiology of contact lens discomfort. Blanka Golebiowski, School of Optometry and Vision Science, University of New South Wales, Sydney, NSW, Australia

11:21 **Keynote Address:** New advances in the understanding of the role of the ocular surface and tear film in contact lens discomfort. Maria Markoulli, School of Optometry and Vision Science, University of New South Wales, Sydney, NSW, Australia

11:38 **Keynote Address:** New advances in the management, treatment, and clinical trial design for contact lens discomfort. Joseph B. Ciolino, Massachusetts Eye and Ear Infirmary, Schepens Eye Research Institute, and Harvard Medical School, Boston, MA, USA

11:55 **Poster Viewing & Lunch**

Prime Time TFOS Debates 2

Chairpersons - Donald Korb (USA), Paul Karpecki (USA), Céline Portal (France)

13:15 **Debate 1:** Are there good animal models for human dry eye disease?

It depends on the definition of "good" – Seunghee Cha, Oral and Maxillofacial Diagnostic Sciences/Oral Biology, University of Florida College of Dentistry, Gainesville, FL, USA

No – Austin K. Mircheff. Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

13:45 **Debate 2:** Do contact lenses cause clinically relevant meibomian gland dysfunction?

Yes – Reiko Arita, Itoh Clinic, Saitama, and University of Tokyo, Tokyo, Japan

No – Eric B. Papas, School of Optometry & Vision Science, University of New South Wales, Sydney, Australia.

TFOS Dry Eye WorkShop II: Updates, Part 1

Chairpersons - Jennifer P Craig (New Zealand), Masaki Fukui (Japan), J Daniel Nelson (USA)

14:15 **Introduction.** J. Daniel Nelson, HealthPartners Medical Group and Clinics, St Paul, MN, USA

14:20 **Keynote Address:** Definition & classification. Kelly K. Nichols, University of Alabama at Birmingham School of Optometry, Birmingham, AL, USA

14:35 **Keynote Address:** Sex, hormones & gender. Sruthi Srinivasan, Centre for Contact Lens Research, School of Optometry and Vision Science, University of Waterloo, Waterloo, Canada

14:50 **Keynote Address:** Epidemiology. Fiona Stapleton, School of Optometry and Vision Science, University of New South Wales, Sydney, NSW, Australia

15:05 **Keynote Address:** Pathophysiology. Anthony J. Bron, University of Oxford, Oxford, UK

15:20 **Keynote Address:** Clinical Trials. Gary D. Novack, Pharma•Logic Development, San Rafael, CA, USA

15:35 **Poster Session III (with Coffee & Tea)**
Chairpersons - Murat Dogru (Japan), Driss Zoukhri (USA)

TFOS Dry Eye WorkShop II: Updates, Part 2

Chairpersons - Kai Jin (Japan), Charles McMonnies (Australia), Louis Tong (Singapore)

16:25 **Keynote Address:** Tear film. Mark DP Willcox, School of Optometry and Vision Science, University of New South Wales, Sydney, NSW, Australia

16:40 **Keynote Address:** Iatrogenic dry eye disease. José Gomes, Department of Ophthalmology, Paulista School of Medicine, São Paulo, Brazil

16:55 **Keynote Address:** Pain & sensation. Carlos Belmonte, Medical School, University Miguel Hernandez and Neurosciences Institute of Alicante, Alicante, Spain

17:10 **Keynote Address:** Diagnosis. James Wolffsohn, Aston University, School of Life and Health Sciences, Aston, UK

17:25 **Keynote Address:** Management & Therapy. Lyndon Jones, Centre for Contact Lens Research, School of Optometry and Vision Science, University of Waterloo, Waterloo, Canada

17:40 **Keynote Address:** Public awareness & education. Katherine Hammitt, Sjögrens Syndrome Foundation, Bethesda, MD, USA

Closing Remarks

17:55 David A. Sullivan, Schepens Eye Research Institute, Massachusetts Eye and Ear and Harvard Medical School, Boston, MA, USA

Closing Reception

18:00 – 19:00

Poster Session III

Chairpersons - Murat Dogru (Japan), Driss Zoukhri (USA)

1 IMPAIRED FUNCTION OF PERIPHERALLY INDUCED REGULATORY T CELLS IN HOSTS OF HIGH RISK OF GRAFT REJECTION. Takenori Inomata,[1,2,3] Jing Hua,[1,2] Antonio Di Zazzo,[1,2] and Reza Dana.[1,2] Schepens Eye Research Institute,[1] Massachusetts Eye & Ear Infirmly,[2] Department of Ophthalmology, Harvard Medical School, Boston, MA, USA, Juntendo University Faculty of Medicine,[3] Department of Ophthalmology, Tokyo, Japan.

2 PRO-INFLAMMATORY CYTOKINES ASSOCIATED WITH CLINICAL SEVERITY OF DRY EYE DISEASE OF PATIENTS WITH DEPRESSION. Mrugacz Małgorzata[1], Ostrowska Lucyna[2], Bryl Anna[1], Szulc Agata[3], Beata Zelazowska-Rutkowska[4], Mrugacz Grzegorz[5] [1] Department of Ophthalmology and Eye Rehabilitation, Medical University of Białystok, Poland, [2] Department of Clinical Nutrition, Medical University

of Białystok, Poland, [3] Department of Psychiatry, Medical University of Warsaw, Poland, [4] Department of Paediatric Laboratory Diagnostics, Medical University of Białystok, Poland, [5] Centre for Reproductive Medicine, Białystok, Poland; 15-267 Białystok, Poland

3 DRY EYE DISEASE EXPERIMENTAL MODELLING. Brzheskiy V.V.,[1] Popov V. Yu.,[1] Kalinina N.M.[2] [1]Saint Petersburg State Medical Pediatric University, Russia [2] The Nikiforov Russian Centre of Emergency and Radiation Medicine, Russia

4 THE EFFECT OF AMBIENT TITANIUM DIOXIDE MICROPARTICLE EXPOSURE TO THE OCULAR SURFACE ON THE EXPRESSION OF INFLAMMATORY CYTOKINES IN THE EYE AND CERVICAL LYMPH NODES. Youngsub Eom,[1] Jong Suk Song,[1] Hyun Kyu Lee,[1] Boram Kang,[1] Hyeon Chang Kim,[2] Hyung Keun Lee,[3] Hyo Myung Kim.[1] Korea University College of Medicine,[1] Department of Preventive Medicine, Yonsei University College of Medicine,[2] Department of Ophthalmology, Yonsei University College of Medicine,[3] Seoul, South Korea

5 EXACERBATION OF CLOSED EYE LEUKOCYTE INFLAMMATION IN DRY EYE DISEASE. Cameron K. Postnikoff[1], Kelly K. Nichols.[1] [1]School of Optometry, University of Alabama at Birmingham, Birmingham, AL, USA

6 IMMUNE-NERVE CROSS-TALK IN THE CORNEA: THE ROLE OF PLASMACYTOID DENDRITIC CELLS ON CORNEAL NERVE SURVIVAL. Pedram Hamrah,[1,2] Arsia Jamali,[1,2] Maria Lopez,[1,2] Victor Sendra,[1,2] Deshea L. Harris,[1,2] Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, [1] Schepens Eye Research Institute/Massachusetts Eye and Ear, Department of Ophthalmology, Harvard Medical School,[2] Boston, MA

7 LANGERIN+ CELLS PREVENT OCULAR SURFACE INFLAMMATION AND FACILITATE SUBBASAL NERVE REGENERATION IN DRY EYE DISEASE. Hyung K. Lee, Eun Y. Choi, Chul H. Lee, Hyungoo Kang, Areum Yeo, Hyemi Noh, Eung K. Kim, Institute of Vision Research, Department of Ophthalmology, Yonsei University College of Medicine, Seoul, Republic of Korea

8 PLASMACYTOID DENDRITIC CELLS ARE CRITICAL FOR THE MAINTENANCE OF CORNEAL ANGIOGENIC PRIVILEDGE. Arsia Jamali,[1,2] Maria Lopez,[1,2] Victor Sendra,[1,2] Deshea L. Harris,[1,2] Pedram Hamrah,[1,2] Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine,[1] Schepens Eye Research Institute/Massachusetts Eye and Ear, Department of Ophthalmology, Harvard Medical School,[2] Boston, MA

9 EXPRESSION OF VAMP8 IN CHRONIC OCULAR GRAFT VS HOST DISEASE. Masaki Fukui,[1,2] Yoko Ogawa,[1] Shin Mukai,[1] Teru Azato,[1] Mizuka Kamoi,[1] Kazuo Tsubota.[1] Department of Ophthalmology, Keio University School of Medicine,[1] National Hospital Organization Tokyo Medical Center,[2] Tokyo, Japan

10 MADCAM-1 AND ITS RECEPTORS AS NOVEL BIOLOGICAL TARGETS TO ENHANCE CORNEAL GRAFT SURVIVAL. Hamid-Reza Moein[1,2], Maria Lopez [1,2], Deshea Harris[1,2],Pedram Hamrah[1,2] [1]Schepens Eye Research Institute, Harvard Medical School, Boston, MA, USA. [2] Tufts Medical Center, Center for Translational Ocular Immunology, Tufts University School of Medicine, Boston, MA, USA.

11 CLINICAL OBSERVATION OF LEPTIN'S ROLE IN DRY EYE DEVELOPMENT. Jiang Xiaodan, Lu Huibin, Li Xuemin, Peking University Third Hospital

12 TOXICITY OF POVIDONE IODINE TO THE OCULAR SURFACE OF RABBITS. Hyun Seung Kim, Sun Young Kim. Department of Ophthlamology and Visual Science, Yeouido St. Mary's Hospital, College of Medicine, The Catholic University of KOREA, Seoul, KOREA

13 ASSOCIATION BETWEEN AIR POLLUTION AND DRY EYE DISEASE IN SOUTH KOREA: THE POTENTIAL IMPORTANCE OF OZONE. Dong Hyun Kim1, MD, Yoon-Hyeong Choi2, PhD, Hae Jung Paik, MD, PhD1 1Department of Ophthalmology, Gachon University Gil Medical Center, Incheon, Korea 2Department of Preventive Medicine, Gachon University College of Medicine, Incheon, Korea

14 TOWARDS A HOLISTIC UP-TO-DATE MODEL OF THE PATHOPHYSIOLOGY IN DRY EYE DISEASE. Erich Knop and Nadja Knop, Ocular Surface Center Berlin (OSCB), Dept. for Cell and Neurobiology, Center for Anatomy, Charite – Universitätsmedizin Berlin

15 HEAD WORN AUGMENTED REALITY DISPLAYS IN WORKFORCE AND THEIR INFLUENCE ON OCULAR COMFORT AND OCULAR SURFACE PARAMETERS. Boldin Ingrid[1], Rabensteiner Dieter Franz[1], Schwantzer Gerold[2], Wultsch Georg[3], Haleh Aminfar[1], Heidinger Andrea[1], Klein-Theyer Angelika[1] and Horwath-Winter Jutta[1] Department of Ophthalmology, Medical University[1], Institute for Medical Informatics, Statistics and Documentation, Medical University[2], AMEZ Graz occupational health centre[3] Graz, Austria

16 ESTABLISHMENT OF RAT DRY EYE MODEL WITH OCULAR DISCOMFORT BEHAVIOR. Shigeru Nakamura[1],Yusuke Izuta[1], Michiko Shibuya[1], Erina Onishi[1], Hisayo Sakaguchi[1], Kai Jin [1],Toshihiro Imada[1], Kazuo Tsubota[1] Keio University School of Medicine Department of Ophthalmology, Tokyo, Japan[1]

17 INFLUENCES OF INDOOR ENVIRONMENT QUALITY AND DRY EYE IN A MODERN DESIGN OFFICE Mirjam van Tilborg,1,2 Katharine Evans2 1University of Applied Sciences Utrecht, Utrecht, The Netherlands 2School of Optometry and Vision Sciences, Cardiff University, Cardiff, UK

18 CHARACTERISTICS OF ON-ROAD DRIVING PERFORMANCE OF PERSONS WITH DRY EYE DISEASE IN CHINA. Huibin Lu, Ying Wang, Yan Liu, Xiaodan Jiang, Mingzhou Zhang, Xuemin Li, Wei Wang. Department of Ophthalmology, Peking University Third Hospital, Beijing, China

19 HYPERALGESIA IN DRY EYE DISEASE IS ASSOCIATED WITH LOW VIATMIN D. Natasha Pahuja[1], Rohit Shetty[1], Arkasubhra Ghosh[2], Swaminathan Sethu[2] [1] Cornea Refractive services, Narayana Nethralaya. [2] GROW laboratories, Narayana Nethralaya foundation.

20 OCULAR CICATRICIAL PEMPHIGOID: INDUCED BY BIOLOGICS. Manfred Zierhut[1], Deshka Doycheva[1], Christoph Deuter[1], Bianka Sobolewska[1], Martin Schaller[2]. Center of Ophthalmology[1] and Dermatology[2], University of Tuebingen, Germany.

21 BARRIERS TO GLAUCOMA MEDICATION COMPLIANCE AMONG VETERANS: DRY EYE SYMPTOMS AND ANXIETY DISORDERS. Sarah R Wellik[1,2], Jack Stringham[2], Noy Ashkenazy[3], Anat Galor,[1,2] Miami Veterans Administration Medical Center, Miami, FL[1] Bascom Palmer Eye Institute, Miami, FL,[2] University of Miami Miller School of Medicine, Miami, FL[3]

22 REDUCING THE OCULAR AND SYSTEMIC SIDE EFFECTS OF TROPICAMIDE 0,5% EYEDROPS BY REDUCING THE DROP VOLUME. H. van der Heiden[a], N.A.M. Troelstra[b], J. van Lith[b], J.M. Verzijl[ba] Mu-Drop BV. Apeldoorn, The Netherlands. [b] Elisabeth-TweeSteden Ziekenhuis, 5042 AD Tilburg, The Netherlands.

23 A CASE OF SEVERE OCULAR SURFACE DISORDER RELATED AND SEVERE CONJUNCTIVOCHALASIS. Miki Hata[1,2], Masaki Fukui[1,2], Yoshinobu Mizuno[1], Toru Noda[1] National Hospital Organization Tokyo Medical Center, Department,[1]Department of Ophthalmology, Keio University School of Medicine,[2] Tokyo, Japan

24 PREVALENCE OF DEMODEX FOLLICULORUM IN PATIENTS WITH KERATOCONJUNCTIVITIS SICCA. Christina Jacobi[1,2], Julia K. Kurz[2], Friedrich Paulsen[3], Anselm G.M. Jünemann[2,4]. Ophthalmological practice, Nuremberg, Germany[1]; Department of Ophthalmology, University of Erlangen-Nuremberg, Germany[2]; Institute of Anatomy II, University of Erlangen-Nuremberg, Germany[3]; Department of Ophthalmology, University of Rostock, Germany[4].

25 DIFFERENCE IN THE FREQUENCY OF USE OF LACHRYMAL SUBSTITUTES IN PATIENTS WITH MODERATE TO SEVERE DRY EYE DISEASE. Doreen Schmidl[1,2], Katarzyna Witkowska[1,2], Piotr Wozniak[1], Ahmed Bata[1], Klemens Fondi[1], Carina Baar[1], Gerhard Garhöfer[1], Leopold Schmetterer[1,2]. [1]Department of Clinical Pharmacology, [2]Center for Medical Physics and Biomedical Engineering. Medical University of Vienna, Vienna, Austria

26 CORRELATION OF OCULAR SYMPTOMS QUESTIONNAIRES WITH DRY EYE EVALUATION IN PRIMARY SJÖGREN'S SYNDROME. Karim Mohamed-Noriega, MD, Dr Med,[1] Fernando Morales-Wong, MD;[1] Yunuen Bages-Rousselon, MD,[1] Janett Riega, MD,[2] Dr Med; Mario Garza, MD, PhD,[2] Jesús Mohamed-Hamsho, MD, Dr. Med.[1] Department Of Ophthalmology, Autonomous University Of Nuevo Leon (UANL), Faculty Of Medicine, University Hospital, Monterrey, Mexico.[1] Department Of Rheumatology, Autonomous University Of Nuevo Leon (UANL), Faculty Of Medicine, University Hospital, Monterrey, Mexico.[2]

27 NEUROPATHIC PAIN AS A DISTINGUISHING FACTOR AMONG SJÖGREN AND NON-SJÖGREN SYNDROME PATIENTS WITH DRY EYE DISEASE. Jacqueline Faustino[1], Carolina Maria Modulo[1], Adriana Batista Murashima[1], Eduardo Melani Rocha[1]. [1]FMRP, University of São Paulo, USP, Ribeirão Preto – SP. Department of Ophthalmology, Otorhinolaryngology, and Head and Neck Surgery.Brasil.

28 OCULAR SURFACE PAIN AND AS A DISCRIMINANT SYMPTOM IN DRY EYE DISEASE.Jacqueline Faustino[1], Carolina Maria Modulo1, Adriana Batista Murashima1, Luis Fernando Nominato 1, Ana Carolina Dias1, Eduardo Melani Rocha1.1 FMRP,University of São Paulo,USP, Ribeirão Preto-SP Department of Ophthalmology, Otorhinolaryngology and Head and Neck Surgery.Brasil

29 CHANGES IN CORNEAL ENDOTHELIAL MORPHOLOGY AND CORNEAL THICKNESS IN PATIENTS WITH DRY EYE DISEASE AND SJÖGREN'S SYNDROME. Mizu Ono,[1] Takenori Inomata,[1] Yoshimune Hiratsuka,[1] Tina Shiang,[2] Akira Murakami.[1] Juntendo University Faculty of Medicine,[1] Tokyo, Japan, Boston University School of Medicine,[2] Boston, MA USA.

30 RECOMMENDATIONS OF THE P.I.C.A.S.S.O. (ITALIAN PARTNERS FOR THE CORRECTION OF OCULAR SURFACE ALTERATIONS) BOARD FOR THE DIAGNOSIS AND THERAPEUTIC MANAGEMENT OF PATIENTS WITH TEAR DYSFUNCTIONS. Pasquale Aragona[1], Emilia Cantera[2], Rita Mencucci[3], Maurizio Rolando[4], Pierangela Rubino[5],[1] Professor of Ophthalmology, Biomedical Sciences Department - University of Messina, Italy, [2]Israelitico Hospital, Roma, Italy, [3]Clinica Oculistica di Firenze, Italy, [4]IsPre Oftalmica, Ocular Surface Center, Genoa, Italy, [5]Dirigente Medico, AOU di Parma, Italy

31 BASELINE CHARACTERISTICS OF PARTICIPANTS IN THE DRY EYE ASSESSMENT AND MANAGEMENT (DREAM) STUDY. Penny Asbell,[1] Maureen Maguire,[2] Maxwell Pistilli,[2] Ellen Peskin[2], Kathy McWilliams[2], Eric Kulinski[1] for the DREAM Research Group. [1]Icahn School of Medicine at Mt. Sinai, New York, NY, [2]School of Medicine, University of Pennsylvania, Philadelphia PA.

32 Clinical and neurophysiological commonalities among chronic corneal pain patients enrolled in a clinical trial. Doruk D*[1], Chanes L*[1,2], Jacobs DS[3], Merabet L[4], Valero-Cabré A[2] & Fregni F[1] *Equally contributing. [1]Spaulding Neuromodulation Center,Spaulding Rehabilitation Hospital, Harvard Medical School, Charlestown,MA, USA [2]Université Pierre et Marie Curie,CNRS 7225-INSERM S975,Institut du Cerveau et la Moelle épinière, Paris, France [3]Boston Foundation for Sight, Needham, MA, USA [4]Laboratory for Visual Neuroplasticity, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, MA,USA

33 HARNESSING NON-TRADITIONAL, 10-YEAR, REAL WORLD DATA TO GENERATE PATIENT INSIGHTS INTO DRY EYE DISEASE. Debra A Schaumberg,[1] Stephen Doogan,[2] Timothy Kaan,[3] Matthew McLoughlin,[3] Cindhuja Pandian,[3] Steven Zhang.[1] Shire,[1] Real Life Sciences,[2] Kinapse,[3] USA

34 TOWARDS A NOVEL IN-VITRO ANTERIOR EYE MODEL FOR OCULAR SURFACE EVALUATION. Francesco Menduni, James S. Wolffsohn, Antonio Fratini, Leon N. Davies. Ophthalmic Research Group, Aston University, Birmingham, UK.

35 EPIDEMIOLOGY OF DRY EYE DISEASE SYMPTOMS IN BRAZIL. Julia Silvestre de Castro, Iara Borin Selegatto, Marilia Menezes Trindade Ferrer, Lucas Yunes Cominatto Barbosa, Monique Possari Minari, Rosane Silvestre de Castro, José Paulo Cabral de Vasconcelos, Carlos Eduardo Leite Arieta, Mônica Alves. University of Campinas – UNICAMP, Discipline of Ophthalmology, Faculty of Medical Sciences, Brazil.

36 PREVALENCE OF DRY EYE DISEASE IN THE ADULT INDIAN POPULATION. Noopur Gupta,1 Praveen Vashist, 1Vivek Gupta,1 Meenakshi Wadhwani,1 Radhika Tandon, 1 1Dr. Rajendra Prasad Centre for Ophthalmic Sciences, AIIMS, New Delhi, India.

37 A RELATIONSHIP BETWEEN NUTRITION, BODY COMPOSITION AND SIGNS BUT NOT SYMPTOMS OF DRY EYE. Isabelle Jalbert, Kam Chun (Terry) Ho, Pei Schier Tan, Fiona Stapleton, School of Optometry and Vision Science, UNSW Australia

38 SELF-REPORTED COMPLIANCE IN SYMPTOMATIC VERSUS ASYMPTOMATIC PATIENTS WITH EVAPORATIVE DRY EYE. Christen Kenrick,[1] Caroline Blackie,[2] Donald Korb.[1,2] Korb & Associates,[1] TearScience,[2] Boston, MA, USA

39 THE RELATIONSHIP BETWEEN CORNEAL NERVE MORPHOLOGY AND SUBJECTIVE SYMPTOM IN DRY EYE DISEASE. Hidenaga Kobashi, MD, PhD[1,2]; Kazutaka Kamiya, MD, PhD[1] [1]Department of Ophthalmology, University of Kitasato School of Medicine, Kanagawa, Japan. [2]Schepens Eye Research Institute, Massachusetts Eye and Ear Infirmary, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts.

40 21ST CENTURY DIGITAL DEVICE USE AND OSDI. Justin T. Kwan,[1] Jennifer Harthan,[2] Leslie O'Dell,[3] Scott G. Hauswirth,[4] Clare Halleran,[5] Katherine Mastrota,[6] Milton M. Hom.[7] Marshall B. Ketchum University,[1] Fullerton, CA; Illinois College of Optometry,[2] Chicago, IL; Private practice,[3] York, PA; Minnesota Eye Consultants,[4] Minneapolis, MN; Private practice,[5] Clarenville, NL, Canada; Omni Eye Services,[6] New York, NY; Private practice,[7] Azusa, CA.

41 THE ASSOCIATION BETWEEN SYMPTOMS OF DRY EYE SYNDROME AND METABOLIC OUTCOME IN A GENERAL POPULATION IN KOREA. Jong Woon Park .National Health Insuranse Service Ilsan Hoapital

42 TEST EFFICACY OF THE MODIFIED SCHEIN QUESTIONNAIRE. Jerry R. Paugh, O.D.,Ph.D.[1], Andrew Loc Nguyen, Ph.D[2] [1]Southern California College of Optometry, Fullerton, CA, [2]California State University at Fullerton

43 ASSESSMENT OF DRY EYE PATIENTS USING QUESTIONNAIRES – A REVIEW. Alberto Recchioni[1,2,3], Tugce Ipek[1,2,4], Andreas Hartwig[1,2], Clare O'Donnell[1,2] 1 Optegra Eye Sciences, Berlin, Germany 2 Aston University, Birmingham, UK 3 University of Valencia, Valencia, Spain 4 Universidad Complutense de Madrid, Madrid, Spain

44 A NOVEL IMAGING METHOD TO EVALUATE DRY EYE SYNDROME. Raanan Gefen[3], Fanny Segev[1], Noa Gefen[1], Leejee H. Suh[2], Danielle Trief[2], Yoel Cohen[3], Yoel Arieli[3], Avner Belkin[1], Alon Harris[3,4], Meir Medical Center, Israel[1], Columbia University Medical Center[2], AdOM advance optical technologies Ltd. [3], Eugene and Marilyn Glick Eye Institute and Indiana University School of Medicine[4]

45 BILATERALITY IN DRY EYE DISEASE: IMPLICATIONS FOR CLINICAL TRIALS. Michael A. Lemp.[1,2,3] , Benjamin D. Sullivan[3] , Georgetown University[1], George Washington University[2], TearLab Corp.[3]

46 ANGIOGENIN AS BIOMARKER OF DRY EYE. JeaChan Kim, Jung Huh. Department of Ophthalmology, Chung-Ang University Hospital.

47 CASE-CONTROL STUDY OF CORNEAL FINDINGS IN DIABETIC AND NONDIABETIC PATIENTS. Machiko Shimmura-Tomita, Hiroko Takano, Nozomi Kinoshita, Fumihiko Toyoda, Yoshiaki Tanaka, Rina Takagi, Mina Kobayashi, Akihiro Kakehashi. Department of Ophthalmology, Saitama Medical Center, Jichi Medical University, Saitama, Japan

48 RELATIONSHIP BETWEEN FLUORESCEIN BREAKUP PATTERNS AND CLINICAL MANIFESTATIONS IN DRY EYE. Norihiko Yokoi[1], Georgi As. Georgiev[2], Hiroaki Kato[1], Aoi Komuro[1], Yukiko Sonomura[1], Chie Sotozono[1], Kazuo Tsubota[3], and Shigeru Kinoshita[4]. Department of Ophthalmology[1] and Department of Frontier Medical Science and Technology for Ophthalmology[4], Kyoto Prefectural University of Medicine, Kyoto, Japan, Department of Optics and Spectroscopy, Faculty of Physics, St. Kliment Ohridski University of Sofia, Sofia, Bulgaria[2], Department of Ophthalmology, Keio University School of Medicine, Tokyo, Japan[3]

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74 PERMEATION AND PERVAPORATION OF WATER THROUGH CONTACT LENS MATERIALS. Zohra Fadli, Ph.D., Charles Scales, Ph.D., Bernardo Santa Maria, M.S., and Donald Riederer, Ph.D.

75 EFFECT OF 3% DIQUAFOSOL SODIUM OPHTHALMIC SOLUTION ON SOFT CONTACT LENS WEARERS. Yukiko Sonomura,[1,2] Norihiko Yokoi,[2] Rieko Sakai,[2] Aoi Komuro,[2] Hiroaki Kato,[2] Chie Sotozono,[2] and Shigeru Kinoshita[3] [1]Department of Ophthalmology, Kyoto Yamashiro General Medical Center, Kyoto, Japan, and [2]Department of Ophthalmology and [3]Department of Frontier Medical Science and Technology for Ophthalmology, Kyoto Prefectural University of Medicine, Kyoto, Japan

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Abstracts

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CONCENTRATION OF MUC16 AND MUC5AC USING THREE TEAR COLLECTION METHODS.

Anna F. Ablamowicz[1] and Jason J. Nichols.[1] University of Alabama at Birmingham, School of Optometry[1]

Purpose: To determine the optimal tear collection method for analysis of ocular surface mucins MUC5AC and MUC16.

Methods: Fifteen subjects without ocular surface disease were recruited. Subjects presented for tear collection on three separate days for three different tear collection methods with order of method randomized. All samples from the right eyes were processed to investigate MUc5AC whereas left eye samples were processed for MUC16. Ten micrograms of protein were loaded per lane into a 1% (w/v) agarose gel and run in electrophoresis buffer for two hours. After overnight capillary transfer, membranes were incubated with either MUC5AC antibody CLH2 or MUC16 antibody OC125 for western blot analysis. Blots were developed with ECL and chemiluminescent signals captured with the Odyssey Fc (LI-COR). The relative amounts of MUC5AC and MUC16 were quantified with densitometry using software and compared for statistically significant differences between tear collection methods using the Kruskal-Wallis test in SPSS.

Results: Samples containing less than ten micrograms of protein were not used for analysis which left thirty-seven samples out of forty-five. All lanes displayed identifiable bands greater or around 460 kDa. Calculated MUC16 average signal intensities from capillary, schirmer, and flush samples were 5.16 (s=1.1), 2.55 (s=2.0), and 2.21 (s=0.51), respectively ($H=18.1$, $p<0.001$). Post-hoc pairwise comparison showed significant differences between capillary and both schirmer and flush ($p < 0.001$). Calculated MUC5AC average signal intensities from capillary, schirmer, and flush samples were 2.10 (s=0.95), 2.74 (s=0.82), and 1.56 (s=0.24), respectively ($H=9.5$, $p=0.009$). Post-hoc pairwise comparisons showed a significant difference between schirmer and flush samples ($p=0.011$).

Conclusions: MUC5AC and MUC16 are present in human tears and can be captured using various tear collection methods. While capillary tear collection yielded the highest relative concentration of MUC16, schirmer tear collection yielded the highest MUC5AC concentration. Therefore, the tear collection method chosen depends on the mucin of interest.

COLLAGEN FIBER ORIENTATION AND THICKNESS IN THE HUMAN AMNIOTIC STROMA BEFORE AND AFTER CELL CULTURE.

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Purpose: Orientation and thickness of collagen fibers have been associated to the physical cues that modulate different cell lineages. Evidence suggests that they could be altered by cell culture procedure–induced stimuli. We have evaluated orientation and thickness of collagen fibers in the stroma from the denuded human amniotic membrane (dHAM), before and after culture of limbal progenitor epithelial cells (LEPCs).

Methods: Uncultured dHAM and samples of dHAM containing rabbit LEPCs cultured for two, seven, and 15 days (C-2, C-7 and C-15 groups) were processed to paraffin inclusion and sectioned at 7 μm. Sections were stained with Ponceau SS (pH 2.5), and evaluated using polarized linearly light (Olympus BX-53Pol microscope) and video image analysis (Image J software). Values of gray average (GA, pixels) related to collagen birefringence brightness intensities were established for calculating parallel orientation ratios [POR = (GAmax / GAmin)]. Thickness of fibers was inferred from interference colors caused by birefringence anomalous dispersion. Yellow and red colors were attributed to thicker fibers, while green was attributed to thin fibers (20–40 nm).The percentage of areas covered by fibers in different colors was calculated. Differences were significant when $p \leq 0.05$

Results: The POR of the collagen fibers were 1.02 in uncultured dHAM, 1.17 in C-2, 1.26 in C-7 and 1.17 in C-15 ($p<0.05$ uncultured vs. cultures samples). C-7 and C-15 groups showed higher percentage of thick collagen fibers (38.28% and 48.32%) compared to the NC-HAM group (3%) ($p<0.05$).

Conclusions: Our results demonstrated that the culture procedure–induced stimuli altered the orientation (parallelism) and the thickness of collagen fibers in the dHAM stroma. [This research was supported by grants from FAPESP (Proc. 2012/17308-5, 2013/01494-7, and 2013/25533-1) and CNPq (467289/2014-0)].

CONCANAVALIN A-POSITIVE GLYCOPROTEINS IN THE NUCLEI OF CORNEAL LIMBAL EPITHELIAL CELLS.

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Purpose: The nuclear matrix of adult cells possesses glycoproteins, which stabilize DNA and contribute to the formation of pericentromeric heterochromatin. Some of these glycoproteins form granules detectable by topochemical reactions with Concanavalin A (ConA), a lectin from *Canavalia ensiformis*. Alterations in the nuclear localization of ConA-positive glycoproteins have been observed during development of some cell lineages. This study evaluated the distribution of ConA-positive glycoproteins in the nuclei of progenitor and differentiated limbal epithelial cells (LECs).

Methods: Explants of rabbit corneoscleral limbus were processed to paraffin inclusion and sectioned at 7 μm. A part of the material was submitted to immunohistochemistry [using anti-k3/k12 (clone AE5) and anti-delta p63 antibodies (clone 4A4) Abcam]; and the other was incubated in PBS buffer containing 0.5 mg/dL ConA (Sigma-Aldrich), pH 6.0, for 30 min. Horseradish peroxidase and diaminobenzidine were used to detect the reaction. All material was evaluated under an Olympus BX-53 microscope coupled with image analysis software (Image J). The fractions of nuclear areas containing ConA-positive glycoproteins were evaluated and surface plot were constructed for progenitor and differentiated LECs.

Results: The progenitor LECs (p63 positive) presented with biggest glycoprotein granules distributed in the nuclear periphery near the nuclear envelope. In contrast, the nuclei from differentiated LECs (k3/k12 positive) showed glycoprotein granules of homogeneous size that were dispersed into the entire nuclear matrix.

Conclusions: Progenitor and differentiated LECS did differ to nuclear distribution of ConA-positive glycoprotein granules. Our results suggest that topochemical reactions with ConA may be a useful technique to discriminate LECs in varying development stages. [CNPQ467289/2014-0]

EXPRESSION OF P63 AND CHROMATIN FUNCTIONAL STATES FROM LIMBAL EPITHELIAL CELLS GROWN ON SYNTHETIC VERSUS DENUDED HUMAN AMNIOTIC MEMBRANE.

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Purpose: Denuded human amniotic membrane (dHAM) has been used for expanding limbal epithelial cells (LECs). There are, however, certain concerns with dHAM, including its structural heterogeneity. To circumvent these concerns, synthetic membranes have been proposed as replacements for dHAM. Evidence suggests that membranes from chitosan (Chi), alginate (Alg) and fucoidan (Fuc) are candidates for limbal therapy. This study evaluated expression of p63 and chromatin functional states in culture of LECs grown on membrane from Alg-Chi-Fuc and dHAM.
Methods: Chi-Alg-Fuc membranes were fabricated by ionic and thermal reticulation. Fragments of amniotic membrane were denuded using EDTA. LECs were obtained from rabbit limbus and then cultured on Algi-Chi-Fuc membrane or dHAM for 14 days. Immunohistochemistry against p63 (clone 4A4) was performed for detecting progenitor cells. Chromatin functional states were studied in samples stained with Feulgen reaction, and by using an optical microscope coupled with software (Image J). Optical density (OD) related to chromatin condensation and integrated optical density (IOD) related to DNA amount were quantified.
Results: No significant differences in expression of p63 were observed between samples studies (5.8% dHAM vs. 3.5% Algi-Chi-Fuc membrane; $p>0.05$). The mean OD values were 0.57 ± 0.01 for LECs cultured on Algi-Chi-Fuc membrane and 0.54 ± 0.01 for cells grown on dHAM ($p<0.01$). Mean IOD values were higher for cells grown on Algi-Chi-Fuc membrane (25.18 ± 12.08 vs. 23.06 ± 11.12 on dHAM, $p<0.01$).
Conclusions: Membrane from Alg-Chi-Fuc is a viable substrate for expanding LECs. The cells grown on this substrate presented more condensed chromatin and DNA than cells expanded on dHAM. [This research was supported by grants from FAPESP (Proc. 2013/01494-7 and 2013/25533-1) and CNPq (467289/2014-0)].

THE EFFECT OF CONTACT LENS WEAR ON THE LID MARGIN EPITHELIUM.

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Purpose: To establish if the duration of contact lens (CL) wear affects the cellular morphology of the lid margin epithelium. Methods: This was a cross sectional study of 100 individuals with different exposures to CL wear. These were divided equally into 5 groups: short, moderate and long experience of CL wear, previous CL wearers (PWs) who had ceased wear for at least 6 months prior to the study, and healthy non-wearers (NWs) as controls. Impression cytology samples were collected from the central upper lid margin (lid wiper area) using Millipore Millicell filter paper. After fixing, samples were stained with periodic acid Schiff (PAS) and haematoxylin for cell morphology analysis. The samples were then photographed with an automated upright microscope system at 40×, and subsequently graded in a masked fashion according to the Nelson 0 – 3 scale that takes into account the shape of epithelial cell and nuclei, nucleocytoplasmic ratio, and goblet cells density. Lid wiper (LW) staining in this study was assessed with the aid of lissamine green and graded using the Korb (0-3) scale. One-way Kruskal–Wallis analysis of variance followed by the Dunn's multiple comparison tests was used for statistical comparison.
Results: The Nelson grade for lid margin epithelium morphology was significantly different between groups (Kruskal–Wallis, $p = 0.003$). Abnormal epithelial morphology as defined by grades 2 and above, was evident in 66.7% of CL wearers with short experience and 76.5% of CL wearers with moderate experience (Nelson's grade of 2 or 3). This was significantly higher than NWs of whom only 21.5% showed > grade 1 (post hoc Dunn $p= 0.02$ and 0.005 respectively). There was no significant difference between NWs and either CL wearers with long experience (41.2% > grade 1, $p = 0.2$), or PWs (29.5% > grade 1, $p =0.6$). LW staining did not significantly differ between groups (Kruskal–Wallis $p = 0.5$) or correlate with the Nelson grade (Spearman rank correlation $r = 0.02$, $p = 0.08$).
Conclusion: Metaplasia of the marginal epithelium was significantly greater in the early to moderate stages of CL wear as evidenced by altered cytoplasmic and nuclear characteristics as well as reduction in goblet cell density. Increasing squamous metaplasia supports the view that mechanical irritation is responsible for lid margin (LW) changes in CL wear. The observation of the marginal epithelium suggests mild adaptation after many years of CL wear, while ceasing CL wear seems to lead to a recovery. LW staining did not reflect the underlying morphological changes.

CONJUNCTIVAL EPITHELIAL CELLS CHANGES AFTER THE TREATMENT WITH 0.2% XANTHAN GUM EYE DROPS IN MODERATE DRY EYE.

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Purpose: To study the effect of xanthan gum (XG) eye drops on the conjunctival cytology of patients with moderate dry eye.
Methods: This prospective, double masked, controlled trial (ClinTrials no: NCT01959854) included 30 patients (21 F/9 M), age 60-79 yrs, divided in two groups of 15 subjects each and treated with 0.2% XG eye drops (group 1) or 0.5% carboxymethilcellulose (CMC) (group 2) qid. Inclusion criteria were: age> 60 and OSDI score >12 and <33. Exclusion criteria were previous disease or treatment other than dry eye and use of tear substitutes, use of contact lenses. After a run-in period of 7 days with saline qid, patients underwent OSDI questionnaire and impression cytology (IC) biopsy at baseline (T0) and after one month (T1). For the IC seven parameters were considered: specimen cellularity, cell-to-cell contacts, nucleous/cytoplasm ratio, chromatin aspect, goblet cells distribution, keratinization, inflammatory cells presence. Parameters were scored from 0 (absence of alteration) to 3 (evident alterations); a total score was obtained adding up the results of each parameter. For statistical analysis the Wilcoxon rank sum test and the Mann-Whitney U-test were used.
Results: In group 1 a significant amelioration was found for the following parameters: cellularity (T0=0.65 ± 0.48; T1=0.35 ± 0.47; m±SD, $p=0.05$), chromatin (T0=1.25 ± 0.48; T1=0.85 ± 0.49; $p=0.02$), keratinization (T0=1 ± 0.72; T1=$0.\ 5\pm0.5$; $p=0.006$) and total score (T0=5.8 ± 1.28; T1=3.65 ± 1.69; $p<0.0001$). In group 2, only the total score showed a statistically significant difference (T0=5.04 ± 1.42; T1=4.34 ± 1.46; $p=0.01$). The comparison between groups showed a significant difference in favor of group 1 for keratinization at T1 ($p=0.02$).
Conclusions: The treatment with XG, a molecule with muco-adhesive and anti-oxidant properties, was able to ameliorate the conjunctival epithelium of moderate dry eye patients better than CMC. [Research supported by a grant from SIFI]

RECOMMENDATIONS OF THE P.I.C.A.S.S.O. (ITALIAN PARTNERS FOR THE CORRECTION OF OCULAR SURFACE ALTERATIONS) BOARD FOR THE DIAGNOSIS AND THERAPEUTIC MANAGEMENT OF PATIENTS WITH TEAR DYSFUNCTIONS.

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Purpose: At present, there is no published literature that supports the systematic, practice oriented approach for the management of patient

with tear film dysfunction. In this paper, the PICASSO group aims to provide a modern approach to tear dysfunction, supported by a flowchart, which can be used for the management of this disorder.
Methods: Literature revision and clinical experience of a group of 5 experts in ocular surface diseases has been collected to provide: a) review of risk factors for dry eye, b) current anamnestic procedures (questionnaires, time relation of symptoms, seasonality) c) low tech diagnostic manoeuvres and specific tests for the detection of tear film disturbances leading to recognition of the level of disease and of the ocular system elements involved.
These data will represent the basis for the therapeutic approach providing elements of an appropriate effective therapeutic approach.
Results: a multi item flow chart for tear film dysfunction, with point by point explanatory guide, leading from the diagnosis to a rational treatment, has been built.
Conclusions: Prompt and correct diagnosis a treatment will provide a better quality of life to dry eye patients. The PICASSO work group delivers a guide, whose core is a flowchart that will help the general ophthalmologist to achieve a correct diagnosis and management of patients with tear film dysfunctions, contributing to improve patient's quality of life.
This paper was supported by unrestricted grant from Théa Farma.

THE OCULAR SURFACE GLYCOCALYX BARRIER.

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Carbohydrates have been traditionally considered sources of energy for the living organism. However, it is now becoming evident that carbohydrates also play important roles in determining cell function. A large number of carbohydrates are located on the cell surface, where they modulate a wide variety of cell-cell and cell-pathogen interactions. This communication results in a varied spectrum of cellular events, such as secretion of bioactive substances, recruitment of immune cells to areas of cellular damage, or cancer cell metastasis. We are interested in elucidating the structure and function of transmembrane mucins, a group of highly glycosylated, high-molecular-weight glycoproteins that constitute a major component of the protective biofilm on epithelial cell surfaces. Due to their extremely large size, they extend above other components of the plasma membrane, therefore constituting the outermost interface between the epithelial cell and the external environment. Our current studies involve investigating the interactions between transmembrane mucins and multivalent carbohydrate-binding proteins in the ocular surface epithelial glycocalyx. This field of investigation is yielding clues to the understanding of the pathogenesis of ocular surface diseases in which the glycocalyx barrier is compromised.
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CONTACT LENSES CAUSE CLINICALLY RELEVANT MEIBOMIAN GLAND DYSFUNCTION.

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Meibomian glands secrete lipids (meibum) that form the outer lipid layer of the tear film and thereby prevent excessive evaporation of tear fluid. Meibomian gland dysfunction (MGD) is a major cause of evaporative dry eye, which is more prevalent than aqueous-deficient dry eye. Noninvasive meibography with infrared light and an infrared CCD camera can detect morphological changes of meibomian glands in both upper and lower eyelids, whereas tear interferometry allows qualitative and quantitative evaluation of the lipid layer of the tear film. To examine the possible effects of contact lens wear on meibomian gland morphology and the lipid layer of the tear film, we have performed noninvasive meibography and tear interferometry in non–contact lens wearers as well as in wearers of soft contact lenses or rigid gas-permeable lenses.
The morphology of meibomian glands was significantly altered in wearers of each type of lens compared with non–lens wearers. Pre-corneal LLT was significantly reduced in soft contact lenses wearers. Contact lens wear is thus associated with adverse effects on meibomian gland morphology and function that can give rise to contact lens discomfort.
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BASELINE CHARACTERISTICS OF PARTICIPANTS IN THE DRY EYE ASSESSMENT AND MANAGEMENT (DREAM) STUDY.

Penny Asbell,[1] Maureen Maguire,[2] Maxwell Pistilli,[2] Ellen Peskin[2], Kathy McWilliams[2], Eric Kulinski[1] for the DREAM Research Group. [1]Icahn School of Medicine at Mt. Sinai, New York, NY, [2]School of Medicine, University of Pennsylvania, Philadelphia PA.
Purpose: To describe patients enrolled in the DREAM Study, a multicenter clinical trial to evaluate omega-3 fatty acid supplements for moderate to severe dry eye disease (DED).
Methods: Candidates are evaluated at 2 Visit, 2 weeks apart. Adult patients need an Ocular Surface Disease Index (OSDI) score of 25-80 at Visit 1 and 21-80 at Visit 2. One or both eyes must have 2 reproducible signs of DED: 1) Conjunctival lissamine green staining score ≥1 out of a maximum score of 6; 2) corneal fluorescein staining score ≥4 out of 15); Tear break-up time ≤7 seconds, and Schirmer's test (with anesthesia) ≥1 and ≤7mm/5 minutes. Patients using other DED treatments are eligible if they commit to continuing the treatments during DREAM.
Results: Among the first 476 patients enrolled, the mean (standard deviation - SD) age was 58.1 (13.3) years, 384 (81%) were female, 67 (14%) Hispanic, 347 (73%) White, 56 (12%) Black, 19 (4%), Asian, and 432 (91%) had both eyes qualify. OSDI total scores were distributed over the entire allowable range with a mean (SD) of 46.7 (15.7) at Screening and 41.7 (15.6) at Baseline. The mean score for signs was similar at Baseline and Screening visits. The mean (SD) score at the Baseline visit was 3.0 (1.4) for conjunctival staining, 3.8 (2.7) for corneal staining, 3.1 (1.5) for tear break-up time, and 9.6 (6.6) for Schirmer's test. Aside from artificial tears, 173 (36%) used cyclosporine drops, 100 (21%) used warm lid soaks, 54 (11%) used lubricating ointment, 53 (11%) used lid scrubs, and 22 (5%) had punctal plugs.
Conclusion: DREAM enrolled patients with a mean OSDI score in the severe range even though many were using treatments for DED.
DREAM is supported by NIH grants U10 EY022879 and U10 EY022881.

UNIQUE CHALLENGES AND UNMET NEED FOR THE TREATMENT OF OCULAR SURFACE DISEASE.

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About 25% of the U.S. population reports some abnormality of exposed ocular surface. Proper management of OSD can often be challenging. Some of the challenges lie in accurate testing (using both objective and subjective methods) and differential diagnosis of OSD, detection of OSD in preliminary stages to facilitate prevention and development of therapies. There is a need for alleviating symptoms, understanding and targeting the underlying cause of the disease, and consideration of various socio-economic factors influencing OSD.
We conducted a 5 year Pubmed database search using the search terms 'ocular surface', 'dry eye', 'Sjogren syndrome', 'blepharitis', 'meibomitis', 'keratitis', 'ocular allergy', and 'ocular surface disease'. We also conducted a similar search of www.clinicaltrials.gov spanning a 5 year period. These publication and studies were subdivided into four

main categories: research, diagnosis, therapy and prevention. Reported research challenges include lack of suitable animal models due to inherent differences between human and animal tear compositions, disparity in signs and symptoms in most drug trials, and challenges in determination of novel lipid structures for lipid-based drug delivery due to technical and logistical hurdles. Reported challenges in the diagnosis of OSD include difficulty in grading the severity of OSD and determining clinical improvements based on available testing methods. Reported challenges in therapy include limited amount of medication to overcome OSD in general, and also the ones that tackle the root cause. Reported challenges in prevention include the availability of screening tests with high sensitivity and specificity that are also cost-effective and simple.
By addressing these unique challenges in the treatment of OSD, the ophthalmic community will be able to make important discoveries that could be translated to novel treatments aimed at addressing these unmet needs.

THE EFFECT OF A NEW OCULAR SURFACE MODULATOR IN CONTROLLING INFLAMMATION IN AN IN VITRO MODEL OF DRY EYE.

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Purpose: Inflammation plays an important role in dry eye syndrome (DES) pathogenesis. The aim of this study was to assess the effect of an ocular surface modulator on inflammatory markers compared to substitute tears in an in vitro model of DES.

Methods: A reconstructed human corneal epithelium (HCE) model challenged by the introduction of sorbitol in the culture medium for 16 hours was used to induce corneal damage and inflammation similar to DES. In the study group HCE cells were treated with topical application of 30 ml of the ocular surface modulator T-Lysyal, in the control group with a substitute tear containing sodium carboxymethylcellulose 0.5%, glycerine 1%, and castor oil 0.25%. A negative control treated with saline solution was used for comparisons. After 16, 22, and 46 hours the following parameters were quantified: mRNA expression of TGFb1, Metalloprotease 1(MMP-1), ICAM-1, Caspase 14 (CASP14), and CD44.

Results: The study group showed significant reduction of TGFb1 and MMP-1 compared to controls at all time points. ICAM-1 expression was increased after 22 hours in the study group only, while CD44 and CASP 14 were increased in the control group after 16 hours.

Conclusions: This study has shown for the first time that it is possible to control inflammation by using a modulator of the ocular surface. Further in vivo studies are certainly necessary to confirm these Results.
[This research was supported by grants from Sildeha Switzerland and Farmigea Italy]

EFFECT OF MATRIX REGENERATION THERAPY ON CORNEAL EPITHELIAL HEALING FOLLOWING EPI-OFF CROSS-LINKING IN PATIENTS WITH KERATOCONUS.

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Purpose: In the present study, we demonstrated the effect of a new type of matrix therapy agent (ReGeneraTing Agent [RGTA]; Cacicol®, Thea Pharma, France) on corneal epithelial healing following cross-linking (CXL) in patients with keratoconus.

Methods: 40 Patients with progressive keratoconus undergoing epi-off CXL were included in a randomized, double-masked, parallel group study. Patients were randomized immediately after surgery to receive either RGTA or hyaluronic acid 0.1% eye drops every other day until corneal epithelial wound closure was achieved. Wound healing was evaluated from slit lamp photographs using fluorescein staining and with ultrahigh-resolution optical coherence tomography (OCT)

Results: Epithelial wound healing was significantly faster in the RGTA group as compared to the hyaluronic acid group (4.4±1.3 days versus 6.1±2.3 days; p=0.008). The defect size was smaller in the RGTA group than in the hyaluronic acid group, an effect that was already significant at the second post-operative day (OCT: p=0.045; photo: p=0.027). The correlation between the defect size as measured with OCT and the defect size as measured with slit lamp photography using fluorescein staining was highly significant (r=0.89, p<0.001).

Conclusions: RGTA eye drops seem to promote corneal epithelial wound healing after CXL in patients with keratoconus. OCT can be used as a reliable, non-invasive method in estimation of corneal wound healing providing a three-dimensional evaluation of the corneal defect.

CLINICAL OUTCOMES FOLLOWING USE OF THE DUAL POLYMER HYDROXYPROPYL GUAR/HYALURONIC ACID-BASED LUBRICANT EYE DROPS IN PATIENTS WITH DRY EYE.

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Purpose: To evaluate efficacy and safety of the new dual polymer hydroxypropyl guar/hyaluronic acid-based eye drops (SYH; Systane™ HYDRATION) in patients with dry eye.

Methods: In a 6-week, prospective, multicenter, double-masked, parallel-group, non-inferiority (NI) study, patients were randomized 1:1 to receive SYH (n=50) or Hyabak® 0.15% (HBK; n=49) 4 times daily (QID) for 42 days. The primary endpoint was change from baseline (BL) in Total Ocular Surface Staining (TOSS) score at Day 42. Secondary endpoints included change from baseline in impact of dry eye on everyday life (IDEEL) treatment satisfaction scores & tear film breakup time (TFBUT) at Day 42.

Results: At Day 42, least squares mean (LSM) change (standard error [SE]) from BL in TOSS was −1.16 (0.24) & −0.92 (0.23) in the SYH and HBK groups, respectively; treatment difference was −0.24 (95% CI: −0.90, 0.42); upper limit of 95% CI was <2 (NI margin). At Day 42, LSM change from BL in other assessments in the SYH and HBK groups were as follows: IDEEL scores (effectiveness and inconvenience) were 9.62 vs. 12.80 & -10.32 vs. 2.24, treatment differences were −3.18 (p=0.4817) & −12.56 (p=0.0001), respectively; TFBUT was 0.46 s & 0.61 s, respectively; treatment difference was −0.30 s (p=0.58). Incidences of ocular adverse events were similar between the two groups; 2 serious adverse events were reported (1 in each group), both treatment unrelated.

Conclusion: The new SYH eye drops showed improvements in ocular staining that was non-inferior to HBK following 42 days of QID use, with no new safety findings in patients with dry eye. (Study was supported by Alcon Research, Ltd.,Fort Worth,TX)

ORIGIN OF CORNEAL NEUROPATHIC PAIN.

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Pain arising from actual or threatened damage to tissues is called nociceptive pain. In contrast, neuropathic pain appears as a result of lesion or malfunction of the somatosensory system. Ocular surface pain originates at peripheral sensory nerve terminals (nociceptors) of trigeminal ganglion (TG) neurons innervating the eye. These are morphologically and functionally heterogeneous, being preferentially activated by mechanical forces (mechano-nociceptors); low temperatures and hyperosmolarity (cold thermoreceptors); and irritant chemicals, endogenous inflammatory mediators and noxious mechanical stimuli and heat (polymodal nociceptors). Their nerve impulse discharges are conveyed to the brain, evoking conscious sensations referred to the eye. Environmental aggressions, disturbed tearing, wounds, surgery or infections acting on the eye surface cause a variable level of local inflammation and of nerve injury. Inflammation enhances the sensitivity to natural stimuli of polymodal and mechano-nociceptors (sensitization), evoking spontaneous nociceptive pain and hyperalgesia, while the sensitivity of cold thermoreceptors is depressed. When inflammation is accompanied by a parallel damage of peripheral receptor terminals, these respond less or become insensitive to natural stimuli. Still, the injured nerve stumps may generate an aberrant activity that evokes spontaneous, neuropathic pain. Healing of the wounded tissues usually reverses inflammation and regenerates broken nerve terminals reversing pain. However, when chronic inflammation and/or extended peripheral nerve damage occur, TG neurons innervating the eye surface experience permanent changes in the expression of ion channels and receptor proteins. These lead to profound and sustained membrane excitability changes both at peripheral nerve branches and cell bodies which generate aberrant, ectopic nerve impulse activity which is the cause of peripheral neuropathic pain sensations and dysesthesias.

HOW COMMON ARE EYELID DISORDERS ACROSS EUROPE?

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Purpose: To determine the incidence and characteristics of eyelid inflammatory disorders encountered during general ophthalmology consultations in Europe.

Methods: A two-page survey was conducted on ten consecutive patients attending for routine ophthalmology appointments across centers in 9 countries (2012-14): Poland (2584), Spain (1925) Portugal (415), Turkey (398), Germany (375), The Netherlands (230), France (185), Belgium (78) and Denmark (60). Ophthalmologists recorded reason for visit, ocular history, symptoms, examination of eyelids and ocular surface, diagnosis of MGD or dry eye, impact on daily life, and management of eyelid disorders.

Results: 6,250 patients were recruited; 61.6% were female and mean age was 57.2±17.6yrs.

Over 3/4 of the sample were diagnosed with eyelid disorders (77.7%). Rosacea, atopic dermatitis, seborrheic dermatitis, dry eye, AMD, diabetes, cataract, allergy and MGD were significantly linked to the presence of eyelid disorder ($p<0.05$). Meibomian Gland Dysfunction (MGD) was diagnosed in 53.2% and dry eye in 60.9% of patients. Among MGD diagnoses, 36.8% were hyposecretory, 37.3% were obstructive and 38.0% had a hypersecretory MGD.

Management included warming (49.5%), cleansing (67.7%), massage (53.6%), and also eye drops for dry eye (81.7%). The impact of eyelid disorder on daily life concerned vision for 56.7%, daily activities/work (53%), leisure (43.1%), and also on emotions (20.6%) and sleep (17.6%).

Conclusion: The incidence of eyelid disorders is underestimated in routine clinical practice. The impact of eyelid disorder on daily life is notable. This survey highlights the importance of examining eyelids more closely during routine eye examinations. This research was supported by Laboratories' Thea

HEAD WORN AUGMENTED REALITY DISPLAYS IN WORKFORCE AND THEIR INFLUENCE ON OCULAR COMFORT AND OCULAR SURFACE PARAMETERS.

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Purpose Visual picking more and more replace voice guided solutions in workforce. The impact of these head worn augmented reality displays on ocular comfort, the ocular surface and tear function is still uncertain. In this study we compared the effect of these two commissioning systems on subjective and objective ocular parameters.

Methods A total of 25 young asymptomatic volunteers performed commissioning over 10 hours on two consecutive days. One day the operator was guided in the picking process by the augmented reality displays, on the other day, he was guided by the voice system. Subjective symptoms, ocular surface and tear function parameters were compared between the two groups.

Results In the visual condition the visual analogue scale (VAS) values, according to subjective dry eye symptoms, were significantly higher at the end of the commissioning than the baseline measurements. In the voice condition, the VAS values remained stable during the commissioning.

The tear break-up time (BUT) values declined significantly in the visual in the right eyes, that were exposed to the displays, the left eyes in the visual condition showed only a minor decline, whereas the BUT values in the voice condition remained unchanged.

No significant differences in the tear meniscus height values before and after the commissioning were observed in either condition.

Conclusions: In our study, the use of visually guided picking solutions was correlated with post-task subjective symptoms and tear film instability. Further studies in this field which focus on dry eye syndrome and asthenopia are needed.

[No commercial relationships]

UNIQUE CHALLENGES AND UNMET NEEDS FOR THE TREATMENT OF OCULAR SURFACE DISEASES IN EUROPE.

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Among the 240 new products approved by EMA in 2010-2015, the number of true innovative medicine (first –in-class) was very limited. In Ophthalmology, drugs innovation was almost absent and without the Lucentis/Avastin querelle, ophthalmology could have been forgotten by regulators. This lack of novelties is particularly evident for the treatment of ocular surface diseases. The reasons why innovation has been so poor could be ascribed to the reduced investments because of the long and difficult regulatory pathway to obtain marketing authorization and market access and for the poor quality of clinical trials despite the high potential of advanced therapies and the many unmet needs of eye diseases. In contrast the number of OTC products and medical devices increased a lot in the last few years. Two major improvement have been made in the this field, even if, at least one of them, was a novelty just for Europe. In fact, the approval of Ikervis (Cyclosporin eye drops) in May 2015, let this compound to be available also in Europe following many attempts for the other cyclosporine Restasis already available for many years in USA and other countries. This new compound targets dry

eye disease (exact indication wording: Treatment of severe keratitis in adult patients with dry eye disease, which has not improved despite treatment with tear substitutes. Probably, the real novelty is the approval by EMA in Feb 2015 of Holoclar (ex vivo expanded autologous human corneal epithelial cells containing stem cells, implant) –for treatment of limbal stem cell deficiency [exact indication wording: treatment of adult patients with moderate to severe limbal stem cell deficiency (defined by the presence of superficial corneal neovascularisation in at least two corneal quadrants, with central corneal involvement, and severely impaired visual acuity), unilateral or bilateral, due to physical or chemical ocular burns.

In this speech, perspectives of new agents targeting inflammation, tear film stability and mechanisms of wound healing on the ocular surface will be discussed based on the unmet needs for clinical practice.

LIPID ORDER, SATURATION AND SURFACE PROPERTIES OF HUMAN MEIBUM.

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Purpose: Tear film stability decreases with age however the cause(s) of the instability are speculative. The meibum lipid phase transition temperature and lipid hydrocarbon chain order at physiological temperature (33˚ C) decrease with increasing age. It is reasonable that stronger lipid-lipid interactions could stabilize the tear film since these interactions must be broken for tear break up to occur. We tested the hypothesis that the more saturated meibum from infants may contribute to tear film stability.

Methods: NMR spectroscopy was used to measure human meibum and tear film lipid composition. Infrared spectroscopy was used to measure lipid structure. Langmuir trough technology was used to measure meibum rheology.

Results: Human meibum and tear lipids were saturated catalytically. Saturation of native human meibum did not change the minimum or maximum values of hydrocarbon chain order so at temperatures far above or below the phase transition of human meibum, saturation does not play a role in ordering or disordering the lipid hydrocarbon chains. Saturation did increase the phase transition temperature in human meibum by over 20˚C, a relatively high amount. Surface pressure-area studies showing the late take off and higher maximum surface pressure of saturated meibum compared to native meibum suggest that the saturated meibum film is quite molecularly ordered (stiff molecular arrangement) and elastic (molecules are able to rearrange during compression and expansion) compared with native meibum films which are more fluid agreeing with the infrared spectroscopic results of this study.

Conclusion: Higher surface pressure observed with films of saturated meibum compared to native meibum suggests greater film stability especially under the high shear stress of a blink. [This work was supported by Kentucky Lions Eye Foundation and an unrestricted grant from Research to Prevent Blindness Inc., and R01 EYO 26180, DB].

MEIBOGRAPHY: INTER-RATER RELIABILITY.

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Purpose: The tear film lipid layer holds an important role in maintaining the integrity and health of the anterior surface of the eye. The meibomian glands found in eyelids are responsible for producing most of the lipids of the tear film. Dysfunction of the meibomian glands leads to increased evaporation of tears, which may lead to dry eye. Meibography is a method used for assessing the drop out of meibomian glands. The aim of this study was to evaluate the reliability between two different examiners when rating meibography images.

Methods: The Sirius 3D scheimpflug camera (C.S.O., Florence, Italy) was used to photograph the everted upper and lower eyelids of the right and left eye of 52 subjects. The grade of meibomian gland loss was subjectively graded using the five-grade Meiboscale (Pult, 2012) and the percentage of gland loss was calculated using Phoenix Meibography software (version 3.0.1.021, bon Optic VertriebsGmbH, Lübeck, Germany). Data was analyzed using MedCalc for Windows (version 16.4.3, MedCalc Software, Ostend, Belgium).

Results: The inter-rater reliability for the Meiboscale grade of meibomian gland loss was calculated using weighted Cohen's kappa (linear weights). The result for all 208 images was K_w = 0.542 (95 % CI 0.454 to 0.630), which indicates a moderate agreement. The inter-rater reliability for the percentage of meibomian gland loss was calculated using intraclass correlation coefficient. The result for all 208 images was ICC = 0.794 (95 % CI 0.737 to 0.839), which indicates a substantial agreement.

Conclusions: Imaging is an invaluable tool when managing patients in clinical practice. When performing meibography to evaluate meibomian gland loss, using software to calculate the percentage of gland loss gives a better inter-rater agreement than subjective grading of the images.

[Dr. Källmark is the owner of a private dry eye clinic. The authors have no commercial interests in any concept or product discussed.]

STEADY-STATE CORNEAL OXYGEN CONSUMPTION PROFILES DURING CONTACT LENS WEAR.

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Purpose: Oxygen transmissibility, partial pressure profiles and flux values provide useful information about oxygenation of the cornea during contact lens wear but do not fully specify metabolic activity. The oxygen consumption profile through the cornea is the ideal representation of metabolic state but it cannot be directly measured. Here we develop profiles using a set of empirically derived parameter measurements and the application of well-known diffusion theory.

Method: Unidimensional steady state oxygen consumption profiles were generated using the metabolic diffusion model of Chhabra et al (OVS, 2009) for the central cornea with open-eye wear of contact lenses of varying Dk/t– presented here in units of $x10^{-9}$ (cm/sec)(mlO_2/ml.mmHg). The partial pressure of oxygen at the cornea-aqueous interface is assumed to be invariant at 24 mmHg. A Michaelis-Menten constant of 0.4mmHg was assumed.

Results: At very low Dk/t values, say 2, there is very little consumption evident at the anterior 200 μm of the stroma or posterior epithelium. At a Dk/t of 10, the posterior epithelium and anterior stroma are predicted to consume oxygen at positive but sub-normal levels, but consumption falls to near-zero at the central stroma. With Dk/t values of 20 and above, the entire cornea consumes oxygen at an equivalent rate to when unrestricted by contact lens wear. The predictions are strongly dependent upon the accuracy of the Harvitt-Bonanno model (IOVS 1998) of altered oxygen consumption during acidosis.

Conclusion: Corneal oxygen consumption profiles allow the metabolic state of the cornea during contact lens wear to be characterized. The predicted critical Dk/t value of about 20 to prevent reduced metabolic activity is consistent with clinical measures of corneal edema. Further understanding of changes to the partial pressure of oxygen at the posterior corneal surface with changes in lens Dk/t are required to increase model accuracy.

Commercial Relationships. 1. Employee of JJVC. 2. Consulting fee from JJVC.

THE UTILITY OF A NORMAL TEAR OSMOLARITY TEST IN SYMPTOMATIC PATIENTS.

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Purpose: To explore the diagnostic utility of a normal tear osmolarity test in patients with symptoms suggestive of dry eye disease (DED). Methods: A prospective observational study of 50 patients was conducted. Patients underwent tear osmolarity testing (TearLab™) if they endorsed one or more of the following symptoms of potential DED: visual acuity fluctuations, ocular surface irritation (including foreign body sensation, grittiness, pruritis, or dryness) and conjunctival injection. Patients were included for study if they had a normal tear osmolarity test (value <308 mOsm/L in each eye, and an inter-eye difference <8 mOsm/L). A cornea specialist then performed an anterior segment examination in patients selected for study. The main outcome measure was the presence of an alternate diagnosis to explain the patient's symptoms.

Results: Mean tear osmolarity was 293.33 mOsms/L (± 6.70), with a mean difference of 0.94 mOsms/L (± 3.18) between the eyes. An alternate diagnosis was established in 100% of patients with normal tear osmolarity testing. Eleven patients (22%) had more than 1 diagnosis present. The most frequent diagnoses included allergic conjunctivitis (24%) and anterior blepharitis (24%). Other common diagnoses encountered were epithelial basement membrane dystrophy (12%), keratoneuralgia (12%), contact lens intolerance (8%), conjunctivochalasis (8%), computer vision syndrome (6%) and trichiasis (6%). Another 4% of symptomatic patients with normal osmolarity had a history of established DED treated with long-term topical cyclosporine A. Of note, there was a statistically significant association between pruritis and diagnosis of allergic conjunctivitis ($p<0.001$).

Conclusions: Common symptoms of DED overlap significantly with a wide variety of other ocular surface diseases making symptomatology alone an insensitive diagnostic tool. If a normal tear osmolarity test rules out traditional DED then the clinician must use the exam and other diagnostic tools to find alternate diagnoses to explain the symptoms.

Pertinent Disclosures: C.Starr has a financial interest in TearLab Inc.

CYCLOSPORINE A LOADED LIPOSOMES FOR DRY EYE DISEASE TREATMENT.

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Purpose: Therapeutic approaches for dry eye disease (DED) include the use of artificial tears and anti-inflammatory agents. The purpose of this study was the design and characterization of a liposomal formulation similar in composition to natural tears combined with the anti-inflammatory agent cyclosporine A (CsA). Efficacy studies in animals (dogs suffering DED) were also performed.

Methods: Liposomes loaded with CsA (0.1%) were prepared. pH, osmolarity and in vitro tolerance (in human corneal and IOBA conjunctival cell lines) of the ophthalmic formulation were determined. The Schirmer test was performed in dogs suffering DED.

Results: The mean size of liposomes resulted 348.6±16.0 nm. The formulation presented neutral pH with an osmolarity value of 200.5±2.8 mOsm/L. Cellular viability resulted higher than 80% in both cell lines. The Schirmer test results showed that the lachrymal production in dogs with DED significantly increased ($p<0.05$) after one month of treatment.

Conclusions: The results observed in this work suggest that the liposomal formulation similar to natural tears in composition and containing CsA (0.1%) may be beneficial in the treatment of DED.

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EPIDEMIOLOGY OF DRY EYE DISEASE SYMPTOMS IN BRAZIL.

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Purpose: Scarce information is available about epidemiological and clinical characteristics of Dry Eye Disease (DED) in Brazil. This study aims to estimate the prevalence of DED and to investigate its risk factors in our country.

Methods: A previously reported questionnaire for the assessment of DED symptoms was translated into portuguese and validated in pilot study. This tool comprises questions about the DED diagnosis and the magnitude of symptoms, as well as risk factors. This questionnaire was then used in an ongoing population-based cross-sectional study in the 5 different regions of the country in order to achieve representative samples.

Results: Questionnaire translation and validation into portuguese was performed without difficulty. The study already included of 985 subjects aged 34.14 ± 14.87 year old. Prevalence of DED diagnosis was 8.8%; symptoms were absent in 12.3%, mild in 54.9%, moderate in 27.5% and severe in 5.3%. Risk factors that were significantly associated with DED were: aging OR=1.72 (95%CI 1.06-2.78), female sex OR 1.87 (95%CI 1.37-2.55), menopause OR 2.16 (95%CI 1.39-3.37), contact lens wear OR 2.00 (95%CI 1.41-2.83) and antidepressant use OR 2.01 (95%CI 1.24-3.21). Diabetes, visual display use, connective tissue diseases, ocular surgery and others medications were not associated with DED.

Conclusions: the translation and validation of this questionnaire enabled its application in a larger population sample to determine the prevalence of DED symptoms in the brazilian population, correlate risk factors and compare distinct regions of the country. We founded that DED symptoms are most frequently reported as mild to moderate intensity and aging, female sex, menopause, contact lens wear and antidepressants correlates with DED. Financial Support: Fapesp grant#2014/19138-5

ARE THERE GOOD ANIMAL MODELS FOR HUMAN DRY EYE DISEASE? IT DEPENDS ON THE DEFINITION OF "GOOD".

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Developing a perfect animal model for dry eye disease (DED) is a daunting task as it requires duplicating the complexity of pathophysiology and the entire spectrum of clinical symptoms observed in patients. Animal models for DED include but are not limited to: 1) mouse models with induced or spontaneous development of Sjögren's syndrome (SjS)-like disease, 2) dog models with spontaneous dry eye conditions, 3) rabbits applied with a preservative or a neuroreceptor

blocker, and 4) animals with surgical manipulation and/or environmental stressors for improved stability and chronicity of DED. Of those, rabbits have been commonly utilized for their large ocular surface, which allows standard dry eye clinical tests on the animals. However, because these models do exhibit limitations that are generally intrinsic to species, lack of a reliable animal model has posed a challenge in the field, hindering successful clinical translations.

Nevertheless, it is unquestionable that animal models have advanced our understanding of disease pathogenesis associated with DED in various ways, as exemplified in the clinical use of cyclosporine for DED, and anti-BAFF therapy/detection of anti-muscarinic receptor autoantibodies in SjS patients. Improved animal models that enable a therapy targeting underlying etiology and clinical symptoms simultaneously are expected to emerge. It would also be valid to utilize a number of animal models that collectively permit a dual approach, as dryness in the eyes can be irreversible even after targeted therapy for the cause.

Considering that over 90% of Nobel Prizes in Physiology or Medicine involve animal studies, the benefits of using animal models certainly surpass the risk of failing clinical trials. Current animal models are good enough as each model provides a piece of key information that is fundamental to advancing the field of DED. In the end, it may not be a perfect animal model that leads to a cure but it is we, researchers, who assemble the key information available and draw a big picture out of lessons we learn from numerous "good-enough" animal models.

TOPICAL, NON-INVASIVE TREATMENT FOR DRY EYE IN CONTROLLED HUMAN AND ANIMAL STUDIES.

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Purpose: A novel route for drug administration to specified non-ocular skin regions elicits rapid secretion, in seconds to minutes, of endogenous tear film components that bring about sustained comfort (greater than 12 hours) to dry eye sufferers.

Methods: A double-blind Phase 2 study (NCT02078661) was conducted to assess safety and efficacy for dry eye syndrome involving 75 subjects divided into 25 placebo and 25 at each of 0.25% and 1% levels. Approximately 0.25 g of PG101 gel containing low doses (2 mg or less) of an endogenous neurosteroid or placebo was massaged onto forehead skin.

Dry eye symptoms and signs were assessed at 30 and 60 minutes following test drug or placebo application on Days 1 and 14. Subjects applied test drug or placebo twice daily on Days 1 to 14, and filled out daily diaries. Results. Multiple dry eye symptoms and signs were significantly improved over the placebo and/or baseline values ($p \leq 0.05$): Ocular discomfort, dryness, grittiness, mucus discharge, corneal staining, interblink interval, and conjunctival redness.

In a rat animal model afferent neurons in a rostral brainstem region (Vi/Vc, subnucleus interpolaris/ subnucleus caudalis) are known to activate secretion of tear film components. Rats treated with drug had significantly higher ($p<0.05$) cFos gene activity than rats treated with placebo. Tear film secreted can also be visualized by the Tearscope. Meniscus height and Non-Invasive break-up time (NIKBUT) increases can be measured by Keratograph 5M.

Conclusion: Low-dose drug administration to specified skin regions can provide remote chemical signaling that activates neurons controlling tear film secretion. Data from the rat animal model confirm the postulated mechanism of action whereby low dose drug binds to receptors in the epidermis, in turn activating rapid chemical neural signaling via cranial nerve V (trigeminal) and possibly cranial nerve VII (facial) to afferent neurons that control tear film secretion.

RESTORATION OF CORNEAL TRANSPARENCY BY MESENCHYMAL STEM CELLS.

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Transparency of the cornea is indispensable for optimal vision. During ocular injury, inflammation-induced transforming growth factor (TGF)-β1 drives the differentiation of keratocytes into α-smooth muscle actin (αSMA)-expressing myofibroblasts, which produce disorganized extracellular matrix leading to the development of corneal opacity and scarring. Recently, mesenchymal stem cells (MSCs) have gained prominence due to their inflammation-suppressing and tissue repair functions. Here, we investigated the potential of and underlying mechanisms by which MSCs inhibit stromal fibrosis and restore transparency following injury using a well-characterized sterile injury model of mouse cornea. Our data demonstrated that systemically administered MSCs restore the corneal transparency as demonstrated by decreased corneal opacity scores (evaluated by slit lamp biomicroscopy), reduced α-SMA expression, and decreased TGFβ1 expression in injured cornea of mice treated with MSCs. Moreover, our findings showed that MSCs secret elevated levels of hepatocyte growth factor (HGF) in inflammatory environment, and interestingly, silencing of HGF expression in MSCs abrogated their anti-opacity function and their ability to suppress fibrosis and inflammation. These findings indicate that MSCs exert their anti-opacity function primarily via secretion of higher level of HGF. Interestingly, our data also showed that HGF alone can restore corneal transparency, an observation that has translational implications for the development of cell-free, HGF-based therapy. Funding Support: This work was supported in part by the National Institutes of Health (EY024602), and the Department of defense (W81XWH-15-1-0024).

COMPOSITIONAL ANALYSIS OF Ω-HYDROXY FATTY ACID-BASED DIESTERS IN HUMAN MEIBUM.

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Purpose: Meibum, the secretions from meibomian glands, contains special types of diesters (DEs) not found in other biological systems. These DEs are components of the tear film lipid layer (TFLL) and may play an important role in inhibiting evaporation. One type of DEs in human meibum is *ω* Type I-Ch DEs, each containing components of a fatty acid (FA), a *ω*-hydroxy fatty acid (HOFA) and cholesterol (Ch) with the shorthand FA-HOFA-Ch. The purpose of this study is to determine the molecular composition of *ω* Type I-Ch DEs, which can augment our understanding their role in the TFLL.

Methods: Human meibum samples (~ 13 *μ*g or ~ 16 nL) were collected in microcapillary tubes directly from meibomian gland orifices. Meibum sample solutions were prepared in a mixture of chloroform and methanol. Each solution was directly infused into a Triple TOF 5600 mass spectrometer (Sciex, Framingham, MA) with electrospray ionization in positive ion detection mode. Mass spectrometry (MS) and tandem mass spectrometry (MS/MS) analyses were performed for ions of all lipids and *ω* Type I-Ch DEs, respectively. From the relative ion intensities of intact molecules of these DEs in the MS spectrum and their characteristic fragments in the MS/MS spectra, the percentages of the DEs of different molecular weights and their isomers were determined, respectively. A total of 18 MS/MS spectra for these DEs of different molecular weights were acquired. Combining the information from the MS and MS/MS spectra, the percentages of a total of 91 *ω* Type I-Ch DE species were determined.

Results: The major components of the *ω* Type I-St DEs in human meibum included FA18:1-HOFA32:1-Ch (21%), FA16:1-HOFA32:1-Ch (9%), FA18:1-HOFA34:1-Ch (8%), FA18:1-HOFA30:1-Ch (7%) and FA17:0-HOFA32:1-Ch (6%). The major HOFAs in these DEs contained ultra-long unsaturated carbon chain including 32:1 (47%), 34:1 (20%) and 30:1 (11%).

Conclusions: The composition of *ω* Type I-Ch DEs is determined, which will be helpful for studies on the structure and function of the TFLL.

BUILDING AN EVIDENCE BASIS FOR MANAGEMENT OF OCULAR STEVENS-JOHNSON SYNDROME/TOXIC EPIDERMAL NECROLYSIS.

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Stevens Johnson syndrome and toxic epidermal necrolysis (SJS/TEN) characterize two ends of a spectrum of a rare but devastating mucocutaneous disease, with an incidence of 12 or less cases per million persons per year, and with associated mortality during the acute stage as high as 35%. In survivors of acute SJS/TEN, involvement of the ocular surface with chronic inflammation, dessication, and scarring leading to blindness, is the most significant sequelae, and the most feared, affecting up to 80% of survivors. This presentation will review the current evidence basis for management of acute and chronic ocular SJS/TEN, with a focus on windows of opportunity for intervention that if missed may lead to irreversible worsening of the condition. We will also focus on gaps in the current knowledge base for the disease, and discuss strategies for overcoming existing challenges to a more robust, information-based management algorithm for every stage of the disorder.

TEAR CYTOKINE PROFILES IN MEIBOMIAN GLAND DYSFUNCTION (MGD) TREATED WITH INTENSE PULSED LIGHT (IPL).

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Purpose: Intense pulsed light (IPL) is an emerging treatment modality for meibomian gland dysfunction (MGD). The major mechanism is that IPL eliminates inflammation in the meibomian glands. We have previously reported on the elevation of tear cytokines in MGD patients. Therefore, we conducted a study to analyze the alteration in tear cytokine profiles in MGD patients treated with IPL and to provide evidence for the decrease in inflammation following treatment.
Methods: Twenty patients with grades 2-4 MGD were prospectively enrolled, and were treated with 4 cycles of IPL of 3-4 weeks interval. Tear concentrations of interleukin (IL)-6, IL-10, IL-4, IL-2, IL-17A, interferon gamma (IFN- γ), and tumor necrosis factor alpha (TNF-α) were measured by a multiplex immunobead assay, and the change in tear cytokine levels following IPL treatment was analyzed. Meibomian gland dysfunction was staged according to meibum quality, expressibility of meibum, and lid margin features such as plugging, vascularity, and irregularity. Ocular surface staining, tear breakup time and Ocular Surface disease Index (OSDI) were also performed.
Results: TNF-α significantly decreased serially with treatment. IL-6 and IL-10 showed initial increase followed by a subsequent decrease, however the change was not statistically significant. IL-17A generally showed increasing tendency, which was also not statistically significant.
Conclusions: Inflammatory tear cytokine concentrations declined with IPL treatment in MGD patients. The results of this study suggest that IPL decreases inflammation in MGD, and may be considered as an effective treatment option.
[The authors have no financial interests to disclose.]

THE EFFECT OF TOPICAL DIQUAFOSOL TETRASODIUM 3% ON DRY EYE AFTER CATARACT SURGERY.

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Purpose: To evaluate the effectiveness of 3% diquafosol tetrasodium for treating dry eye after cataract surgery. Methods: Among patients who underwent bilateral cataract surgery, 34, who met the diagnostic criteria for dry eye syndrome 1 week postoperatively, were enrolled. Patients were randomly assigned to receive 3.0% diquafosol tetrasodium ophthalmic solution in one eye and 0.9% saline in the other eye four times daily for 8 weeks. Dry eye severity was measured at 1, 5, and 9 postoperative weeks using the Schirmer 1 test (SIT), tear film breakup time (TBUT), and fluorescein corneal staining. tear meniscus height (TMH), tear meniscus depth (TMD), and tear meniscus area (TMA) measured using Fourier-domain optical coherence tomography and symptom questionnaire scores.
Results: TBUT and corneal staining significantly improved 8 weeks postoperatively in eyes treated with 3.0% diquafosol tetrasodium ($p < 0.01$, $p < 0.01$) and were better than normal saline-treated eyes ($p < 0.01$, $p < 0.01$). SIT did not improve ($p = 0.26$). TMH, TMD, and TMA did not improve at 4 and 8 weeks. All symptom questionnaire scores improved in eyes treated with 3.0% diquafosol tetrasodium (all $p < 0.01$).
Conclusion: The 3.0% diquafosol tetrasodium treatment improved tear film stability and subjective symptoms of dry eye after cataract surgery. Increased mucin production as a result of diquafosol treatment may have caused these results.

EFFECTS AND PROGNOSTIC FACTORS OF KCL 1100® AUTOMATED THERMODYNAMIC SYSTEM FOR MEIBOMIAN GLAND DYSFUNCTION.

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Purpose: To evaluate effect and prognostic factors of automated thermodynamic system (thermal compression therapy device (KCL 1100®)) for Meibomian gland dysfunction (MGD).
Methods: Patients (forty eight eyes of 24 subjects) with MGD were recruited for a prospective clinical trial. Patients received 15-minutes treatment twice a day using the KCL 1100®. Severity of dry eye symptoms were evaluated using the Standard Patient Evaluation for Eye Dryness (SPEED) and Ocular Surface Disease Index (OSDI), and severity of Meibomian gland function was evaluated using the Meibomian Gland Expressibility (MGE), Meibomian Gland Secretion score (MGS), and Lipid Layer Thickness (LLT) measured by Lipiview®. To evaluate ocular surface, we measured tear break-up time (BUT) and fluorescein corneal staining score (Oxford scale). Data are presented for baseline and at 2-week and 1-month post-treatment.
Results: Dry eye symptom (SPEED, OSDI), meibomian gland function (MGE, MGS), and ocular surface index (BUT, Oxford scale) of patients were all improved significantly from baseline to 2-week ($p<0.05$) and also 1-month post-treatment ($p<0.05$). In addition, patients with more severe dry eye symptom and meibomian gland index at baseline examination achieved more improvement in mild to moderate MGD ($p<0.05$). Improvement of Meibomian gland function (MGE) was related to improvement of ocular surface index ($p<0.05$), but not associated with improvement of dry eye symptom (SPEED, OSDI) ($p>0.05$). There was no significant adverse event during treatment.
Conclusions: KCL1100® automated thermodynamic treatment offers an effective and safe treatment for MGD. Also, KCL1100® is more effective to patients with moderate dry eye symptom and meibomian gland dysfunction.
I have no financial interests.

GLUCOCORTICOIDS, SEX AND INFLAMMATION.

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Glucocorticoids are necessary for life after birth and regulate numerous biological processes in man, including glucose homeostasis, protein catabolism, skeletal growth, respiratory function, inflammation, development, behavior and apoptosis. They are also one of the most prescribed classes of drugs in the world particularly for diseases involving inflammation. Interestingly, males and females exhibit distinct differences in the prevalence of many major diseases, including autoimmune diseases, hepatocellular carcinoma, diabetes, osteoporosis, and dry eye disease, which all have important inflammatory components in their etiology. These gender-specific diseases are largely considered to reflect only the actions of sex hormones on the susceptibility to inflammatory stimuli. However, inflammation is recognized to reflect a balance between pro- and anti-inflammatory signals and glucocorticoids are the primary physiological anti-inflammatory hormone in mammals. Synthetic derivatives of these hormones are extensively prescribed as anti-inflammatory agents, irrespective of patient sex. We have explored the possibility that the sexually dimorphic actions of glucocorticoid regulation of gene expression may contribute to the dimorphic basis of inflammatory disease in rats, mice and humans. Surprisingly, glucocorticoid administration resulted in distinct global gene expression patterns in males and females. Pathway analysis identified sex-specific glucocorticoid-regulated genes in several canonical pathways involved in inflammatory disease with sex specific differences in prevalence. Current investigations of glucocorticoid actions in the eye will be presented.

UPDATE ON THE MANAGEMENT, TREATMENT, AND CLINICAL TRIAL DESIGN FOR CONTACT LENS DISCOMFORT.

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Contact lens discomfort (CLD) is the leading cause of patient dissatisfaction with and discontinuation of contact lens wear. The Tear Film & Ocular Surface Society (TFOS) launched the TFOS International Workshop on CLD that aimed to build a global consensus concerning CLD using an evidence-based approach. The Report of the Subcommittee on Clinical Trial Design and Outcomes noted that the CLDEQ-8 questionnaire best approached the most validated device although no specific recommendations could be made on the basis of evidence based review. The Subcommittee on Management and Treatment of CLD recommended managing CLD with a stepwise treatment algorithm that included tear supplements, adjustments of replacement frequency, change of materials and/or care system, among others.

This presentation will review the literature published since the TFOS reports. It will provide updates on new treatment approaches and the published outcomes of clinical trials investigating a range of treatments such as novel rewetting drops, lens materials, punctual occlusion, and other promising approaches. Finally, the presentation will address the most important needs and areas of future research.

STUDYING BOTH SEXES: A GUIDING PRINCIPLE FOR OPHTHALMOLOGY.

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Ophthalmologists have known for centuries that men and women exhibit sex-related differences in a variety of ocular diseases. Nevertheless, it is more important than ever to study both sexes to fully understand differences in the causes, mechanisms, and effective treatments for the diseases in women and men. Although the terms "sex" and "gender" are often used interchangeably, the Institute of Medicine has suggested clarifying their use such that "sex" refers to the classification of living things, generally as female or male according to their reproductive organs and functions assigned by chromosomal complement. "Gender" encompasses to a person's self-representation as a woman, man or gender diverse person, and/or how social institutions respond to a person based on the individual's gender presentation. The NIH now requires researchers to address sex as a biological variable. Sex begins *in utero*, and differences must be considered at all stages of the lifespan, especially when hormonal influences are particularly acute because they are critical in development and not just the obvious aspects of physiology—for example, sex differences in the lacrimal gland, and aging, which seem to have a strong influence on dry eye disease. Further, every cell has a sex, and so the genetic complement is not limited to XX vs. XY chromosomal differences. Hence, it will be a great challenge to figure out genetic versus hormonal influences—as well as their interactions. In the new NIH policy, accounting for sex as a biological variable begins with the development of research questions and study design, includes data collection and analysis of results, as well as reporting of findings. Consideration of sex may be critical to the interpretation, validation, and generalizability of research findings. For example, underreporting of sex is still an issue in animal studies, and the sex of origin of cells and tissues are often ignored. Adequate consideration of both sexes in experiments and disaggregation of data by sex allows for sex-based comparisons and may inform clinical interventions. Appropriate analysis and transparent reporting of data by sex may therefore enhance the rigor and applicability of preclinical research and promote investigation of sex and gender influences in health and disease across the biomedical research spectrum.

MEIBOMIAN GLAND DYSFUNCTION: ONLINE MANAGEMENT USING EYECALM - A COMMERICAL CLINICAL DECISION SUPPORT SYSYTEM COMPARED TO "USUAL CARE" USING PATIENT RELATED OUTCOME MEASURES.

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Purpose: Eyecalm - an online, commercial, clinical decision and self-management support system (CDSS) - has previously been shown to be equally effective in identifying the probable cause of a patient's chronic ocular discomfort as ophthalmologist's consultation. We undertook this study to determine if using this online CDSS to identify and direct self-management was equally acceptable from a patients' perspective as "usual care".

Methods: From October 2015 until April 2016 patients referred to Wirral UTH with chronic ocular discomfort who could potentially use the online CDSS were contacted and - if they consented - assigned to either use The Eyecalm system online or undergo "usual care" by eye clinic attendance. After four weeks of initial self-management by eyelid heating, all patients were reviewed, examined and completed a patient satisfaction survey. The results of the patient satisfaction survey in the Eyecalm group were compared to the "usual care" group.

Results: The mean patient satisfaction score in the Eyecalm group was 22.3 and the mean in the "usual care" group was 20.83 This difference was not statistically significant at $p < .05$, sub-group analysis was not attempted for that reason.

Conclusions: Although Eyecalm patients seemed more satisfied with their care than "usual care" patients the difference was not statistically significant at $p < .05$. This result has caused us to extend the number of patients using The Eyecalm online system to validate these initial results in a study containing more patients.

NOVEL MICRORNA THERAPEUTICS IN SJÖGREN'S SYNDROME DRY EYE DISEASE.

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Purpose: Sjogren's Syndrome (pSS) an inflammatory disease, primarily affecting mucous membrane epithelia leading to the clinical phenotype of dry eyes and dry mouth. Dysregulated expression of Type 1 IFNs and proinflammatory cytokines is associated with pSS. MiR regulated genes may contribute to the pathogenesis of pSS by increasing cytokine production. We have previously shown that miR-744-5p expression was significantly increased, while its predicted gene target Pellino 3- a known negative regulator of type 1 interferons- was significantly reduced in the primary conjunctival epithelial cells (CECs) from primary Sjögren's Syndrome patients. Modulation of miR-744-5p expression is an attractive potential target for the restoration of immune homeostasis at the ocular surface in pSS.

Methods: psiCHECK-2 luciferase constructs were designed such that one contained the potential miR-744 binding sites within the 3' UTR of Pellino3, while the second contained an unrelated fragment with no binding sites as a control vector. Chitosan-antagomiR nanoparticles were formulated. Particle size and charge were determined using Malvern Zetasizer Nano 3000. miR and gene expression were evaluated using real time PCR.

Results: Co-transfection of psiCHECK-2 construct studies containing both of the potential binding sites with a miR-744 mimic demonstrated a significant decrease in luciferase gene expression when compared to the unrelated fragment control. Nanoparticles incorporating antagomiR were fabricated in a range of sizes and concentration.

Conclusions: Our results confirm the direct interaction of miR-744-5p with PELI3, as a negative regulator. An optimised nanoparticle delivery system has therapeutic potential for modulating inflammation at the ocular surface. This work is supported by grants from the RVEEH Research Foundation and MRCG.

DROP VOLUME OF ARTIFICIAL TEAR SOLUTIONS: PHARMACOECONOMIC STUDY.

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Purpose: To determine the mean drop volume produced by artificial tear solutions in different inclination angles and to determine the mean cost of the treatment.

Methods: The drop volume of 3 original bottles of the artificial tear solutions Artelac®, Hylo Comod®, Lacrima® Plus, Systane® UL, Lacrifilm®, Hyabak®, Lacribell®, Ecofilm®, Mirugell®, Plenigell®, Fresh Tears®, Optive® and Endura® were determined at the inclination of 90º and 45º. The mean number of drops in each bottle was determined and a pharmacoeconomic evaluation of the drops was made.

Results: The drop volume ranged from 32.2 to 64.0 µL at 45º and from 29.1 to 65.1 µL at 90º. The difference between drops in each inclination varied from 2 to 24%. The annual cost was from R$2.73 to R$130.73 according to the inclination of the bottle. The Maximum Duration of Treatment (MDT) was from 29.3 to 51.4 days at 45º and from 28.8 to 48.4 days at 90º, being the difference in MDT from 0.5 to 8 more or less days depending on each brand.

Conclusion: None of the eye drops studied presented ideal drops for human eyes once they are bigger than what the ocular surface can suit, leading to a waste of the product and higher cost for the manufacturer and the consumer, as well as a risk of augmenting the systemic absorption or undesired side effects on the skin. We noted that there is a significant variation in the drop volume according to the inclination of the bottle, and that a variation of over 10% would bring financial impact for the patient.

SUPRATARSAL INJECTION OF TRIAMCINOLONE FOR SEVERE VERNAL KERATOCONJUNCTIVITIS.

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Purpose: To evaluate the use of supratarsal injection of triamcinolone acetonide in severe vernal keratoconjuctivitis (VKC) in children.

Methods: Patients with severe allergic keratoconjunctivitis associated with keratitis, gelatinous limbal infiltrates and/or giant papillae, with a history of recurrences and resistance to conventional topical antiallergic agents were included in this open clinical trial. The patients were treated with a supratarsal injection of 20 mg triamcinolone acetonide.

Results: Analysis included 27 injections in 23 eyes of 17 patients with severe allergic keratoconjunctivitis. The mean age was 12.3, range 7-19 years. The mean follow-up time was 39.3 months (SD 19.21). Of the 17 patients, the disease was successfully controlled for an average of 3.6 months (range 1-16) in which the symptoms and signs were significantly improved with complete resolution of lid edema and conjunctival chemosis, significant decline of pannus, keratitis and reduction of giant papillae's size.

Conclusion: The treatment of severe allergic keratoconjuctivitis in children with supratarsal injection of 20mg triamcinolone proved cost-effective, rendered satisfactory results and was well tolerated with little side effects, thus constituting a safe option for severe and challenging cases of VKC. A significant improvement was found in the ocular allergy symptoms and signs, with a reduction in the frequency of acute recurrences.

ASSOCIATIONS BETWEEN CLINICAL MEASURES OF OCULAR SURFACE DISEASE AND TEAR FILM DERIVED NEUROPEPTIDE CONCENTRATIONS.

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Purpose: To determine associations between the concentrations of vasoactive intestinal polypeptide (VIP), calcitonin gene-related peptide (CGRP), neuropeptide Y (NPY), or substance P (SP) and clinical measures of ocular surface disease.

Methods: The clinical assessments included the Ocular Surface Disease Index (OSDI), tear production using Schirmer strips (unanesthetized), inferior palpebral and corneal sensitivity testing using a Cochet-Bonnet aesthesiometer, and average lipid layer thickness using the LipiView. The Keratograph 5M was used to obtain two first non-invasive keratograph tear break up time (NIK-BUT) measures, which were averaged for each subject, and a picture of the inferior lid margin, which was graded for redness on a scale of 0 to 4. Up to 5µL of tears were collected using microcapillary tubes. Peptides retrieved using C18 spin columns were split into four for use in each neuropeptide's ELISA. Spearman correlations between clinical parameters and neuropeptide concentrations were used to assess associations.

Results: Average age of the 56 subjects was 34.8 +/- 15.2 years, and 64.3% were female. VIP concentration was significantly associated with age ($p = 0.03$) and lid margin redness ($p = 0.04$). It was not associated with OSDI score ($p = 0.76$), tear production ($p = 0.20$), conjunctival ($p = 0.46$) or corneal sensitivity ($p = 0.36$), lipid layer thickness ($p = 0.49$), or first NIK-BUT ($p = 0.73$). CGRP, NPY, and SP were not associated

with age (p = 0.47, 0.30, 0.57, respectively), OSDI score (p = 0.82, 0.34, 0.77, respectively), tear production (p = 0.56, 0.50, 0.64, respectively), palpebral (p = 0.94, 0.23, 0.71, respectively) or corneal sensitivity (p = 0.87, 0.15, 0.77, respectively), lipid layer thickness (p = 0.20, 0.43, 0.07, respectively), first NIK-BUT (p = 0.95, 0.58, 0.81, respectively), or lid margin redness (p = 0.76, 0.63, 0.81, respectively). Conclusions. VIP should be investigated further for its relationship between inflammation and age.
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UNIQUE CHALLENGES AND UNMET NEEDS FOR THE TREATMENT OF OCULAR SURFACE DISEASE IN OCEANIA.
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Oceania describes a collection of over 30,000 islands, representing 14 countries, and displays considerable diversity with respect to land mass, population density, remoteness, social and economic development, and even climate. Access to healthcare varies dramatically across Oceania between highly developed countries such as Australia and New Zealand (NZ) and developing nations such as Papua New Guinea and the Solomon Islands, where health care needs are far more fundamental and widespread.
With regard to ocular surface health in Australia and NZ, dry eye certainly presents significant and growing management challenges and there is a recognised need for better treatments. However, even within these highly developed countries, there remain regions of desperate need for better basic health care, particularly amongst, often geographically and culturally isolated, indigenous populations. Indeed, Australia remains the only developed country in which trachoma has not been eradicated. Keratoconus, most prevalent in NZ's M*ā*ori and Polynesian populations, is the leading indication for corneal transplantation in NZ. Different approaches to health between the Tangata Whenua (people of the land) and P*ā*keh*ā* (European New Zealanders) present unique challenges in ensuring equal access to healthcare for all, and reducing disparity in health outcomes for the indigenous peoples. High intensity atmospheric UV radiation exposure, exacerbated by localised depletion of the ozone layer, further predisposes inhabitants of Oceania to vision-threatening, ocular surface diseases such as ptyergium as well as corneal and conjunctival dysplasias or malignancies.
Relative isolation combined with a struggling economy poses distinct challenges for some of the less developed islands of the Pacific, and a paucity of specialised eye doctors and nurses can necessitate reliance on expatriate health care being provided by international aid donors. Thus, with respect to ocular surface disease management in Oceania, a wide variety of unmet needs exist, which are confounded by unique challenges presented by climate, poverty, location and culture.

CLINICAL SAFETY AND TOLERABILITY OF A MANUKA HONEY-BASED PRODUCT DESIGNED TO PROMOTE EYELID HEALTH.
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Purpose: Commensal bacteria play a role in the pathogenesis and propagation of blepharitis. Through its active ingredient, methylglyoxal, Manuka honey is recognised to possess antibacterial and anti-inflammatory properties. This has been employed in developing a topical therapy; Manuka Honey CycloPower™ microemulsion (MHCPME) to aid management of blepharitis and its sequelae. This study reports the results of a clinical safety and tolerability trial that follows favourable preclinical testing.
Methods: In a prospective, randomised, investigator-masked, paired-eye study, MHCPME was applied to one eye of 25 participants for 2 weeks while the contralateral eye remained untreated. Clinical evaluation was performed at baseline, and then at 1 week and 2 weeks post-treatment. Evaluations at each visit included palpebral erythema, bulbar conjunctival hyperaemia, tear lipid layer grade, objective non-invasive tear break up time, tear evaporation rate and osmolarity as well as fluorescein and lissamine green staining of the ocular surface and lid wiper regions. qPCR analysis of the markers IL-6, MMP-9 and MUC5AC was performed at baseline and at 2 weeks.
Results: No major ocular or systemic adverse events were observed following the use of MHCPME. All parameters in both treated and untreated eyes remained within the normal range throughout the study. No differences were noted post-treatment relative to baseline, ($p>0.05$) nor between treated and untreated eyes, at any time point ($p>0.05$).
Conclusion: The absence of adverse tear film or ocular surface changes, attributable to 2 weeks daily application of the MHCPME product, confirms product safety for human use and acceptability to proceed to an investigation of the antimicrobial and anti-inflammatory benefits of the Manuka honey-based product, in vivo.
[This research was supported by a grant from Manuka Health New Zealand Ltd., NZ]

THE EFFECT OF TOPICAL DIQUAFOSOL TETRASODIUM 3% ON TEAR FILM AND CONJUNCTIVAL GOBLET CELLS AFTER CATARACT SURGERY IN PATIENTS WITH DRY EYE DISEASE.
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Purpose: To investigate the changes of diquafosol tetrasodium (DT) 3% treatment on tear film and ocular surface parameters including conjunctival goblet cell densities after cataract surgery in patients with pre-existing dry eye disease (DED)
Methods: A total of 48 eyes of 42 patients with DED who underwent uneventful cataract surgery were included. In total, 25 eyes of 22 patients were treated with DT 3% tears (group A) while 23 eyes of 20 patients were treated with sodium hyaluronate (SH) artificial tears (group B) postoperatively, along with topical instillation of antibiotics and steroid. Ocular surface disease index (OSDI), tear film break-up time (TBUT), Schirmer test, and keratoepitheliopathy score were measured at baseline and at 1, 4, and 12 weeks postoperatively. Conjunctival impression cytology analysis was performed at baseline, and at 4 and 12 weeks postoperatively. Results: In both groups, ocular surface parameters were significantly aggravated 1 week postoperatively than at baseline. Compared with group B, group A showed significantly lower OSDI scores at 4 and 12 weeks, longer TBUT at 1, 4, and 12 weeks, and lower keratoepitheliopathy score at 1 and 12 weeks ($P < 0.05$). A significant improvement in the impression cytologic findings including conjunctival squamous cell metaplasia and goblet cell densitiy were observed at 4 and 12 weeks postoperatively in group A when compared with group B.
Conclusions: In patients with DED, DT 3% eyedrops application after cataract surgery can assist in the early reduction of dry eye symptoms and improvement of ocular surface environment.

EXPERIENCE OF THE FIRST OCULAR SURFACE-DRY EYE SERVICE IN ATHENS.
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Purpose: To present the set-up and first year results of the ocular surface-dry eye service of the clinic. Methods. 150 patients (101 women and 49 men) with ocular surface complaints were examined as following: history, OSDI questionnaire, number and type of blinking, complete slit lamp examination of the ocular surface, photography, TBUT, fluorescein stain (Oxford grading system) and schirmer test. Patients underwent specific examinations: precorneal tear film evaluation with corneal topography, lipid layer and tear meniscus evaluation with tearscope, tear osmolarity testing with tearlab, Meibomian gland discharge evaluation with MGEvaluator, Meibomian gland retroilumination evaluation and microscopic eyelash examination for demodex diagnosis, whenever necessary.
Results: According to their diagnosis, patients were divided into the following categories: MGD (46 patients- 30,7%), disorders of the lids (24 patients-16%), disorders of the conjunctiva (7 patients- 4,7%), OSD-toxic (20 patients-13,3%), demodex (14 patients- 9,3%), autoimmune (13 patients- 8,7%), infection (2 patients- 1,3%) and combined disorders (24 patients- 16%). Based on the findings appropriate medical or surgical treatment was administered. Specifically for MGD patients, heating of the glands was performed with a special mask (Blephasteam®) followed by MGD decompression and eyelash cleansing. For symptomatic demodex patients, 100% tea tree oil lid cleansing per week for 6 weeks was performed. Examination of the 150 patients according to protocol lead to targeted and personalized treatment with positive outcomes for the patients.
Conclusions: The department's purpose, to introduce in clinical practice, a diagnosis protocol, based on DEWS and MGD workshop principals for patients with ocular surface problems, followed by targeted treatment, was achieved. Patient satisfaction was high especially for those that had many previous unsatisfactory treatments. These kind of services must work independently to provide better care for this category of patients.

STAPHYLOCOCCUS AUREUS-INDUCED MUCIN SECRETION BY CONJUNCTIVAL GOBLET CELLS: DEPENDENCY ON NLRP3 INFLAMMASOME ACTIVATION AND RELEASE OF MATURE IL-1β

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Purpose: We have demonstrated that pathogenic S. aureus activates the NLRP3 inflammasome in conjunctival goblet cells, resulting in secretion of the pro-inflammatory cytokine IL-1β and the mucin MUC5AC. We now determine if NLRP3 inflammasome activation is required for S. aureus-induced mucin secretion and if this secretion is dependent upon the release of mature IL-1β. Methods: Cultured human conjunctival goblet cells were incubated for 72 h with siRNA for NLRP3 or TLR 2 or scrambled siRNA. Cells were stimulated with toxigenic S. aureus RN6390. Cells were also stimulated with IL-1β or S. aureus RN6390 with: (1) IL-1 receptor antagonist (IL-1Ra, Anakinra), (2) intracellular Ca2+ chelator (BAPTA/AM), (3) extracellular regulated kinase (ERK) 1/2 inhibitor (U0126), or (4) vehicle control. High molecular weight glycoconjugate (HMGC) secretion including MUC5AC was measured by enzyme linked lectin assay (ELLA).
Results: NLRP3 and TLR2 siRNA, but not scrambled siRNA, significantly inhibited goblet cell secretion induced by toxigenic S. aureus RN6390. Mature IL-1β alone stimulated goblet cell secretion in a dose-dependent manner. IL-1Ra significantly blocked goblet cell secretion stimulated by S. aureus RN6390 or IL-1β alone. IL-β-induced mucin secretion was blocked by chelating intracellular Ca2+ or inhibiting ERK1/2 activity. Conclusions: Conjunctival goblet cell-derived mature IL-1β mediates S.aureus-induced mucin secretion by increasing intracellular [Ca2+] and activating ERK1/2. Moreover, the S. aureus-induced production of mature IL-1β is dependent upon the triggering of both NLRP3 and TLR2 expressed on goblet cells. Conjunctival goblet-cell-derived IL-1β induced by pathogenic S. aureus is an inducer of both immune cell recruitment that clears pathogens and of mucin secretion that enhances the mucosal surface barrier to infection. Supported by NIH EY EY022415.

SURFACE INTERACTIONS OF CATIONIC NANOEMULSIONS WITH HUMAN MEIBUM FILMS.

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Purpose: Ikervis® (IKV) cationic nanoemulsions (CNE) improve tear film stability in vivo possibly via the effect of CNE oil phase on tear film lipid layer (TFLL). Consequently the interactions of human meibum (MGS) films were studied with IKV and with binary and ternary mixtures of its constituents. The binary mixtures consisted of 2% mid chain triglycerides (MCT)/0.005% cetalkonium chloride (CKC) or 2% MCT/0.3% Tyloxapol (Tylo). The ternary mixture was MCT/CKC/Tylo (2%/0.005%/0.3%). The effect of 0.1µM bovine submaxillary mucin (BSM) on CNE/MGS interactions was also studied.
Methods: MGS and CNE oils were spread at the air/water interface of a Langmuir surface balance in range of 2D ratios (20/1, 10/1, 5/1, 3/1, 2/1 and 1/1) at two measurement regimes: (i) fixed MGS amount or (ii) the inclusion of CNE is accompanied by proportional decrease of MGS content. The films performance at dynamic area cycling was evaluated. The layers dilatational rheology was probed via the step/relaxation method. Films structure was registered with Brewster Angle microscopy.
Results: The binary mixtures showed limited spreading and miscibility with MGS. The ternary mixture and IKV spread and mixed well with MGS. At fixed MGS amount, the inclusion of CNEs enhanced the structure, properties and elasticity of the layers. When the CNE/MGS amounts were simultaneously varied, the films remained primarily elastic, but at high (≤3/1) CNE content the elasticity slightly decreased and heterogeneities in layers structure were observed. BSM enhanced the ternary mixture (IKV)/MGS interactions.
Conclusions: At physiologically relevant MGS/CNE ratios MCT/CKC/Tylo and IKV interact favorably with MGS films. The impact of BSM suggests that polyanionic polysaccharides can enhance CNE/TFLL interactions in vivo. [Collaborative study grant by Santen SAS, Evry, France]

SAFETY AND EFFICACY OF EXCISION OF THE HORISONTAL CANALICULUS IN SEVERE AQUEOUS DEFICIENT DRY EYE.

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Purpose: To investigate safety and efficacy of excision of the horizontal canaliculus (HC), a novel alternative technique to punctal occlusion, for severe aqueous deficient dry eye prospectively.
Methods: Twenty-six canaliculi of 17 eyes of 13 consecutive patients (5 Sjögren syndrome (SS), 6 Ocular cicatricial pemphigoid, 1 Stevens-Johnson syndrome and 1 non-SS) consisting of 3 males and 10 females were enrolled in this study (mean age; 61.6 ± 20.4 years). All patients had experienced repeated extrusion of punctal plugs and failed surgeries of conventional punctal occlusion. Twenty-two canaliculi underwent partial removal of the HC. In 4 canaliculi, simple incision was performed around center of the HC. Tear meniscus height

(TMH), ocular surface damage and tear film lipid layer interferometry (TFLLI) were measured preoperatively and 1, 3, 6 and 12 months postoperatively. Dry eye symptoms were also assessed using dry eye-related quality-of-life score (DEQS) questionnaire and visual analogue scale (VAS).

Results: Rate of occluded canaliculi at final follow-up was 84.6% (22 of 26 canaliculi). Two of 4 (50%) canaliculi undergone simple incision were recanalized postoperatively and performed partial removal of the HC thereafter. TMH significantly increased 1 month after surgery (0.27 ± 0.10 mm, P<0.00005) compared to preoperative values (0.13 ± 0.07), and was maintained during 12 months. Epithelial damage and TFLLI grades significantly decreased at all the time points of postoperative examinations. Preoperative DEQS showed 59.0 ± 22.2 points, and significantly decreased at 6 months postoperatively (29.8 ± 24.8, P=0.0225). VAS scores also significantly improved. None of complications other than conjunctival wound dehiscence in one canaliculus were recorded.

Conclusions: Excision of the horizontal canaliculus was safe and effective for severe aqueous deficient dry eye. This techinique may be an alternative to conventional punctal occlusion.

LIMBAL STEM CELLS.

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Limbal stem cells (LSCs) maintain the normal homeostasis and wound healing of corneal epithelial cells. This concept is further proven by lineage tracing experiments using transgenic mouse models. Due to the lack of specific markers of LSCs, identification and characterization of LSCS have been challenging. Despite the difficulty, additional surface markers including ABCB5 and Frizzled 7 have been identified and used to characterize the LSC population. Recent studies also have elucidated several signaling pathways, such as Wnt and Notch signaling that play important roles in the self-renewal and differentiation of LSCs. Methods to evaluate in vivo LSC function are being developed using in vivo imaging techniques. These new advances in the understanding of LSC biology will facilitate the development of future therapies of limbal stem cell deficiency.

CONJUNCTIVAL INFLAMMATION AFTER PUNCTAL PLUGGING FOR SEVERE DRY EYE.

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Purpose: to investigate conjunctival inflammation after punctal plugging for severe dry eye

Methods: In this prospective study, HLA DR expression was assessed on conjunctival impression cytology specimens harvested in 8 patients (10 eyes) with severe keratoconjunctivitis sicca (related to Sjögren's syndrome or Graft versus host disease) before and 1 month after punctal plugging. Clinical efficacy was also graded.

Results: After punctal plugging, HLA DR expression increased in all eyes but 2. Mean HLA DR showed a 35% increased from 38621±28840 to 52464±26196 at 1 month (p<0.05). Meanwhile, global symptoms measured by visual analog scale dropped from 88±23 to 12±15 mm, and total ocular surface staining score decreased from 11.7±3.2 to 2.1±1.1. Conjunctival hyperhemia also decreased or remained stable.

Conclusions: Despite the low number of patients included, this study shows that punctal plugging is an efficient treatment of keratoconjunctivitis sicca, allowing for major reduction of symptoms and of corneoconjunctival epitheliopathy. However, subclinical inflammation is increased probably by the reduced tear turnover. The clinical significance and consequences of this inflammation remain unclear.

SAFETY AND EFFICACY OF 0.1% (1 MG/ML) CYCLOSPORINE CATIONIC EMULSION (CSA CE) IN PATIENTS WITH DRY EYE DISEASE AND SJÖGREN'S SYNDROME: EXPERIENCE FROM THE FRENCH EARLY ACCESS PROGRAM.

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Purpose: Dry eye disease (DED) associated with Sjögren's syndrome (SS) may be severe and difficult to treat. The efficacy and safety of 0.1% CsA CE in patients with DED and SS was assessed in a French early access program (EAP).

Methods: French national authorities approved a temporary authorization for use (ATU) of 0.1% CsA CE (Oct 2013–Jun 2015). All patients had severe keratitis as per corneal fluorescein staining (CFS) score of 3–5 on the Oxford scale and/or presence of filaments and/or corneal ulcers. Efficacy was assessed at Months 1, 3, 6 and 12, and safety was also monitored.

Results: A total of 1212 patients enrolled. At inclusion, 1164 patients (99.0%) had no improvement despite use of tear substitutes; 49.6% were CsA treatment naïve, and 50.4% were switched from RESTASIS® (0.05% CsA anionic emulsion) (43.8%) or hospital CsA formulations (6.6%). Analysis focused on 590 (48.7%) patients with SS (mean age 63 years, 91% female, mean symptom duration 5.8 years). Improvement and stabilization in signs of DED (keratitis) were observed in 38–49% and 41–48% of patients, respectively; 8.6% achieved CFS Grade 0 at Month 6. Improvement and stabilization in DED symptoms were observed in 49–52% and 44–46% of patients with SS, respectively. The most frequent adverse events were moderate and local and included instillation site pain, eye irritation and eye pain (21%, 16% and 13% of events, respectively).

Conclusions: Data from the French EAP suggest the benefit of 0.1% CsA CE in stabilizing or improving corneal damage and symptoms in patients with DED with severe keratitis and SS. This research was supported by Santen. S.D. reports commercial relationships with Alcon, Allergan, Bausch&Lomb, Horus, Santen, Théa. B.C. is a clinical investigator and consultant for Alcon, Allergan, AMO, Horus Physiol, RVO, Santen, Théa. P.-J. P. is a consultant for Abbott, Alcon, Allergan, Santen, Théa. D.B.-G. reports commercial relationships with Alcon, Allergan, Santen, Théa. M.A., J-S.G., D.I. are employees of Santen.

EFFICACY OF INTENSE REGULATED PULSED LIGHT THERAPY IN MEIBOMIAN GLAND DYSFUCTION RELATED DRY EYE.

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Purpose: To report the efficacy of intense regulated pulsed light (IRPL) therapy in meibomian gland dysfunction (MGD) related dry eye.

Methods: This prospective non controlled study included 20 patients (40 eyes) with MGD and evaporative dry eye, who failed lid hygiene. IPL was applied on the peri ocular area with the E-Eye device (E-Swin, France) at day 0, 15, 45. At each visit and also at day 75, symptoms (evaluated by visual analog scale, EVA and SPEED questionnaire), fluorescein BUT and meibum grading were performed.

Results: Compared to day 0, mean global symptom VAS at day 75 decreased from 69 to 55 (p=0.048), and mean SPEED score decreased

from 22 to 19 (p=0.03). 70% of cases had more than 20% decrease of EVA or SPEED. BUT increased from 4.2 to 5.9 s (NS). The number of permeable meibomian glands (out of 15 glands) increased from 5.9 to 8.1 (p=0.04).
Conclusions: IRPL seems to be an interesting option for treating MGD related dry eye, although BUT was not significantly changed in our study.

CLINICAL AND NEUROPHYSIOLOGICAL COMMONALITIES AMONG CHRONIC CORNEAL PAIN PATIENTS ENROLLED IN A CLINICAL TRIAL

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Purpose: To describe clinical and neurophysiological commonalities in a small series of patients enrolled in a clinical trial of transcranial direct current stimulation (tDCS) for chronic corneal pain (CCP).
Methods: Demographics and clinical data were obtained from the trial database and retrospective review of medical records. Patients' pressure-pain thresholds (PPT) on the affected area (ophthalmic division of the trigeminal nerve) and on a control site (thenar area) were compared to those of a gender-matched healthy control population enrolled in the same clinical trial (t-test).
Results: Data on the effectiveness of tDCS for CCP was inconclusive in this small trial that enrolled only 5 patients. There were remarkable commonalities among the patients despite the broad inclusion criteria for the trial. All patients were male, young, and had bilateral disease. They all had high levels of educational attainment. Four patients were in the 3rd or 4th decades, had either bilateral LASIK or systemic treatment with isotretinoin as apparent precipitating factors; two had self-reported psychiatric comorbidities and a third had an undiagnosed sensory syndrome. The 5th patient was an outlier in terms of his age, the absence of any apparent precipitating factors and the clinical presentation, which included dystonic features. Patients had reduced PPT on the affected area (p=.010) and on the control site (p=.046) as compared to controls. Conclusions: Commonalities among CCP patients point to avenues for future investigation as to pathophysiology, prevention and treatment of what is newly appreciated as a relatively intractable form of dry eye disease. Altered PPT may be a marker of CCP or CCP susceptibility.

A RANDOMISED, DOUBLE-MASKED, PLACEBO-CONTROLLED CLINICAL TRIAL OF TWO FORMS OF OMEGA-3 SUPPLEMENTS FOR TREATING DRY EYE DISEASE.

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Purpose: To assess the efficacy of two forms of oral long-chain omega-3 (*ω*-3) essential fatty acid (EFA) supplements, phospholipid and triglyceride, for treating dry eye disease (DED).
Methods: This study was a single-centre, double-masked, placebo-controlled randomised clinical trial. Participants (n=60) with DED were randomised (1:1:1) to one of: placebo (olive oil) or matched doses (1000mg/day eicosapentaenoic acid + 500mg/day docosahexaenoic acid) of *ω*-3 EFAs in either predominantly phospholipid (krill oil) or triglyceride (fish oil) form. Primary outcome measures were mean change in: i) tear osmolarity and ii) DED symptoms (OSDI) between Days 1&90. Secondary outcomes included mean change in key clinical signs (tear stability, tear production, ocular surface staining, bulbar redness, meibomian gland integrity) and tear inflammatory cytokines.
Results: 54 participants completed the study. At Day 90, tear osmolarity was reduced from baseline with *ω*-3 EFAs in predominantly phospholipid (-18.6 [SD:16.7] mOsmol/L, n=18, p<0.001) and triglyceride (-19.8 [SD:19.6] mOsmol/L, n=19, p<0.001) forms compared with placebo (-1.5 [SD:18.2] mOsmol/L, n=17). OSDI score was reduced at Day 90 relative to baseline in the phospholipid *ω*-3 EFA group only compared with placebo (-18.6 [SD:10.2] versus -10.5 [SD:13.5], p=0.02). At Day 90, there were relative improvements in tear-break-up-time and ocular bulbar redness, compared with placebo, for both forms of *ω*-3 EFAs. Basal tear levels of the pro-inflammatory cytokine IL-17A were reduced only in the phospholipid *ω*-3 EFA arm compared with placebo at Day 90 (-27.1 [SD:46.2] versus +46.5 [SD:125.5] pg/mL, p=0.02). Conclusions: A moderate daily dose of both forms of long-chain *ω*-3 EFAs, for 3-months, resulted in reduced tear osmolarity and increased tear stability in people with DED. Krill oil may confer additional therapeutic benefit, with improvements in symptoms and lower basal tear levels of IL-17A, relative to placebo.
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COMFORT AND WETTABILITY OF DAILY DISPOSABLE CONTACT LENSES.

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Purpose: To explore the association between comfort and wettability of daily disposable (DD) contact lenses (CLs).
Methods: Sixty habitual DDCL DAILIES®TOTAL1® (DT1, n=29) and clariti®1day (c1d, n=31) wearers attended a baseline visit wearing their CLs. Digital videos of the pre-lens tear film were captured using Tearscope illumination following 3 hrs in a controlled, reduced humidity environment (20%RH). Subjects were refitted with MyDay™ and 1-DAY ACUVUE® TruEye® (TE) DDCLs and videos captured following 10 ± 3 days and 3hrs at 20%RH. A post hoc analysis of non-invasive break up time (NIBUT) and minimum protected area (MPA) of the CL surface was conducted by masked investigators. Comfortable wearing time (CWT) and satisfaction with end of day comfort (SEODC) were assessed for each DDCL. Results. NIBUT was longer with DT1 than with MD and TE (Mean: DT1 9.2s, MD 6.3s, TE 5.1s; p=0.052 & p=0.006; UCL=0.03 & <0 respectively); MPA for DT1 was also superior to MD and TE (Mean DT1 95.4%, MD 84.4%, TE 82.9%, p=0.002 & p<0.001 respectively; UCL<0). For habitual c1d wearers, NIBUT was similar for all CLs but MPA was greater for c1d and MD than TE (c1d 89.0%, MD 88.4%, TE 76.2%, p=0.001 and p=0.002 respectively). CWT was 2hrs longer with DT1 than MD and TE (Mean: DT1 13.2, MD 11.1, TE 11.1; p=0.005) but similar for c1d wearers refitted with MD and TE (Mean: c1d 11.1, MD 10.4, TE 11.0; p>0.05). SEODC was higher for DT1 than MD and TE (DT1 50%, MD 28%, TE 24%) and higher for habitual c1d wearers with c1D and TE (c1d 38%, MD 19%, TE 39%). Conclusion. Wearers of DT1 reported the longest CWT and greatest SEODC. This DDCL also provided superior wettability following exposure to 20%RH indicating that on-eye wettability may be an effective predictor of overall comfort.
This study was sponsored by Alcon Inc.

THE EFFECT OF AMBIENT TITANIUM DIOXIDE MICROPARTICLE EXPOSURE TO THE OCULAR SURFACE ON THE EXPRESSION OF INFLAMMATORY CYTOKINES IN THE EYE AND CERVICAL LYMPH NODES.

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Purpose: To investigate the expression of inflammatory cytokines in the anterior segment of the eyeball and cervical lymph nodes after exposure to airborne Titanium dioxide (TiO_2) microparticle for five days.

Methods: Twenty-eight rats were randomized to TiO_2-exposed (n=14) or control (n=14) groups. Rats in the TiO_2-exposed group were exposed to airborne TiO_2 particles for two hours twice daily for five days, while those in the control group were not exposed to TiO_2. Lactic dehydrogenase (LDH) activity (n=4) and MUC5AC levels (n=4) were measured in the tears, the serum immunoglobulins (Ig)G (n=4) and IgE (n=4) were assayed using enzyme-linked immunosorbent assay, and the size of cervical lymph nodes (n=6) was compared between the two groups. In addition, the expression of interleukin (IL)-4, IL-17, and interferon (IFN)-γ in the anterior segment of the eyeball and cervical lymph nodes was measured by immunohistochemistry, real-time polymerase chain reaction (RT-PCR), and Western blot analysis (n=4).

Results: Tear LDH activity and cervical lymph node size were increased after TiO_2 exposure, while there was no significant difference in tear MUC5AC levels. Serum IgG and IgE levels were found to be significantly elevated in rats exposed to airborne TiO_2. IL-4 expression was increased in the anterior segment of the eyeball and lymph nodes following TiO_2 exposure, as measured by immunostaining, RT-PCR, and Western blot. In addition, IL-17 and IFN-γ levels were also increased following TiO_2 exposure compared to controls as measured by immunostaining. Conclusions. Exposure to airborne TiO_2 induced ocular surface damage and attenuated the ocular surface protection provided by mucin. The Type 2 helper T cell pathway seems to play a dominant role in the ocular immune response following airborne TiO_2 exposure.

SMART GLASSES: FUTURE USES & LIMITATIONS FOR HEALTHCARE.

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As the world moves from Analog to Digital service models, there remains a gap in Digitizing people. We have digitized how we consume music, entertainment, education, and core services like banking, where software can replace physical packages and buildings. By digitizing these services, they can now be made to be available anywhere, anytime, on-demand, and at scale. A desire to listen to music, to watch your favorite sports team, or to shop, can instantaneously be served online via the cloud. However, until now the world has not been able to digitize people, or the ability to deliver services to people. Patients still visit specialists at physical locations for assessment. This is changing. Using Smartglass and other mobile technologies, HD video, and other innovations, we are now able to virtualize people and expertise and make those skills available anywhere, anytime, on-demand, and at scale, for multiple different industries. This innovation is allowing healthcare organizations to rethink how research, teaching, patient treatment, and overall healthcare services are provided, not only domestically, but globally.

Teaching hospitals leverage the innovation to change how students, globally can virtually 'participate' in a surgery, seeing through the eyes of the surgeon, and discussing the activity live. And, students can have an "over-the-shoulder" coach and mentor consortium to be called upon when expert need arises.

In rural locations, from small towns in Texas to the poorest of communities in emerging world countries, access to specialized services for treating cancer, stroke, wound-care, etc are non-existent. Physical distance, and patient mobility are barriers to care that are now non-existent.

Using Smartglass technology, and the software innovation, healthcare organizations are streamlining the entire patient care process; from automating the admittance process, to automating the process to capture care results and creating patient healthcare records. Specialists are now able to extend the reach of their expertise, providing support globally where needed, unconstrained by physical location.

With a rapidly increasing global population, and aging population, traditional models to provide healthcare are no longer viable. Technology, and innovation is the force-multiplier (or "Workforce Mulitplier") that can allow any healthcare worker to be as smart as the smartest healthcare professional globally. The benefits are just now being realized, and new applications are being discovered by users as they integrate smartglass solutions into daily operations. However, like all new innovations there are limitations. In this presentation we will introduce the audience to innovations in smartglass, assisted reality, and augmented reality. This presentation will discuss specific use cases being deployed today, and discuss current limitations, and future industry trends.

PERMEATION AND PERVAPORATION OF WATER THROUGH CONTACT LENS MATERIALS.

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Purpose: Evaporation of water through a contact lens can dehydrate the front surface and is one of the main routes by which water is removed from the ocular environment. Measuring water transport through contact lenses is important for understanding its influence on ocular hydration and comfort. New methods to measure permeation and pervaporation rates have been developed and were used to measure various lens materials.

Methods: Permeation experiments (n=3 per material) were carried out using a diffusion cell where the lens was used as a membrane separating two reservoirs of saline. The rate at which isotopically labeled water traversed the lens was measured using nuclear magnetic resonance spectroscopy. Pervaporation experiments (n=3 per material) were carried out gravimetrically in a dynamic vapor sorption instrument that provided complete control over temperature and humidity of the environment.

Results: Water permeation rates were found to range from 5 to 50 $\mu L/min/cm^2$, while water pervaporation rates were found to be 0.5 to 1.5 $\mu L/min/cm^2$. Taken together, these results indicate that evaporation from the surface of the lens is the rate limiting step to water loss from the contact lens. This is further substantiated by demonstrating that the evaporation rate is independent of lens thickness. Tests on in-vitro lenses show that for some materials, adsorption of protein and lipids from the tear film can increase the rate of evaporation.

Conclusions: Evaporation is the rate limiting step to loss of water from the front surface of the lens and is material dependent. Adsorption of tear film components can significantly increase the rate of water loss from the lens by evaporation. [Authors are employees of Johnson & Johnson Vision Care, Inc

NEUROPATHIC PAIN AS A DISTINGUISHING FACTOR AMONG SJÖGREN AND NON-SJÖGREN SYNDROME PATIENTS WITH DRY EYE DISEASE.

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Purpose: Ocular surface pain or discomfort has been used as an element in the diagnosis of dry eye syndrome, including Sjögren's syndrome (SS). The present work compared clinical characteristics of

patients with confirmed SS and inconclusive cases, (NONSS). The goal of the present work is to investigate whether a set of signs and symptoms can distinguish the two groups.
Methods: This study has approval from the local Ethics Committee. Two random samples of patients were evaluated: SS with dry eye (n = 54), incomplete SS (NonSS) with dry eye (n= 22) (American-European Criteria for SS). The evaluation consisted of a comprehensive protocol that included six variables: Index of Ocular Surface Disease (OSDI); Pain Detect (Neuropathic pain); breakup time of the tear film (TBUT); vital staining corneal fluorescein(CF), Schirmer test (ST) and Patient Health Questionnaire (PHQ9). The SAS JMP Software, version 10.0. DED diagnosis was made if: ST <10 mm and/or TFBUT ≤ 6 s and/or the CF > 3.
Results: The groups were similar in age, sex, OSDI (SS=50.19±20.1 and nonSS=47.22±20.48 for OSDI , p=0,8515) and PhQ9 (SS=12.54±9.61 and nonSS=17.4±6.94, p=0.3938) , TFBUT (SS=2.96±2.05; and nonSS=3.95±3.33, p=0.3025). Neuropathic pain score was higher on non SS group (SS=10.11±7.01 and nonSS=19.5±9.41, p=0.0033*). CF and ST were significantly lower in SS group (3.2±2.91 and 1.36±2.55, p=0.0043* for CF and 8.33±10.33 and 12.54±10.96, p=0.0309* for ST, respectively.
Conclusions: The results revealed that SS and non-SS groups are distinguishable conditions considering ocular surface signs and neuropathic pain symptoms. This finding suggests that is useful to address neuropathic symptoms to discriminate between SS and nonSS patients. Further studies will investigate whether other signs and symptoms can contribute to differentiating SS and nonSS.
Financial Support: FAEPA, CNPq, FAPESP, NAP-FTO.

OCULAR SURFACE PAIN AND AS A DISCRIMINANT SYMPTOM IN DRY EYE DISEASE.

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Purpose: Ocular surface pain or discomfort has been used as an element in the diagnosis of dry eye syndrome, including Sjögren's syndrome (SS). The present work compared clinical characteristics of patients with confirmed SS and inconclusive cases, who did not fit on the American-European Criteria for SS (non SS). The goal of the present work is to investigate whether a set of signs and symptoms is able to distinguish the two groups of diseases usually identified with dry eye.
Methods: This study has approval from the local Ethics Committee. Two random samples of patients were evaluated: SS with dry eye (n = 54), incomplete SS (Non SS) with dry eye (n= 26). Evaluation consisted of a comprehensive protocol that included six variables: Index of Ocular Surface Disease (OSDI); Pain Detect® (Neuropathic pain); breakup time of the tear film (TBUT); vital staining corneal fluorescein(CF), Schirmer test (ST) and Patient Health Questionnaire (PHQ9). The SAS JMP Software, version 10.0 was used. DED diagnosis: ST <10 mm and/or TFBUT ≤ 6 s and/or the CF>3. Severity was categorized based on a method adapted from the Dry Eye Workshop (DEWS, 2007).
Results: The groups were similar in age, sex, OSDI and PhQ9 (10.75±8.86 and 19.2±8.19, p=0.0905) scores. TFBUT where SS achieved 49.39±19.73; and nonSS 46.64±20.03, p=0.8347. Neuropathic pain score was higher on non SS group (9.53±6.15 and 19.8±8.85, p=0.0003*). CF and ST were significantly lower in SS group (3.31±2.98 and 1.53±2.46, p=0.0061 for CF and 8.08±10.13 and 12.32±11.44, p=0.0481 for ST, respectively.
Conclusions: The results revealed that SS and non SS groups are distinguishable conditions considering signs and neuropathic pain symptoms.Further studies will investigate whether other signs and symptoms can contribute to differentiate SS and nonSS and the implication to the understanding of the pathophysiology of those diseases.
Financial Support: FAEPA, CNPq, FAPESP, NAP-FTO.

DEFINITION AND CLINICAL ENDPOINTS FOR CHRONIC NEUROPATHIC PAIN.

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This presentation will provide a general overview of characteristics, mechanisms, and assessment of neuropathic pain.
Chronic neuropathic pain is persistent pain that is caused by a lesion or disease of the somatosensory nervous system. In cases of obvious trauma or disease of the nervous system, diagnosis of neuropathic pain may be straightforward, but, for other cases, a thorough history and physical exam, including the evaluation of somatosensory function, are essential to guide diagnosis. In recent years, standardized assessment tools have been developed to assist with neuropathic pain diagnosis, and to measure the severity of signs and symptoms related to neuropathic pain, for both research and clinical purposes. Although a number of mechanisms related to neuropathic pain have been identified, defining the specific mechanisms implicated in pain on a patient-by-patient basis is not yet possible. Thus, for many types of neuropathic pain, particularly those due to central somatosensory nervous system dysfunction, treatment is often inadequate.
Grant support: Supported by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Clinical Sciences Research EPID-006-15S (Dr. Galor), NIH Center Core Grant P30EY014801, Research to Prevent Blindness Unrestricted Grant (institutional), NIH NIDCR RO1 DE022903 (Dr. Levitt)

CHARACTERIZATION OF DRY EYE DISEASE AND MEIBOMIAN GLAND DYSFUCNTION AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION.

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Purpose: this study aimed to describe incidence, clinical features and outcome of dry eye disease (DED) and meibomian gland dysfunction (MGD) associated with ocular graft-versus-host disease (oGVHD) in allogeneic hematopoietic stem cell transplantation (allo-HSCT) patients to better understand diagnosis and treatment endpoints.
Methods: cross-sectional study of ocular surface disorders related to allo-HSCT. We performed a comprehensive ocular evaluation, including, symptom score (OSDI), tear break-up time (TBUT), Schirmer's test, ocular surface staining, meibomian gland score. Indeed, indications for allo-HSCT, human leukocyte antigen, gender and donor matching, systemic manifestation and treatment were noted.
Results: GVHD occurred in 80% of 42 allo-HSCT patients (age 54.6±8.8 yo) included in the study at 191.2 ± 96.6 days after the

procedure. GVHD risk factors identified included female gender, relapse, HLA, gender and donor mismatch. oGVHD was noted in 75% of chronic GVHD. GVHD oral and dermatological involvement showed a significant association with oGVHD. Ocular surface disorders were frequently observed after HSCT as noted by results of OSDI 18.1±13.1, TBUT 5.1±3.5 sec, corneal fluorescein staining 3.6±4.1, Schirmer 8.1±8.7 and MGD scores in 88%. Results demonstrate that MGD is significantly increased in patients with ocular GVHD as well as prior to HSCT, in our study 66.7% presented besides normal tear volume (14.8±10.2), TBUT (8.7±4) and no other ocular surface signs. Conclusions: This study suggests that DED and MGD in GVHD patients is likely to be a multifactorial process that also occurs prior to HSCT, possibly due to underlying diseases and/or secondary to chemotherapy or irradiation. Diagnostic criteria and ocular endpoints must be carefully evaluated in order improve outcomes and avoid complications.
Financial Support: Fapesp grant#2014/19138-5

EYE DISEASE FROM DIAGNOSIS TO TREATMENT: A SURVEY OF PATIENTS WITH AND WITHOUT SJÖGREN'S SYNDROME IN EUROPE.

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Purpose: Dry eye disease (DED) has high prevalence, and the potential association with systemic autoimmune conditions, such as Sjögren's syndrome (SS), may complicate the patient experience/journey. In order to better determine these experiences, we conducted a large European survey of DED patients.

Methods: A specifically developed electronic survey with 35 questions was used in DED patients with and without SS. The questions related to time to diagnosis, diagnosing process and treating physicians, treatments used and impact on quality of life (QoL), among others. Inclusion criteria were: health care professional (HCP)-diagnosed DED, over 40 years of age, no contact lenses, and use of some form of topical eye treatment daily for six months or more.

Results: A total of 1154 DED patients (472 Sjögren's) from France, Germany, Italy, Spain and the UK participated in the survey. In Sjögren's patients, longer time to diagnosis correlated with higher impact on QoL ($r=0.113$; $p=0.017$). In both groups, seeing more HCPs before diagnosis was related to higher impact on QoL (31% who saw one vs 50% who saw more than one reported high QoL impact; χ^2 $p<0.0001$). Interestingly, 54 respondents (37 Sjögren's) saw an ophthalmologist who did not diagnose their condition before seeing a second HCP who correctly diagnosed DED, and these patients reported a higher impact on QoL (57% vs 39%; χ^2 $p=0.01$).

Conclusions: While differences exist between DED patients with and without SS, the time taken and number of HCPs seen before diagnosis appear to be important factors related to QoL. Our data suggest that earlier diagnosis and treatment may have a significant beneficial impact on QoL of patients with DED.

COMMENSAL OCULAR MICROFLORA AND TEAR PARAMETERS IN A NORMAL POPULATION.

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Purpose: We assessed a normal aging population for associations of ocular commensal microflora burden of the lower lid margin with tear parameters comprising invasive and non-invasive tear break up time (TBUT), tear meniscus height, and tear osmolarity.

Methods: Subjects (184), aged 25 to 66 years with no systematic conditions, pre-existing ocular irritation, injury or infection were recruited. Ocular swabs were taken from the lower lid margin of the left eye for cultivation. Non-invasive tear break-up-time (NITBUT) was measured between full eye opening after a blink and appearance of first visible break or initiation of a reflex blink. An average of the three consecutive readings was recorded. Tear meniscus height was measured using Tearscope and the graticule in slit lamp biomiscrosope at 16X magnification, in increments of 0.1 mm. Tear osmolarity was measured using TearLab Osmometer. The fluorescein (invasive TBUT) was measured after two full blinks and stopped after the first tear film break was observed. An average of the three consecutive readings was recorded.

Results: Colony count ranged from 0 to 1500 cfu/swab. Gram positive burden was negatively correlated with NIBUT ($r = -0.17$, $p = 0.021$) and invasive TBUT ($r = -0.19$, $p = 0.009$), as well as tear meniscus height ($r = -0.26$, $p < 0.001$). There was a significant ($p = 0.006$) decrease in invasive TBUT (13 s vs 22 s) and a significant ($p = 0.034$) increase in osmolarity (304 mOsm vs 296 mOsm) for subjects whose swabs showed the presence of Gram positive bacteria versus samples with no viable bacteria. There was no correlation for cultivation of fungi and any tear parameters.

Conclusions: Higher numbers of Gram positive bacteria obtained from the lower lid margin were associated with decreased TBUT and NITBUT and increased tear osmolarity indicating an association of increased ocular Gram positive burden and decreased tear film stability.

IS ANYBODY THERE?

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Purpose: Indirect evidence from microbial DNA sequencing and the results of experiments utilizing germ-free or antibiotic treated mice are the basis for the notion that the ocular surface hosts a bacterial microbiome important for maintaining ocular surface health. For the conjunctiva, culture positive results provide direct evidence for small numbers of a few species in ~60% of people. Whether the cornea supports a microbiome despite its many defenses against microbes remains an open question. An obstacle to progress is that some bacteria are unculturable by standard methods. Additionally, some culturable bacteria can transition into viable but non culturable (VBNC) states when stressed. Here, we developed alternative direct methods based on the principle that bacteria are large enough for observation using a microscope.

Methods: Two methods were developed to visualize bacteria in the context of mouse corneas. One utilized a click chemistry reaction to label only metabolically active bacteria; the other labeled all bacteria irrespective of viability or shape. Both methods were used on mouse corneas with or without P. aeruginosa inoculation. Additionally, an osmoprotective medium was used to explore if corneas harbored L-forms, a type of VBNC state.

Results: No bacteria were detected on uninoculated corneas by any of the methods. All of the methods, however, detected inoculated P. aeruginosa validating their use in mouse eyes in situ. P. aeruginosa were not seen transitioning into L-forms after inoculation onto the cornea.

Conclusions: The healthy C57BL/6 mouse cornea does not host a bacterial microbiome. Thus, positive findings using germ free or antibiotic treated mice are likely due to bacteria elsewhere at the ocular surface or beyond. Factors involved in maintaining the germ-free status of the cornea warrant further investigation, as do the mechanisms by which they are compromised to enable infection in susceptible people.
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OCULAR SURFACE IN LATIN AMERICA: UNIQUE CHALLENGES AND UNMET NEEDS.

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The current population of Latin America is 422,670,933, which is equivalent to 5.69% of the total world population. Most of Latin America is located in the tropics and the climate is predominantly wet and hot, which creates predispositions to peculiar diseases. For instance, there is an increased incidence of pterygium noted in Latin America. Higher incidence is associated with chronic sun exposure (ultraviolet light), older age, male sex, and outdoor activity. Corneal visual impairment encompasses a wide variety of infectious and inflammatory eye diseases that cause scarring of the cornea. Trachoma is responsible for nearly 4.9 million blind, mainly as a result of corneal scarring and vascularization. Ocular trauma and corneal ulcerations are significant causes of corneal blindness. They are often underreported but they are estimated at 1.5 to 2.0 million new cases of unilateral blindness every year. Among the causes of childhood ocular surface diseases, we can list xerophthalmia, new-born conjunctivitis, and rarer ocular infections like herpes and keratoconjunctivitis. New strains of old diseases with different immunological characteristics, increased virulence, and different responses to antibiotics are often responsible for new outbreaks of diseases. Onchocerciasis and leprosy, although better controlled by the public health entities, are still significant causes of blindness. When we discuss eye allergy treatment we question how can we improve eye allergy medication therapy? Perhaps low adherence to the treatment in Latin America continues to play a major impediment to effective management of this condition. Environmental dry eye disease has also to be discussed since several countries in Latin America have high levels of pollution. Corneal graft and Eye Banks face divergent circumstances, such as economic limitations, social dilemmas, political and institutional religious barriers, and varying levels of education. Ultimately, the Latin American region is considered one of the most inequitable in the world in terms of distribution of goods and services, social determinants, and health. The availability of eye care services varies from country to country within the region, and the number of ophthalmologists per million population in the richest countries may be nine times more than in the poorest. Access to ophthalmological assistance is problematic in countries with isolated areas in the rainforest or high mountains, poor road systems and lack of public transportation.

EXPRESSION OF VAMP8 IN CHRONIC OCULAR GRAFT VS HOST DISEASE.

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Purpose: Dry eye is the most common eye disorders caused by chronic graft-versus-host disease (cGVHD) after allogeneic hematopoietic stem cell transplantation. Soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) proteins are known to be required for exocrine glands to release secretory granules, and we reported that one of the SNARE proteins was reduced in the lacrimal glands in Sjögren syndrome (SS) patients. However, the correlation between SNARE proteins and cGVHD has yet to be reported. In this study, we investigated whether the SNARE protein VAMP8 was implicated in the development of lacrimal gland and conjunctival cGVHD.

Methods: We examined the human lacrimal glands and conjunctiva impaired by cGVHD, and used the SS-affected lacrimal glands and conjunctiva as control subjects. In addition, we collected the lacrimal grands from cGVHD-impaired mice and syngeneic controls 2 to 8 weeks after bone marrow transplantation (BMT). We then conducted immunohistochemical and histopathological examination of these samples and measurement of the gene expression of VAMP 8.

Results. The human conjunctiva affected by cGVHD had thinner epithelia and showed the lower protein level of VAMP8 compared with the SS control subjects. The protein expression of VAMP8 in the human lacrimal glands was decreased in the case where lacrimal gland epithelia were damaged. Tear secretion in mice with cGVHD was significantly reduced 8 weeks after BMT in comparison with those without cGVHD. We also investigated the ratios of VAMP 8 gene expression in the murine lacrimal glands with to without cGVHD 2, 3, 5 and 8 weeks after BMT. The values were 0.31, 0.20, 2.24 and 1.12, respectively.

Conclusion: This study has suggested that the cGVHD-affected lacrimal glands and conjunctiva display the decreased protein and mRNA levels of VAMP8 and that they are involved in the pathogenic processes of dry eye induced by cGVHD in both animal model and humans.

IMPACT OF MICROBIOTA ON RESISTANCE TO OCULAR *PSEUDOMONAS AERUGINOSA*–INDUCED KERATITIS.

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Purpose: The existence of the ocular microbiota has been reported but functional analyses to evaluate its significance in regulating ocular immunity are currently lacking.

Methods: We compared the relative contribution of eye and gut commensals in regulating the ocular susceptibility to *Pseudomonas aeruginosa*–induced keratitis.

Results: We find that in health, the presence of microbiota strengthened the ocular innate immune barrier by significantly increasing the concentrations of immune effectors in the tear film, including secretory IgA, complement proteins, and iron scavenging proteins. Consistent with this view, Swiss Webster (SW) mice that are typically resistant to *P. aeruginosa*–induced keratitis become susceptible due to the lack of microbiome. This was exemplified by increased corneal bacterial burden and elevated pathology of the germ free (GF) mice when compared to the conventionally maintained SW mice. The protective immunity was found to be dependent on both eye and gut microbiota with the eye microbiota having a moderate, but significant impact on the resistance to infection. These events were IL-1ß–dependent as corneal IL-1ß levels were decreased in the infected GF and antibiotic-treated mice when compared to the SPF controls, and neutralization of IL-1ß increased the ocular bacterial burden in the SPF mice.

Conclusions: Cumulatively, these data underline a previously unappreciated role for microbiota in regulating susceptibility to ocular keratitis. We predict that these results will have significant implications for contact lens wearers, where alterations in the ocular commensal communities may render the ocular surface vulnerable to infections. Further, we will discuss the cellular and molecular mechanisms of how colonizing with different gram-positive commensals including *Coagulase Negative Staphylococcus sp, Streptococcus sp*, *Propionibacterium sp* affects resistance to *P. aeruginosa*-induced infections in susceptible C57Bl/6 mice.

DIAGNOSIS AND MANAGEMENT OF CORNEAL SOMATOSENSORY DYSFUNCTION.

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Purpose: To review the diagnosis and management of corneal somatosensory dysfunction in patients with dry eye symptoms.
Methods: Prospective, cross sectional study and review of the literature
Results: In this talk, we will summarize data on patient reported (ocular pain questionnaires) and physician assessed (confocal microscopy, corneal and cutaneous quantitative sensory testing, conjunctival blood flow) metrics that provide insight on cornea pain. Pathophysiological implications of testing (peripheral, central sensitization, co-morbid conditions) will be discussed. We will further review how these techniques may alter the treatment of dry eye symptoms, including topical and systemic approaches to modulate corneal somatosensory function.
Conclusions: Corneal somatosensory dysfunction likely underlies chronic dry eye symptoms in some individuals. New diagnostic techniques and treatments are needed to individualize management algorithms in dry eye. Grant support: Supported by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Clinical Sciences Research EPID-006-15S (Dr. Galor), NIH Center Core Grant P30EY014801, Research to Prevent Blindness Unrestricted Grant (institutional), NIH NIDCR RO1 DE022903 (Dr. Levitt)

TEAR DYNAMICS EVALUATION WITH FLUORESCEIN PROFILOMETER AND OPTICAL COHERENCE TOMOGRAPHY

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Purpose: To describe a newly-developed method for tear dynamics assessment with fluorescein profilometer and optical coherence tomography-based method of Tear Turnover Rate (TTR) assessment, to evaluate clinical utility of the methods, search for correlation between TTR and other measures of tear film.
Methods: Twenty-six subjects (18F and 8M) aged 34.8±16.3 years and two special cases (severe dry eye disease and keratoconus) volunteered for the study. It consisted of medical history review, McMonnies questionnaire (McMQ), slit lamp examination, and the assessment of TTR using our newly-developed profilometry method (TTR_{FTP}) and OCT-based measurement of dynamic changes in tear meniscus morphology (TTR_{OCT}). Estimates of TTR were contrasted against each other, patient age, daytime, McMQ score, fluorescein tear film break-up time (FTBUT), and blink frequency.
Results: The group mean TTR_{FTP} and TTR_{OCT} was 45±24% and 24±16% at 30-second and 60-second mark after the beginning of measurements, respectively. For TTR_{FTP}, statistically significant correlations were found with McMQ score (r^2=0.139, p=0.033) and FTBUT (r^2=0.158, p=0.024). For TTR_{OCT}, statistically significant correlations were found with FTBUT (r^2=0.338, p=0.001), blink frequency (r^2=0.256, p=0.004), and the time between subject's awakening and the beginning of measurements (r^2=0.158, p=0.024). The pilot study showed that TTR_{OCT} measurements are repeatable and that tear meniscus height has higher indicative value than tear meniscus depth for TTR estimation. The case of keratoconus showed probable association between corneal steepness and TTR while the case of dry eye subject showed high decrease in TTR .
Conclusions: The study shows that fluorescein profilometry could be exploited for assessing TTR. Measurements are repeatable and may be used for dry eye diagnosis, following dynamic changes in the tear film. Acknowledgements. This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 642760.

CONJUNCTIVAL GOBLET CELL REGULATION BY ALLERGIC MEDIATORS.

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Purpose: To determine if Th2 cytokines IL4, IL5 and IL13, players in allergic conjunctivitis, directly regulate mucin production in rat conjunctival goblet cells (GCs).
Methods: First passage GCs were grown from male Sprague-Dawley rat conjunctiva. Due to its role in goblet cell signaling $[Ca^{2+}]_i$ was measured with the dye Fura2. GCs were stimulated with IL4, IL5, or IL13 (10ng/ml) for 24 h and histamine (10^{-5}M) for 2 h and proliferation was measured with AlamarBlue. The media were analyzed for high molecular weight glycoconjugate secretion using an enzyme-linked lectin assay.
Results: IL4 increased peak in $[Ca^{2+}]_i$ by 117.2±11.9 nM (p=0.00006), IL5 by 114.0±36.3 (p=0.019), and IL13 by 251.2±95.9 (p=0.039). After 2.5 min, 15 min, or 24 h treatment with the cytokines, the effect of histamine was measured. IL4 blocked histamine-mediated increase in $[Ca^{2+}]_i$ at 15min, IL5 at 2.5 min, and IL13 at 2.5 min, 15 min, and 24 h. Histamine has 4 receptors (H1-4): all present in GCs. An H1 agonist, histamine dimaleate (HD, 10^{-6}M) was used to study its interaction with the cytokines. The increase in $[Ca^{2+}]_i$ induced by HD (348.6±37.2 nM) was equivalent to histamine (309.2±58.6 nM). In addition, after 2.5 min pretreatment, IL5 and IL13 reduced the effect of HD, similarly to histamine. This suggests that histamine effect was mainly produced through H1. HD blocked IL13-mediated increased in $[Ca^{2+}]_i$, but not IL4 or IL5. To analyze this interaction we explored the cellular Ca^{2+} pools used by HD and IL13. Responses were reduced in the absence of extracellular Ca^{2+} and in the presence of thapsigargin that depletes intracellular Ca^{2+} stores indicating that the same Ca^{2+} stores are used. IL13 also stimulated GC proliferation. After 24 h, Th2 cytokines increased mucin secretion.
Conclusions: Th2 cytokines, and specially IL13, affect multiple processes that regulate mucin production and secretion by conjunctival GCs. [Funding: NIH EY019470; Government of Spain MAT2013-47501-C2-1-R and BES-2011-046381]

IN VITRO EFFECTS OF SEX HORMONES IN HUMAN MEIBOMIAN GLAND EPITHELIAL CELLS.

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Purpose: Meibomian gland dysfunction (MGD) is considered the most common cause of dry eye disease (DED). Sex hormones show a significantly influence to MGD pathogenesis although their involvement is not completely understood. Therefore, in the present study we evaluated the effect of dihydrotestosteron (DHT) and β-estradiol (β-Est) on an immortalized human meibomian gland epithelial cell line (HMGEC).
Methods: HMGEC were stimulated with 1 nM β-Est and 10 nM DHT for 24 hours. Protein expression of sex hormone receptors was investigated by western blot. Ultrastructural morphology, Sudan III lipid staining, cell proliferation as well as vitality assays were performed. Furthermore, expression of MGD-associated markers for keratinization (hornerin, involucrin and CK6), proliferation (CK5 and CK14) and lipid synthesis (fatty acid synthase and stearoyl-CoA desaturase) were analyzed by real time RT-PCR.

Results: Western blot revealed presence of androgen receptor (AR), estrogen receptors α and -β (ERα, ERβ) and progesterone receptor (PR) in HMGEC. PR, ERα and ERβ expression was significantly increased after cultivation with serum, whereas sex hormones stimulation showed no further effect. Both sex hormones did not influence cellular morphology and lipid accumulation compared to untreated HMGEC. Cell proliferation was slightly induced through application of sex hormones. However, both sex hormones modulated gene expression of MGD-associated markers. Especially keratinization genes HRNR and COR were induced after application of sex hormones to HMGEC cultivated in serum-free medium. Conclusion. In HMGEC DHT and β-Est altered gene expression of MGD-associated markers and promote keratinization process. Based on our results HMGEC are a possible in vitro model for further studies of (hyper)keratinization processes that occur during MGD.
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CORRELATION BETWEEN TEAR FILM LIPID LAYER BY INTERFEROMETRY AND SYMPTOMS IN PATIENTS DIABETICS WITH MEIBOMIAN GLAND DYSFUNCTION.

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Purpose: To assess the tear film lipid layer pattern in type 2 diabetes patients and healthy subjects, the correlation of the symptoms between the Ocular Surface Disease Index (OSDI) symptom questionnaire and the National Eye Institute Vision Functioning Questionnaire (NEI-VFQ).

Methods: Case-control study; All patients were investigated for the presence of meibomian gland dysfunction/MGD according to the meibomian glands/MG secretion's quality and viscosity, MG's morphology, and lipid layer thickness/LLT. The LLT was measured using interferometry Polaris system prior and subsequent to a 10-min period. The Ocular Surface Disease Index (OSDI) symptom questionnaire and the NEI-VFQ were correlated. The results between groups were analyzed using the statistical Kruskal-Wallis and Mann-Whitney tests, association between variables was explored by Spearman's correlation.

Results: 73 subjects were studied (37 diabetics and 36 controls). The mean age was 59 ± 8. 71% of participants presented MGD (76% diabetics and 67% controls). The symptoms through OSDI questionnaire was significantly higher (p=0.016) in the diabetic group with a lower NEI-VFQ (67.86; p = 0.002). Positive correlations were found in diabetic group between corneal staining and symptoms with OSDI questionnaire. NIBUT was lower in the diabetic group (sg 2.47 ± 1.2), with a significant inverse correlation (52.22%) with MG inflammation and a moderate correlation (32,4%) with corneal staining. The LLT presented a positive correlation between the meibomian gland alteration as hyperkeratinisation and inflammation (p=0.0005).

Conclusions: A correlation was found between NIBUT, inflammation and obstruction of the MG in type 2 diabetes patients. The LLT is lower in diabetic group than in normal subjects, which implies a decreased tear film stability and increased subjective symptoms associated with a decreased quality of life. Commercial Relationships: none

CLINICAL FEATURES OF MEIBOMIAN GLAND DYSFUNCTION IN PATIENTS WITH DIABETES TYPE 2.

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Purpose: To assess the state of the Meibomian glands of patients with diabetes type 2 and healthy patients, and their relationship to tear function and status of ocular surface, with correlations between time stability of the tear film, the state of the glands meibomian and symptoms.

Methods: Case-control study; All patients were investigated for presence of diagnosis meibomian gland dysfunction/MGD by criteria for International Work Shop in MGD. The volume of tear secretion was studied with phenol red thread test/PRTT and tear meniscus height was measured with optical coherence tomography/OCT. Lipid layer tear and pattern was performed using Polaris interferometry system, and morphology of the glands with Marx line; quality of meibomian secretion expression was studied. The OSDI symptom questionnaire and the National Eye Institute Vision Functioning Questionnaire (NEI-VFQ) were correlated. The results between groups were analyzed using the statistical Kruskal-Wallis and Mann-Witney, and correlations by Spearman.

Results: A total of 73 subjects were studied, 37 diabetics and 36 controls. The mean age was 59 ± 8. The symptoms through OSDI questionnaire was significantly higher (p=0.016) in the diabetic group with a lower NEI-VFQ (67.86; p = 0.002), relative to controls. 71% of participants presented MGD, 76% diabetics and 67% healthy participants. Diabetic group showed major changes in hyperkeratinisation and inflammation in MG (p=0.0005), with secretion type toothpaste (75%). NIBUT was lower in diabetic (2.47 ± 1.2 sc), with a significant inverse correlation (52.22%) with the inflammation of MG. Tear meniscus heigh, lipid pattern and PRTT presented no statistical difference between groups.

Conclusions: MGD occurs most frequently in patients with type 2 diabetes, accounting for evaporative dry eye having a high degree of correlation with inflammation and obstruction of the MG. The value of Hb1Ac has a high degree of correlation with the NEI-VFQ in patients with DGM.

Commercial relationships: none

A NOVEL IMAGING METHOD TO EVALUATE DRY EYE SYNDROME.

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Purpose: Dry eye syndrome (DES) is a multi-factorial condition that is difficult to diagnose, in part due the inconsistent results of objective testing methodologies. The study purpose was to evaluate the Tear Film Imager (TFI), a novel hyperspectral testing methodology using three dimensional white light tomography (3D-WLT), to measure key parameters of tear film composition that are abnormal in the dry eye state..

Methods: DES severity was graded using conventional DES testing methods, including: Schirmer test, tear breakup time (TBUT), tear meniscus height, corneal fluorescein staining and a patient questionnaire. Subsequently, each patient underwent a two-minute TFI test followed by a retest after 30 minutes. The TFI measures the aqueous layer thickness (ALT) at a nanometer level and calculates average ALT as well as the ALT rate. In addition, the TFI measures the lipid layer thickness (LLT) at a sub-nanometer level and establishes average LLT and lipid breakup time (LBUT).

Results: 40 subjects were included. DES severity clinical grading was as follows: 22 severe, 9 mild and 9 controls. The TFI quantitative measurements diagnosed DES subjects with 97% sensitivity and 70% specificity. The TFI LBUT measurement correlated well (Pearson 0.91, p<0.01) to TBUT and distinguished lipid from aqueous layer abnormalities. The TFI ALT measurements were highly agreeable

(Pearson 0.88, p<0.01) between the two measurements and clearly distinguished aqueous tear deficiency patients. The TFI ALT rate measurements demonstrated notable differentiation between the DES subjects and distinguished the presence of evaporative dry eye conditions.
Conclusions: TFI results demonstrated strong agreement with traditional diagnostic methodologies, doing so in a fast, noninvasive manner. The TFI shows promise in distinguishing different etiologies of DES based on quantifiable measured data.

SURFACE INTERACTIONS OF DIQUAFOSOL AND CHLOHEXIDINE GLUCONATE WITH HUMAN MEIBUM FILMS.
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Purpose: To perform a surface chemistry study of the interactions between the chlorhexidine gluconate (CHX) preserved 3% diquafosol tetrasodium solution (DIQUAS) with tear film (TF) constituents. The interactions of TF compounds with CHX solution (0.001, 0.0025, 0.005, 0.01, 0.02%) were also probed and compared with our published data on the effect of benzalkonium chloride (BAC) solutions in identical concentrations.
Methods: Langmuir surface balance measurements were utilized to examine the interactions between the pharmaceuticals and films of human meibum and rabbit corneal cell lipid extracts. Surface pressure (π) –area (A) isocycles were used to assess the sample's performance at dynamic area changes. The dilatational rheology of the layers was probed by stress-relaxation studies. Lipid film morphology was monitored by Brewster Angle microscopy. The viability of DQS and CHX treated Statens Seruminstitut Rabbit Cornea (SIRC) cell cultures was also evaluated. Results. CHX was essentially inert to the surface films while even after penetration in the films DIQUAS compounds mixed well with the lipid molecules. Thus after inclusion of DIQUAS or CHX in the trough subphase the surface layers maintained rough continuous multilayer structure and non collapsible π/A isotherms. The Fourier analysis of π relaxation transients revealed that the lipid films (pure and in presence of DIQUAS or CHX) remained primarily elastic in the frequency range of 10^{-5}-1 Hz. SIRC cells confluence and viability were also maintained after exposure to DIQUAS or CHX. In contrast BAC solutions even at ≤0.005% perturbed the lipid films structure and properties and impaired SIRC confluence and viability.
Conclusions: Surface chemistry studies present criteria for preclinical in vitro molecular scale characterization of the interactions between eyedrop compounds and TF constituents. [This research was supported by grant from Santen Pharmaceutical Co., Ltd., Osaka, Japan.]

HUMAN MEIBOMIAN GLAND EPITHELIAL CELLS PROTECT CORNEAL EPITHELIAL CELLS FROM BAK INDUCED TOXICITY.
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Purpose: The purpose of this study is to determine the critical cytotoxic BAK concentration on telomerase-immortalized Human Corneal Limbal Epithelial Cells (HCLE) using a series of concentrations and different exposure times, and find a way to prevent this damage.
Methods: HCLE were exposed to different BAK concentrations (0.0005% to 0.005%) incubated for 5, 10, or 15 minutes. In another set of experiments, the cells were incubated in conditioned media from immortalized Human Meibomian Gland Epithelial Cell line, at the time of BAK application. Cell proliferation/viability was assessed by MTT assay.
Results: Exposure of HCLE cells to BAK 0.001% or 0.002% for 10 minutes reduced the viability by more than 50%. Simultaneous treatment with Meibomian gland epithelial cell line (kindly provided by Dr David Sullivan, Schepens Eye Research Institute) conditioned media completely reversed the toxicity due to 0.001% and restore viability to near 90% in 0.002% BAK. (P Value <0.05)
Conclusions: These results indicate that BAK induced cell damage might be reduced using secreted factors by meibomian gland epithelial cells. Further studies are needed to determine the mechanism of this protective effect.

DEVELOPMENT OF AN MGD GRADING SCALE FOR USE IN CLINICAL PRACTICE.
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Purpose: Meibomian gland dysfunction (MGD) has a prevalence ranging from 3.5-6.8%, which may partly be due to the lack of standardised diagnostic criteria used between studies. While grading systems have been developed to report the observable features of MGD, their ability to grade key features quickly in clinical setting to allow tracking of change over time has not been optimised. The purpose of this study is to develop a clinical grading scale to sensitively detect change in MGD quickly, without requiring extra technology, other than a slit lamp.
Methods: Two subject groups, whom underwent intervention between baseline (BL) and final visit (F), were analysed: Group A comprised 35 subjects(mean age 37+15 years, range 20-70, 12 male) and Group B comprised 46 postmenopausal women, diagnosed with dry eye, (mean age 64.5+5.2 years, range 53-83). Stage 1 determined parameters sensitive to change by identifying parameters with %change>20% between BL and F. All techniques were timed to allow the quickest battery with the highest sensitivity to be determined. Stage 2 used ROC analysis (Group A:control, Group B:showing MGD signs) to determine the minimum combination of parameters and shortest clinical grading time to give maximum sensitivity and to optimise the area under curve (AUC) and 95% confidence intervals (CI).
Results: Parameters with %change>20% were Marx line (M), vascularity (V), telangiectasia (T), capping (C), secretion expressibilty (E), secretion quality (Q) and number of expressible glands (N). N and M were not reliable parameters for grading disease progression due to their high variability between visits without an intervention. The greatest AUC and highest sensitivity arose from a combination of QET (.750), ET (.727) or QETV (.703). Due to the high co-linearity between Q and E (r=.701) the combination selected was ET which took 2.0 minutes to perform.
Conclusions: Meibomian glands are fundamental for the maintained health and integrity of the ocular surface. This study has identified a combination of parameters, sensitive to disease change, for time-efficient clinical MGD grading.

INFLUENCE OF A NATURAL EYE DROP EMULSION ON NON-IMMUNE MEDIATED ALLERGIC REACTION.
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Purpose: It is known that allergic conjunctivitis is characterized by a thickening in the lipidic layer of tears possibly as a defense mechanism for increased tear film instability. Here, we investigated whether a natural lipid-based o/w buffered emulsion (EMU) may contribute to support ocular defense mechanisms in allergy. To this end, we studied the effect of EMU following ocular instillation in a model of non-immune mediated allergic reaction in rat.
Methods: Twenty-one male Wistar rats (180 g) housed in standard

conditions were assigned to 3 different groups. On the day of the experiment, treatment groups were administered 10 µl of either PBS or 10% EMU at 60, 40 and 10 min before compound 48/80 administration. To assess for extravasation, 1 ml of a sterile 1% Evans blue (EB) solution in 0.9% NaCl was injected i.v. to anaesthetised rats 10 min prior to instillation of 10 µl of compound 48/80 (250 µg). Thirty minutes following challenge, animals were sacrificed and the ocular globe, the upper and lower lids were removed, weighed and left for 24 h in 0.5% sodium sulphate and acetone (3:7, v/v). Solution were then spun at 1800 rpm for 10 min and the supernatant read at 620 nm to measure the amount of dye.

Results: Administration of compound 48/80 to control animals produced extravasation of EB up to 220.8±68.3 µg/g of tissue. In eyes treated with 10% EMU, EB was significantly reduced by 37.6±7.1 % with respect to controls ($p<0.05$, one-way ANOVA plus Dunnett's post test). Conversely, PBS inhibited EB accumulation by 9.5±7.7 failing to attain any significant effect with respect to controls.

Conclusions: A natural lipid-based 10% o/w emulsion significantly attenuated the allergic response in an animal model of ocular allergy. Therefore, it is possible to conclude that administration of tears substitutes containing specific natural lipids may contribute to the homeostasis of ocular surface and provide support in the management of ocular allergies.

NEW ADVANCES IN THE UNDERSTANDING OF THE NEUROBIOLOGY OF CONTACT LENS DISCOMFORT.

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The 2013 TFOS report on neurobiology of contact lens discomfort (CLD) assimilated the existing knowledge about ocular surface neurobiology. Examining learnings from normal neuroanatomy and dry eye research, the report identified possible neurobiological mechanisms specific to CLD. Contact lens wear was proposed to generate CLD by complex interaction of components including induction of hyperosmolarity, desiccation, thermal effects, chemical mediators in lens solutions and possibly those resulting from inflammation, in addition to mechanical stimulation due to physical interaction. The report recommended future research should improve understanding of sensory input from the lid margins, palpebral and bulbar conjunctiva and the roles of post-receptor and central processing in modulating ocular surface sensation. Sensitive assessment techniques at all stages of the neural pathway were important to understand the subtle response of CLD.

Since publication, progress has been made in the areas highlighted by the report. Unsurprisingly, new knowledge has been generated mostly in areas not specific to contact lenses, although many findings can be extrapolated to understanding CLD. Examples include recognition of corneal cold receptors as osmoreceptors, modelling of hyperosmolarity over the ocular surface, consideration of neuropathic pain in the aetiology of symptoms of dry eye, progress in understanding neuro-immune cross-talk, and development of advanced techniques for assessment of nerve morphology and of nerve terminal neurochemistry. Contact-lens specific advances include determination of lens effects on tear neuropeptides, identification of marked and reversible corneal nerve reorganisation during orthokeratology lens wear, characterisation of conjunctival and lid margin sensitivity during lens wear and validation of a contact-lens specific ocular symptoms questionnaire.

Future research should continue to focus on developing advanced techniques and application of current technologies to investigation of structural and functional aspects of neurobiology which are specific to CLD. Key aspects which will improve understanding of CLD include characterisation of the neuroanatomy of conjunctival tissues, visualisation of corneal nerve terminals in vivo, and clarifying the role of CNS and neuroimmune influences.

USE OF AUTOLOGOUS SERUM IN ADVANCED SURFACE ABLATION CORNEAL REFRACTIVE SURGERY.

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Purpose: To evaluate the efficacy of topical autologous serum (TAS) versus its vehicle (BSS) in patients undergoing advanced surface ablation (ASA) corneal refractive surgery.

Methods: Thirty-six eyes of 18 patients who bilaterally underwent ASA surgery were included. After surgery, in a random manner, one eye of each individual received TAS (treatment group) and the contralateral eye received BSS (control group), one drop four times daily, for 3 months. Symptoms (OSDI), LogMAR uncorrected visual acuity (UCVA), tear osmolarity (TearLab), conjunctival hyperemia, tear break-up time (BUT), conjunctival and corneal staining, Schirmer test with anesthesia and corneal sensitivity (Belmonte's esthesiometer), were evaluated before surgery (baseline) and at 1, 3 and 6 months after surgery.

Results: Seven males and eleven females were included, mean age: 34.6±5.8 years. It was found a significant decrease of OSDI values along time ($p<0.004$), being significant between baseline and 3 and 6 months and between 1 month and 6 months; no differences between treatments were found. There was a significant improvement in UCVA up to 3 months in both treatment groups; a significant difference was found between both groups at 1 month (TAS: 0.15±0.21, BSS: 0.07±0.19; $p=0.006$). Tear osmolarity decreased significantly up to 3 months, with a significant difference between groups at 1 month (TAS: 306.5±17.05, BSS: 314±18.04; $p=0.019$). There were significant differences in Schirmer test ($p=0.013$) and mechanical threshold ($p=0.027$) between baseline and 6-months, but no differences were found between treatment groups.

Conclusions: The use of TAS after ASA improved tear osmolarity faster than BSS. Whether this will result in a long-term benefit making it worth the expense has to be further elucidated. No commercial relationships. Study supported by project: VA174U14, Consejería de Educación, Junta de Castilla y León, Spain.

MUCOUS MEMBRANE GRAFTS IN OCULAR CICATRICIAL PEMPHIGOID: SCHIRMER'S TEST AND LONG TERM FORNIX DEPTH OUTCOMES.

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Purpose: Conjunctival fornix reconstruction using a labial, buccal or hard palate mucous membrane graft to restore mucosal surface area, is sometimes necessary for correction of advanced fornix contracture in ocular cicatricial pemphigoid (OCP). The aim of this study was to evaluate long term outcomes of mucous membrane grafts in OCP including fornix depth measurements, and identify optimum criteria for successful fornix reconstruction.

Methods: Retrospective review of 25 OCP eyes receiving mucous membrane graft fornix reconstruction at Moorfields Eye Hospital between 1997 – 2010. Average follow up duration was 54 ± 30 months (Range 8 – 125 months).

Results: Indications included ankyloblepharon (32%), exposure with lagophthalmos (32%) and entropion with lid shortening (36%). For the 12 wet eyes with Schirmer's test ≥5mm, mean fornix depth appeared to be maintained long term and measured 6 ± 1 mm in the lower fornix, and 10 ± 3 mm in the upper fornix. For the 13 dry eyes with Schirmer's test <5mm, mean lower fornix depth was smaller 3 ± 2 mm ($p=0.005$), and upper fornix depth 9 ± 3 mm. Final visual acuity was 0.34 ± 0.3 in the wet eyes, and 0.18 ± 0.3 in dry eyes ($p=0.24$). All eyes were immunosuppressed for at least 4 months prior to the mucous

membrane graft, and systemic immunosuppression was increased post-operatively in 4 eyes. Complications including bacterial keratitis (20%), persistent epithelial defect (16%), surface failure (8%) and recurrent entropion (28%) occurred most frequently in the dry eyes.
Conclusions: Eyes with Schirmer's test 5mm or more do best with mucous membrane grafting in OCP, with long term maintenance of inferior conjunctival fornix and good visual acuity. Control of inflammation with systemic immunosuppression prior to mucous membrane graft surgery, and increased postoperative immunosuppression where necessary, is a requirement for success of the procedure. [This research was supported by the NIHR Biomedical Research Centre at Moorfields and UCL Institute of Ophthalmology. No financial disclosures.]

BIOENGINEERED CORNEA.

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We have previously shown that recombinantly produced analogs of human collagen promoted functional regeneration of corneal epithelium, stroma and nerves when used as substitutes of human donor corneas for treating corneal blindness. These recombinant human collagen (RHC) implants comprised fibrils that were fine and aligned, like those in human corneas. There were noticeable differences such as the uniaxial alignment of the implant fibrils compared to the biaxial alignment in the cornea, and the lack of D-banding of collagen fibrils in the implants. Nevertheless, the aligned fibrils facilitated an orderly in-growth of corneal stromal cells to form a neo-stroma. These RHC implants when reinforced with a second network of MPC, a phospholipid polymer with anti-inflammatory properties, were well-tolerated as pro-regeneration grafts in corneas with severe pathologies (e.g. alkali burn, previous failed graft, HSK scar) that put them at high risk of rejecting conventional donor corneas. The implants alleviated patients from pain and discomfort, and restored corneal integrity. However, RHC replicates native collagen and as such, is a large protein that is difficult to purify and manipulate, leading to cost-prohibition when considering mass production for clinical use, particularly since the majority of cornea blind patients are in developing countries. We therefore examined short peptide analogs of collagen, i.e. collagen-like peptides (CLPs) as more controllable and as more processable mimics for scale-up and manufacturing. Here, we conjugated a CLP to a PEG-maleimide backbone for mechanical strength and stability and the resulting hydrogel was moulded and cross-linked to form corneal implants. Twelve month pre-clinical results from a mini-pig model showed that the CLP-PEG scaffolds allowed regeneration of corneal cells and nerves just as well as the full-length RHC. Our results therefore show that pro-regeneration bioengineered corneas comprising highly aligned fibrils mimicking the highly ordered corneal ECM promotes regeneration of a functional neo-cornea.

EFFICACY OF A SINGLE LIPIFLOW THERMAL PULSATION TREATMENT ON MEIBOMIAN GLAND DYSFUNCTION IN A DRY EYE COHORT FROM ASIA.

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Purpose: To evaluate the effect of LipiFlow treatment on meibomian gland expression, dry eye symptoms, lipid layer thickness and tear film stability in a cohort of dry eye patients from India.
Methods: The data of 54 eyes of 47 patients who had undergone a single 12-minute LipiFlow treatment and who were available at their respective 6 and 12 months follow-up were reviewed retrospectively. The study parameters were SPEED score, number of meibomian gland yielding liquid secretions (MGYLS) (indicative of the number of functional meibomian glands), tear break-up time (TBUT), lipid layer thickness (LLT), and Schirmer test type I (without anesthesia) and II (with anesthesia).
Results: There was a statistical significant improvement in SPEED, MGYLS, LLT and TBUT at post-treatment 6 months from baseline ($p<0.001$). This improvement from pre-treatment levels observed at 6 months was maintained up to post-treatment12-month visit ($p \leq 0.004$ from baseline; $p > 0.05$ from post-treatment 6 months to 12 months). However, there was no significant change in Schirmer test findings (both I and II) at post-treatment 6 or 12 months from baseline.
Conclusion: A single LipiFlow treatment significantly improved signs and symptoms of MGD associated evaporative dry eye and is effective for at least 12 months in Asian Eyes. [The authors have no financial disclosures to make]

TEAR VOLUME CHANGES OVER THE INTERBLINK PERIOD.

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Purpose: The tear volume (TV) is clinically reported by the measurement of the tear prism height, without indication of the measurement time within the interblink (IB) period. The objective of the study was to quantify the change in TV during the IB period within a population of contact lens wearers (CLW) and non-wearers (NW).
Methods: Digital videos of the lower tear prism were captured using non-invasive Tearscope illumination and the lower tear prism was analysed post hoc by masked investigators. The population was made up of 129 CLW (age 33.9 ± 10.0 years) and 134 NW (age 42.6 ± 13.0 years).
Results: The Lower Tear Prism Area (LTPA) was on average significantly smaller at the blink than upon eye opening for the overall population ($p < 0.001$) and for CLW ($p < 0.001$) and NW ($p = 0.002$), with a mean overall change of -0.17 ± 0.91mm^2, associated with large individual variations (range -5.67 to +3.60 mm^2). The individual variations were confirmed by the poor correlation between the LPTA on eye opening and at the blink for the overall population ($r = 0.361$) and for CLW ($r = 0.332$) and NW ($r = 0.272$). Conclusion. TV is not a constant value for a given eye but varies over the IB period and between individuals. Therefore the overall kinetics of the TV during the IB period need to be considered in the context of its relevance to dry eye.

EFFECTS OF HYALURONIC ACID WITH DIFFERENT MOLECULAR WEIGHT ON REPAIR OF MECHANICAL DAMAGE OR UV - INDUCED INJURY FOR HUMAN CORNEAL EPITHELIAL CELLS.

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Purpose: Hyaluronic acid (HA) was commonly used as moisturizing and thickening component in ophthalmic solutions or gel formulations. For this reason, traditionally, HA with higher molecular weight (Mw, > 700 kDa) was employed to achieve certain consistency. However, the effects of HA with different Mw on repair of mechanical damage or UV-induced injury for human corneal epithelial cells (HCEC) have not been studied yet. Here we studied the effects of HA with different Mw on the protection and repair of HCEC from mechanical scratch and UV-induced photo-aging.
Methods: The HCEC were cultured under standard conditions (moist atmosphere, 5% CO_2, 37°C) in RPMI 1640 medium supplemented with 10% fetal bovine serum (FBS). To simulate a mechanical damage on corneal surface, when cell confluence reached 80% to 90%, a gap was manually scratched on monolayer of HCEC by a 10uL pipette tip.

Then the injured HCEC were incubated with fresh RPMI 1640 medium containing 0.1% (w/v) of HA (molecular weights of 6kDa, 380kDa, 890kDa and 1230kDa, respectively). After 16 and 48 hours, the proliferation and migration of HCEC within the gaps were evaluated under microscope and photographed. A combination of UVA (7.2 J/cm^2) and UVB (126 mJ/cm^2) was used to form a photo-aging injury on HCEC. To evaluate the protection and repair effect of HA, HCEC was treated with fresh medium containing 0.1% (w/v) of HA (with different molecular weights mentioned above) 16 hours before and just after UV irradiation, respectively. And the mitochondrial activity of injured HCEC was measured by MTT-assay.
Results: The results of scratch test demonstrated that low Mw HA (6kDa and 380kDa) significantly improved the proliferation and migration of HCEC after mechanical damage. The highest cell density in the gaps was observed in HA-380kDa group. UV irradiation effectively inhibited the proliferation of HCEC (60% relative growth rate of negative control). High Mw HA (1230kDa) showed the best repair activity after UV irradiation (up to 78% relative growth rate) and low Mw HA (6kDa and 380kDa) showed better protection effect from UV irradiation damage (kept above 70% relative growth rate).
Conclusion: 1. Low Mw HA (≤40kDa) represents a powerful repair effect on mechanical damage of cornea, such as friction damage by contact lends; 2. A combination of high Mw HA (≥1000kDa) and low Mw HA (≤40kDa) should be a good choice for protecting and repairing the cornea and resist the UV-induced injury from sunlight.

EFFECTS OF HYALURONIC ACID WITH DIFFERENT MOLECULAR WEIGHT ON REPAIR OF MECHANICAL DAMAGE OR UV - INDUCED INJURY FOR HUMAN CORNEAL EPITHELIAL CELLS.

Xueping Guo, Xiaoou Zhang, Dejie Li. Bloomage Freda Biopharm Co., Ltd. Jinan, Shandong, China.
Purpose: Hyaluronic acid (HA) was commonly used as moisturizing and thickening component in ophthalmic solutions or gel formulations. For this reason, traditionally, HA with higher molecular weight (Mw, > 700 kDa) was employed to achieve certain consistency. However, the effects of HA with different Mw on repair of mechanical damage or UV-induced injury for human corneal epithelial cells (HCEC) have not been studied yet. Here we studied the effects of HA with different Mw on the protection and repair of HCEC from mechanical scratch and UV-induced photo-aging.
Methods: The HCEC were cultured under standard conditions (moist atmosphere, 5% CO_2, 37℃) in RPMI 1640 medium supplemented with 10% fetal bovine serum (FBS). To simulate a mechanical damage on corneal surface, when cell confluence reached 80% to 90%, a gap was manually scratched on monolayer of HCEC by a 10uL pipette tip. Then the injured HCEC were incubated with fresh RPMI 1640 medium containing 0.1% (w/v) of HA (molecular weights of 6kDa, 380kDa, 890kDa and 1230kDa, respectively). After 16 and 48 hours, the proliferation and migration of HCEC within the gaps were evaluated under microscope and photographed. A combination of UVA (7.2 J/cm^2) and UVB (126 mJ/cm^2) was used to form a photo-aging injury on HCEC. To evaluate the protection and repair effect of HA, HCEC was treated with fresh medium containing 0.1% (w/v) of HA (with different molecular weights mentioned above) 16 hours before and just after UV irradiation, respectively. And the mitochondrial activity of injured HCEC was measured by MTT-assay.
Results: The results of scratch test demonstrated that low Mw HA (6kDa and 380kDa) significantly improved the proliferation and migration of HCEC after mechanical damage. The highest cell density in the gaps was observed in HA-380kDa group. UV irradiation effectively inhibited the proliferation of HCEC (60% relative growth rate of negative control). High Mw HA (1230kDa) showed the best repair activity after UV irradiation (up to 78% relative growth rate) and low Mw HA (6kDa and 380kDa) showed better protection effect from UV irradiation damage (kept above 70% relative growth rate).
Conclusion: 1. Low Mw HA (≤40kDa) represents a powerful repair effect on mechanical damage of cornea, such as friction damage by contact lends; 2. A combination of high Mw HA (≥1000kDa) and low Mw HA (≤40kDa) should be a good choice for protecting and repairing the cornea and resist the UV-induced injury from sunlight.

PREVALENCE OF DRY EYE DISEASE IN THE ADULT INDIAN POPULATION

Noopur Gupta,1 Praveen Vashist, 1Vivek Gupta,1 Meenakshi Wadhwani,1 Radhika Tandon, 1 1Dr. Rajendra Prasad Centre for Ophthalmic Sciences, AIIMS, New Delhi, India.
Purpose: To evaluate the prevalence and risk factors for dry eye disease (DED) in a rural population of India.
Methods: This population-based study conducted in the National Capital Region, India included 3595 individuals aged 40 years and above. The participants were selected randomly from 35 rural clusters with total enumerated population of 18015. Demographic details, risk factor assessment, questionnaire administration and comprehensive ophthalmic evaluation were performed. Dry eye was assessed using OSDI questionnaire and a score of more than 35 was taken as an indicator of dry eye. Clinical tests including the Schirmer's I test without anaesthesia and tear film break-up time (BUT) were performed in the community through a portable slit lamp. DED was defined as Schirmer's I test value of less than 10 mm and a break up time of 10 seconds.
Results: The prevalence of DED (on the basis of Schirmer's test and BUT) was 22.89% in this rural population. Out of the 817 subjects with dry eye, 56.3% were females (p=0.38). Subjects aged 70 years and above (p= <0.001), illiteracy (p=0.002), ultraviolet radiation exposure (p<0.001), smoking (p=0.018), co-existent refractive error (p=.009), were more likely contributors of DED. Systemic disease (p=0.052) and exposure to indoor kitchen smoke (p=0.79) appeared to have no effect on the risk of developing dry eye.
Conclusions: Dry eye disease is common in this rural Indian population; increasing age and exposure to indoor kitchen smoke were strongly correlated with its frequency. Measures directed against modifiable risk factors and its timely detection and management may provide a positive impact on public health and prevent sight threatening complications. This research was supported by grants from Indian Council for Medical Research, New Delhi, India.

INTERPLAY BETWEEN EYE MICROBIOME AND DRY EYE DISEASE IN INDIAN PATIENTS.

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Purpose: Dry eye is a chronic ocular surface disease with a high prevalence in the Indian population. There exists a correlation between ocular surface microbes and dry eye disease, wherein traditional culture and molecular techniques have obvious limitations to identify the conjunctival microbiota, and metagenomic studies can provide better insight. The present study is aimed to evaluate the ocular microbiome and determine distinct microbial signatures in dry eye patients.
Methods: Conjunctival swabs were collected from the inferior conjunctival fornix of 20 newly diagnosed patients with dry eye and matched controls under aseptic conditions. 16S rDNA Ion-torrent sequencing technology will be used to sequence the 16S rDNA V4-V5 hypervariable region of all bacteria in the conjunctival swab samples. The operational taxonomic units will be obtained and bioinformatic analyses will be done.
Results: On preliminary analysis, conjunctival swabs demonstrated higher concentration of microbial DNA content in dry eye patients as compared to controls (5.6 to 7.3 ng/µl in controls versus 9.1 to 51

ng/µl in patients with dry eye). These samples with extracted microbial DNA will be further subjected to high quality sequencing to identify distinct genera.
Conclusions: The composition and diversity of microbiota in patients of dry eye are being elucidated. A framework for investigating potential roles played by the diverse microbiota in disease related with the ocular surface will be provided. The study will help us to better understand and determine the link between ocular microbiome and dry eye disease.

NEW DEVELOPMENTS IN OCULAR SURFACE IMAGING.
Rudolf F. Guthoff, University Eye Department Rostock, Germany
Purpose: Evaluation of tearfilm components and overall thickness, epithelial cell subdifferenciation and quantification of subbasal nerve structures are matters of interest for new imaging methods.
Methods: Interference patterns of tearfilm lipid components, spaceresolved tearfilm breakup phenomena, OCT based tearfilm thickness layer measurements, 2 and 3-D reconstruction of epithelial and subbasal nerve fibers by laser scanning in vivo microscopy are demonstrated and evaluated.
Results: Interference patterns simplify and to some extent quantify lipid layer qualitiy. Dry spot mapping during breakup evaluation allows correlations with minute underlying epithelial pathology. Subdifferentiation and quantification of surface-wing-and basal cell morphology as well as localisations of pathogens give deeper insights in destructive and wound healing processes. Subbasal nerve plexus quantification with single images and improved by mapping technique supplies us with new biomarkers for early detection of small fiber neuropathy in various diseases mainly in patients with subclinical diabetes woundhealing in corneal refractive surgery and corneal cross linking.
Conclusions: Literature reviews and own results demonstrate the importance of mostly quantifiable data from ocular surface imaging in diagnoses and followup of localised and systematic diseases effecting the cornea.

AN INFLAMMATORY GENE PROFILE OF HUMAN CONJUNCTIVAL EPITHELIAL CELLS IN DRY EYE DISEASE.
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Purpose: Tear film hyperosmolarity is a core mechanism underlying ocular surface inflammation and, ultimately, dry eye disease (DED). Impression cytology (IC) is a minimally-invasive method of evaluating conjunctival cells to aid in the diagnosis of DED. We investigated the inflammatory gene profile of human conjunctival epithelial cells (HCE), retrieved via IC, in patients with DED compared to healthy controls. In addition, gene expression of an in vitro model of DED was performed to investigate if it was a relevant model of this inflammatory condition.
Methods: HCEs were retrieved using IC, and real-time PCR (qPCR) was performed to determine expression levels of p38, IL1-beta, IL-8, MCP-1 and MMP-9. A human conjunctival epithelial (Chang) cell line was incubated in media containing excess NaCl or sucrose for up to 24 hours. qPCR was performed on Chang cell RNA to investigate the effects of hyperosmolarity on inflammatory markers.
Results: qPCR assays indicated significant up-regulation of all genes analysed in DED patients versus healthy controls. Following hyperosmolar treatment of Chang cells, p38 was significantly upregulated by 100mM and 400mM NaCl, and by 400mM sucrose (all $p<0.0001$). Significant upregulation of IL-1beta, IL-8, MCP-1 (all $p<0.0001$) and MMP-9 genes ($p<0.001$) was observed, following treatment with 400mM NaCl for 24 hours.
Conclusions: In DED subjects, all pro-inflammatory markers analysed were significantly upregulated compared with normal subjects. Moreover, the in vitro model of dry eye (hyperosmolarity) demonstrated significantly increased expression of the inflammation-related genes. These results demonstrate that markers of ocular surface stress are increased in patients with DED and that Chang cells are a relevant in vitro model of ocular surface inflammation.
The authors wish to thank Topivert for their financial support of this research.

EFFECTS OF INTERMITTENT SHEAR STRESS ON CORNEAL EPITHELIAL CELLS USING AN IN VITRO FLOW CULTURE MODEL. EFFECTS OF INTERMITTENT SHEAR STRESS ON CORNEAL EPITHELIAL CELLS USING AN IN VITRO FLOW CULTURE MODEL.
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Purpose: The aim of this study was to establish an in vitro model for culturing a human telomerase-immortalized corneal epithelial (hTCEpi) cell line under adjustable medium flow mimicking the movements of the tear film on the ocular surface.
Methods: Using an IBIDI pump system, cells were cultured under unidirectional, continuous or oscillating, discontinuous medium flow. Cytoskeletal architecture, cell contacts, and cell surface specializations were investigated by immunofluorescence and raster electron microscopy. The protein expression levels of tight junction protein, occludin and desmoplakin were analyzed by Western blot. MUC1, -4 and -16 proteins were localized by immunocytochemistry. Rose Bengal staining was used to assess mucin (MUC) barrier integrity.
Results: Cells subjected to discontinuous shear stress displayed the typical flattened, polygonal cell shape of the superficial layer of stratified squamous epithelia. Stress fiber formation was not aligned to flow direction. Desmoplakin and occludin but not tight junction protein were upregulated under oscillatory shear stress. Cell surfaces showed less bulging under shear stress. MUC1, -4, and -16 protein immunolocalization was most prominent, while Rose Bengal uptake was diminished under unidirectional conditions.
Conclusion: Our findings suggest that shear stress as it occurs at the ocular surface during blinking exerts marked effects on corneal epithelial cells, such as changes in cell structure and protein expression. The described model may be useful for in vitro investigations of ocular surface epithelia as it represents a much more physiologic reproduction of the in vivo situation than the commonly applied static culture conditions.
The authors have nothing to disclose.
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IMMUNE-NERVE CROSS-TALK IN THE CORNEA: THE ROLE OF PLASMACYTOID DENDRITIC CELLS ON CORNEAL NERVE SURVIVAL.
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Purpose: Plasmacytoid dendritic cells (pDCs) are recently identified in the cornea. Despite recent evidence on pro-neuroregenerative roles of certain immune cells, significance of pDCs remains elusive. This study aims to evaluate neurotrophic properties of pDCs in the cornea.

Methods: Resident corneal pDCs were depleted locally by subconjunctival injections of 30ng Diphtheria toxin (DT) in BDCA2-DTR mice. Controls were wild-type C57BL/6 mice receiving DT and BDCA2-DTR mice receiving PBS. Corneal sensation was evaluated via an 8.0 thread; nerve density was measured via NeuronJ on corneas stained for βIII-tubulin. Corneal stroma NGF mRNA levels were measured via qPCR. Spleen and corneas underwent flow cytometry for pDC markers and NGF. Trigeminal ganglion cells (TGCs) were co-cultured with splenic pDCs and neurite outgrowth was measured.
Results: Upon 7-day pDC depletion, nerve density was diminished to $1.1\pm0.7mm/mm^2$ vs. 143 ± 8.1 in control corneas in the center and to 5.3 ± 3.9 vs. 112 ± 9.3 in controls in the periphery of the corneas ($p<0.001$). Corneal sensation was lost following 3-day pDC depletion ($p<0.01$). Upon pDC repopulation for 14 days, nerves regenerated to 81.5 ± 0.2 in periphery and to 48.4 ± 5.0 in central cornea; also, corneal sensation was recovered ($p<0.001$). Upon 3-day pDC depletion, NGF mRNA level was decreased to 48.2% ($p<0.01$). Flow cytometry showed co-staining of pDCs with NGF. Neurite outgrowth was enhanced 4.2 folds by co-culturing TGCs with pDCs versus TGCs mono-culture ($p<0.01$); anti-NGF treatment abolished enhanced neurite outgrowth ($p<0.01$).
Conclusion: Corneal pDCs possess neurotrophic properties by secreting NGF and are vital for corneal nerve maintenance, function, and regeneration.
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A CASE OF SEVERE OCULAR SURFACE DISORDER RELATED AND SEVERE CONJUNCTIVOCHALASIS.

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Purpose: Conjunctiva has two-sides effect for ocular surface; tarorrhaphy is performed on patients with severe ocular surface disorder to protect the cornea, and otherwise lid wiper epitheliopathy, superior limbal keratoconjunctivitis, tear film instability and inflammation are caused by conjunctiva. In this presentation, we report a case of conjunctivochalasis for mal-effect to ocular surface.
Methods: Case presentation.
Results: An 84 year-old-male with uveitis was treated in our hospital for ocular surface disorder. He had previously undergone cataract surgery and Nd:YAG laser posterior capsulotomy for both eyes. Treatment included topical steroids, antibiotics, autologous serum application, and medically prescribed contact lens. The patient's visual acuity was 20/33 for both eyes in 2008, but gradually deteriorated. From October 2015, his left eye showed severe ocular surface disorder with superficial punctate keratopathy (SPK), corneal erosion, and ulceration. The patients' eyes also showed SPK around the cornea limbus in the region affected by the conjunctivochalasis. We believed that the conjunctivochalasis was related to the ocular surface disorder so we performed surgery on the left eye using conjunctival fixation on the sclera in February 2016. After the operation, the ocular surface improved but the condition of the right eye became poor. We performed conjunctival fixation on the sclera of the patients' right eye in April 2016. During the operation, we corrected shrinkage by cutting the conjunctiva. Postoperatively, the ocular surface was clear and this improvement was still evident on follow-up.
Conclusion: We report a case with severe ocular surface disorder caused by severe conjunctivochalasis. The causes of this condition may include friction, tear instability, and inflammation of the conjunctiva. When treating the ocular surface, the effect on the conjunctiva should be considered. [The authors have no interest with financial disclosure.]

GOBLET CELLS DENSITY AFTER USE OF TOPICAL IMMUNOMODULATOR IN THE TREATMENT OF PATIENTS WITH DRY EYE DISEASE.

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Purpose: To determine efficacy and goblet cell density after treatment with an immunomodulating topical medication containing 0.05% ciclosporine A(CsA), for aqueous deficient dry eye(ADDE) and evaporative dry eye(EDE).
Methods: 17 patients were classified as ADDE and 15 as EDE. The following tests were performed during first visit(T0) and after BID treatment of CsA for one(T1) and three months(T3):Ocular Surface Disease Index(OSDI), non invasive break up time(NIBUT), meibography and tear meniscus height(Keratograph, Oculus),Schirmer 1 test, fluorescein break up time(FBUT), fluorescein and lissamine green staining; plus impression cytology(IC) of superior and temporal conjunctiva followed by HE and HLA-DR immunostaining.
Results: CsA treatment significantly improved FBUT and increse tear meniscus height for the temporal region between T0 and T3 for EDE group.It was found a significant positive correlation between FBUT and NIBUT values in EDE patients.There was a significant improvement in impression cytology total score in the temporal conjunctival region for EDE patients between T0 and T3. Moreover, there was an increase in goblet cell counts on the superior region of ADDE patients and a decrease in the percentage of positive cells for HLA-DR staining, both in the superior and temporal regions.
Conclusion: Our findings suggest that topical CsA treatment for ADDE patients improves superior ocular surface inflammation by increasing goblet cell counts and decreasing HLA-DR expression. On the other hand, for the EDE group, CsA treatment showed benefits for meniscus height and BUT, what might have fostered the reduction of ocular surface inflammation observed in IC total score reduction. CsA treatment was considered effective for both DE subtypes, considering minimum dosage for maximum tolerance.
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EUPHRASIA PROTECTS HUMAN CONJUNCTIVAL CELLS FROM ULTRAVIOLET LIGHT-INDUCED CELL DAMAGE.

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Purpose: Euphrasia (Eyebright) has been used in medicine for hundreds of years for treatment of different eye diseases, especially conjunctivitis, blepharitis and dry eye. Several studies revealed antiinflammatory, antibacterial, antifungal and antioxidative effects of the plant. In prior experiments euphrasia was able to protect hyaluronic acid solutions from depolymerisation through the negative influence of ultraviolet light. The capability of euphrasia to prevent human conjunctival cells from oxidative damage caused by UV light was examined.
Methods: Human conjunctival cells (CHANG cells) were cultivated in culture media with 10% FBS and 1% penicilline/streptomycine. For evaluation of protective effects an euphrasia glycerine extract was added to cell suspensions ($1x10^6$ cells/ml) in concentrations of 0,1%, 1% or 10% respectively. Cells were then irradiated with ultraviolet light type A and B for 23 or 30 seconds. Three and six hours after incubation the cell viability has been measured with the Countess 2 FL Cell counter using the ReadyProbes® Cell Viability Imaging Kit (Blue/Green) from Thermo Fisher Scientific and an additional conventional staining with trypan blue.
Results: Irradiation with ultraviolet light type A and B leads to a

marked reduction of cell viability of human conjunctival cells. When using an euphrasia-glycerine extract during irradiation the degree of cell impairment could be significantly reduced. Already a 0,1% solution of euphrasia is able to protect human conjunctival cells from damage through ultraviolet light type A. A protective effect of ultraviolet light type B had been observed, but was not statistically significant.
Conclusion: Ingredients of the plant euphrasia have antioxidative properties and are able to protect human conjunctival cells from damage caused by UV light. Using this plant for treating several eye diseases, especially conjunctivitis, blepharitis and dry eyes seems to be a promising approach and should be further investigated.
No financial interest

ORGAN REGENERATION OF LACRIMAL GLAND AS A NEXT-GENERATION OF REGENERATIVE MEDICINE.
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The lacrimal gland has a critical role in maintaining a physiological homeostatic environment for a healthy ocular surface by tear secretion. A decrease of tear production from the lacrimal glands causes dry eye disease, which is a prevalent eye disease that results in corneal epithelial damage. Regenerative medicine, such as stem cell therapy, is expected to be a promising therapeutic approach to restore the lacrimal gland function.
Lacrimal gland, which has three-dimensional structure including acini and duct with peripheral nerve fibers, develops through a reciprocal epithelial-mesenchymal interactions in a process of organogenesis during embryo. A goal of lacrimal gland regenerative therapy is to replace a damaged lacrimal gland to a functional bioengineered organ. Previously, a novel method to reconstitute a bioengineered organ germ in in vitro three-dimensional cell manipulation between epithelial and mesenchymal stem cells isolated from mice embryonic organ germs (*Nat Methods* 2007). Furthermore, a novel concepts for a fully functioning bioengineered organ by engraftment of a bioengineered organ germ, which can regenerate the developmental process in organogenesis, have been developed in teeth and hair follicle (*PNAS* 2009, *Nat Commun* 2012). To regenerate a functional lacrimal gland organ regeneration, we have regenerated a bioengineered lacrimal gland by the transplantation of the bioengineered germ into the extra-orbital lacrimal gland-depleted mice *in vivo* (*Nat Commun* 2013). The bioengineered lacrimal gland germ could develop *in vivo* and achieved physiological functionalities such as tear secretion in response to nervous stimulation and ocular surface protection. We have also succeeded to regenerate bioengineered harderian gland, which has a function to secrete lipid *in vivo* in mice. These studies provided the possibility of functional organ regeneration via engraftment of a bioengineered gland germ as a next-generation of regenerative therapy.

CELL VIABILITY AND PROTEIN EXPREESION OF HUMAN AMNIOTIC MEMBRANE IN DIFFERENT PRESERVATION METHODS.
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Purpose. To evaluate cell viability and cytokine changes in amniotic membrane (AM) preserved in different time and temperatures Methods. AM were harvested from 4 women undergoing cesarean delivery. After washing, AM was stored at different preservation methods: at 2 different temperatures (-70 and 4°C), in 2 different preservation media (DMEM and DMEM with protease inhibitor), and for different time periods (for 12hours, 1, 3, 7 days). Nonpreserved fresh AM was used as a control. Histological structures of AMs were examined by H&E staining and immunohistochemical staining. Viability of the stored AM epithelium was assessed by LIVE/DEAD® Viability/Cytotoxicity assay. Epidermal growth factor(EGF), basic fibroblast growth factor(bFGF), keratinocyte growth factor(KGF), nuclear factor kappa-light-chain-enhancer of activated B cells(NF-kB), Bid, caspase-3, caspase-9 protein expressions were measured by western blotting. Results. Viability of AM cells decreased during storage. Especially, less than 5% of AM cells preserved at -70°C were alived after 1 day. Higher viability was obtained by storage 4°C with protease inhibitor. Expression of EGF, bFGF, KGF remained stable for up to 1 day and showed significant decrease. Expression of NF-kB, bid, caspase-3, caspase-9 protein was decreased when preserved in DMEM with protease inhibitor. Conclusions. Appropriate conservative methods with protease inhibitor increase cell viability and protein expression. To achieve the maximal therapeutic effects of AM, it is necessary to control conservative method.

CYCLOSPORINE A APPLICATIONS BEYOND DRY EYE DISEASE.
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Purpose: To investigate reports from the literature on the ocular applications of the immunosuppressant drug cyclosporine A other than for inflammatory dry eye disease.
Methods: A literature search on the Scopus, PubMed and Cochrane Library databases as well as ClinicalTrials.gov was performed for reports or trials on topical applications of cyclosporine A for ocular conditions other than inflammatory dry eye disease. Key search terms included "(Cyclosporine OR Restasis)", "(Ocular OR Eye)" and "Topical", with the terms "Dry Eye" and "Keratoconjunctivitis Sicca" excluded. Publications utilizing both commercial preparations of topical cyclosporine A (Restasis, Allergan) and compounded formulations were included.
Results: Initial searches of the literature returned more than 300 publications discussing ocular use of cyclosporine A unrelated to dry eye disease. The earliest reports on the ocular uses of topical cyclosporine A centred on similar applications of cyclosporine A in the rest of the body, namely to aid in prevention of transplant rejection and for severe, chronic inflammation such as uveitis associated with Behcet's disease. The ability of cyclosporine A to modulate the immune response in severe vernal and atopic disease has also been extensively investigated through both applications of compounded and commercially available formulations. Investigators have also reported on cyclosporine's use in chronic inflammatory diseases where long term inflammatory suppression using corticosteroids are a concern such as in immune mediated stromal disease, Thygesson's superficial keratitis, nummular keratitis and scleritis to various degrees of success. A subset of more recent studies have returned to investigate the agent's ability to improve post-surgical outcomes such as post LASIK, pterygium and squamous cell carcinoma removal, debridement for shield ulcers and glaucoma filtration surgery.
Conclusions: Application of topical cyclosporine A to the ocular surface has several other applications beyond dry eye disease and may be beneficial as part of an overall strategy in the long term management of ocular inflammation.

EVALUATION OF THE EFFECT OF CONJUNCTIVOCHALASIS CAUTERIZATION ON TEAR STABILITY AND CONTRAST SENSITIVITY.
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Purpose: To evaluate the tear stability and contrast sensitivity of

patients with conjunctivochalasis (CCh) who were performed CCh cauterization. Design: The study was designed as prospective clinical study Subjects: Thirty-nine eyes with grade 2 to 3 CCh of 39 patients were enrolled. Intervention and Main Outcome Measures: All the subjects were performed CCh cauterization and evaluated before and 3 months after the surgery. Variables evaluated included: ocular surface disease index (OSDI), tear break-up time (TBUT), Schirmer's I test, corneal fluorescein staining, tear meniscus area (TMA), corneal surface irregularity, and contrast sensitivity.

Results: A follow-up of 3 months was achieved in 36 eyes of 36 patients. All events improved significantly after the surgery (P <0.05), except Schirmer's test.

Conclusions: CCh cauterization is an effective method to reconstruct thelower tear meniscus, and improve both tear film stability and corneal surface irregularity, with resultant of increasing contrast sensitivity at the same time.

EVALUATION OF THE SAFETY AND EFFECTIVENESS OF INTENSE PULSED LIGHT IN THE TREATMENT OF MEIBOMIAN GLAND DYSFUNCTION.

Lv Huibin1, Jiang Xiaodan1, Zhang Mingzhou1, Liu Yan1, Hu Xiaodan1, Li Xuemin1, Wang Wei1. 1Department of Ophthalmology, Peking University Third Hospital, Beijing, China

Purpose: This study aims to explore the safety and efficacy of a novel treatment recently emerged– intense pulsed light (IPL) in MGD eyes.

Methods: This study is a prospective and open label study. Forty eyes of 40MGD patients were recruited in the study and received 4 consecutive IPL treatments on day 1, day 15, day 45 and day 75. Ten ocular surface symptoms were evaluated with a subjective face score at every visit and the summation of these scores was defined as a total subjective symptom score. Best spectacle corrected visual acuity, intraocular pressure (IOP), conjunctival injection, upper and lower tear meniscus height (TMH), tear break-up time (TBUT), corneal staining, lid margin and meibomian gland assessments, meibography were also recorded at every visit, as well as the adverse effects on the eye and ocular surface.

Results: Significant improvements were observed in single and total ocular surface symptom scores, TBUT, and conjunctival injection at all the visits after the initial IPL treatment (P<0.05). Compared to baseline, the signs of eyelid margin, meibomian gland secretion quality and expressibility were significantly improved at every visit after treatments, meeting a maximum therapeutic effect after the second treatment. There was no regional and systemic threat observed in any patient.

Conclusion: Intense pulsed light (IPL) therapy is a safe and efficient treatment in relieving symptoms and signs of MGD eyes.

THE EVALUATION OF ANATOMIC STRUCTURE AND TEAR MENISCUS CHANGING AFTER CONJUNCTIVOCHALASIS CAUTERIZATION BY VISANTE OPTICAL COHERENCE TOMOGRAPHY.

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Purpose: To investigate the use of Visante optical coherence tomography (OCT) in the evaluation of Conjunctivochalasis (CCh), focusing on the tear meniscus cross-sectional area and α-angle change before and after conjunctiva cauterization.

Methods: 33 eyes of 17 patients with temporal CCh and dryness who did not respond to any other treatments underwent the conjunctiva cauterization. Ocular surface disease index score (OSDI), tear breakup time (TBUT), and tear meniscus area (TMA) and α-angle detected by Visante OCT, were estimated one month after the operation and compared with the corresponding preoperative values. Results: One month after CCh cauterization, symptoms of dryness estimated by OSDI decreased from 56.57 + 20.39 to 29.49 + 16.68 (P =0.000). TBUT elevated from 1.82 + 0.98s to 3.70 + 1.65s (P =0.000). Cross-section TMA climbed from 650.33 + 341.69μm2 to 2793.27 + 3054.06μm2 (P =0.000). In contrast, α-angle narrowed from 82.36 + 8.66°to 63.84 + 12.11°(P =0.000). The TMA and α-angle altering were significantly correlated with the changing of TBUT (r =-0.512, P =0.002, r =-0.530, P =0.002), respectively. The area under the curve (AUC) of TMA and α-angle was 0.890 + 0.06, 0.747 + 0.10, separately, between which the significance level was 0.09.

Conclusion: Conjunctivochalasis cauterization is an effective way for fornix reconstruction. The removal of redundant conjunctiva contributed to the α-angle narrowing and the effective area in fornixes increasing. Since both TMA and α-angle were correlation with TBUT, α-angle could be another potential indicator for the evaluation of the fornix structure and tear volume.

CHARACTERISTICS OF ON-ROAD DRIVING PERFORMANCE OF PERSONS WITH DRY EYE DISEASE IN CHINA.

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Purpose: To compare the on-road driving performance in patients with dry eye disease (DED) and to determine clinical predictors of visual impairments while driving.

Methods: The study was performed in the eye center of Peking University Third Hospital, China. 87 dry eye patients and 42 controls were included, including 49 patients without any treatment (group A), 38 patients treated with artificial tears (group B) and 42 controls with no dry eye (group C). The best-corrected visual acuity of all study participants was at least 20/20 as standardly measured. They were diagnosed of no eye disease but dry eye. Vision-related quality-of-life questionnaire (Ocular Surface Disease Index (OSDI) daily life related visual function Questionnaire and questionnaire about performances during driving test were collected. Data were compared between groups and analyzed.

Results: Significant differences in all clinical characteristics and OSDI scores were found between dry eye patients and normal controls (P < 0.05). While group A suffered more uncomfortable than group B. The functional limitations related to dry eye were significant in dry eye patients, especially in daily work and using computer. Dry eye disease was correlated with the unsafe driving habits and performances, which may increase the risk of dangerous driving. (p <0.01). The percent of crash and near-crash were 10.33%. The percent of missing targets summed up to 32.17%.

Conclusions: DED can lead to a lot of inconvenience in daily life, including driving. The frequence of unsafe driving habits and performance increased because of dry eye disease.

IMPAIRED FUNCTION OF PERIPHERALLY INDUCED REGULATORY T CELLS IN HOSTS OF HIGH RISK OF GRAFT REJECTION.

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Purpose: Regulatory T cells (Tregs) are crucial for allograft survival. Tregs can be divided into thymus-derived 'natural' Tregs (tTregs) and peripheral 'induced' Tregs (pTregs). Here, we determine whether the suppressive function of Treg subsets is hampered in hosts who are at

high risk for rejecting corneal grafts.
Methods: To induce inflamed (high-risk) graft beds, intrastromal corneal sutures were placed two weeks prior to transplantation in mice. Ipsilateral draining lymph nodes (DLNs) and corneas were harvested at day 0 (ungrafted) and 14 post-transplantation, and analyzed for frequencies of Tregs, tTregs, pTregs, and their expression of co-inhibitory molecules and cytokines. Foxp3 mRNA expression in the cornea was analyzed by real-time PCR, and interleukin-10, transforming growth factor-beta (TGF-β), and interferon (IFN)-γ were measured using ELISA. The suppressive function of Tregs was evaluated using an in vitro proliferation assay, and the proliferation of co-cultured T effector cells was determined via BrdU incorporation. Adoptive transfer of sorted pTreg and tTreg was conducted in high-risk recipients.
Results: In high-risk recipients we found reduced Treg frequencies in the cornea. Reduced function of pTregs correlated with their decreased expression of Foxp3, CTLA-4, IL-10, and TGF-β. Adoptive transfer of pTregs from mice at low risk of subsequent graft rejection was able to rescue graft survival in recipients that were at high risk of rejecting their grafts. tTregs from high-risk and low-risk improved graft survival; however, less successful.
Conclusions: These data suggests that impaired function of pTregs, but not tTregs, mediates the loss of immune tolerance and promotes allograft rejection. This study was supported by the National Institutes of Health/National Eye Institute Grant EY012963 (RD).

OCULAR SURFACE CYTOKINE RESPONSE TO MUCUS MEMBRANE GRAFTING FOR LID MARGIN KERATINIZATION IN STEVENS JOHNSON SYNDROME.

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Purpose: To analyze the changes in cytokine profile post mucus membrane grafting (MMG) for lid margin keratinization in SJS and study the differences in their conjunctival and oral mucosal environments.
Methods: Tear specimen (Schirmers strip), conjunctival and oral mucosal imprint cells were collected from 50 SJS patients warranting MMG at pre and post intervention stages prospectively for one year (n=33; 1 year followup). Out of these cases, oral mucosal imprint were collected from 17 cases pre-operatively. Age and sex-matched healthy volunteers (n=33 eyes each) were recruited. Tear from Schirmers strips was extracted using PBST and the cytokines profiled using 27-plex Pro-human cytokine array. Total RNA was extracted from the imprint cells by TRIzol method. TGFβ-mediated wound healing responses were compared in the epithelial cells of oral mucosa and conjunctiva of SJS cases as well as the conjunctiva of age and sex matched healthy controls by qPCR.
Results: The cytokine profiling of tears revealed significant up and down regulation of pro and anti inflammatory cytokines respectively in almost 80% of the cases. Conjunctival gene expression studies showed a high 10, 67, 173 and 184 folds increase (mean fold change) in TGF-β1, TGF-βRI1, CTGF and Collagen 3 in the SJS conjunctiva, prior to MMG, compared to that of controls, which dropped to 1.3, 11, 13.5 and 19 fold increase (mean fold change) post MMG. However the oral mucosal expression for TGF-β1, CTGF and Collagen 3 was lower by nearly 2.5, 10, 26 folds and higher by 4 folds for TGF-β RII in comparison to normal. Clinical ocular surface inflammation scores improved in all patients.
Conclusions: The anti-inflammatory shift in cytokine profile post MMG was concurrent with a reduction in clinical ocular surface inflammation. Further studies are needed in larger numbers and in eyes that do not require MMG to understand the role of cytokines in the etiopathogenesis of SJS ocular sequelae. Study funded by DST, Govt of India and Medical Research Foundation

UNIQUE CHALLENGES AND UNMET NEEDS FOR THE TREATMENT OF OCULAR SURFACE DISEASE IN VARIOUS REGIONS OF THE WORLD – INDIA (SOUTH ASIA).

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The uniqueness of India lies in her diversity. Equally diverse are the challenges faced in the field of ocular surface disorders in India, and by virtue of geographical proximity and racial similarities, the same holds true for the entire Southern Asia. The need for ocular surface to branch out as a separate entity emerged around a decade back. A seemingly better understanding of the pathophysiology of ocular surface disorders coupled with the huge strides in corneal stem cell therapy along with acceptance and improvisations in keratoprostheses paved the way for the same.
The most common ocular surface disorders encountered in India apart from dry eye and allergic disorders include Stevens Johnson syndrome and chemical injuries secondary to assault with intent to disfigure and accidents related to the "chuna" – edible lime, injury. There exists a need to create awareness among the ophthalmic and medical fraternity in the country to address these issues at the level of prevention and primary acute care in order to reduce the occurrence of chronic vision threatening sequelae. Genetic studies for disease markers are the need of the hour to identify individuals at high risk for SJS. Surface stabilization procedures for the chronic sequelae in more than 800 eyes over 10 years at our tertiary eye care institute helped establish their role highlighting a paradigm shift in the management of ocular SJS. The use of most types of keratoprostheses, both Type 1 and 2, for this subgroup of eyes (80 eyes with SJS) revealed the pros and cons of each.
Tear proteomics would probably be able to pinpoint causative factors in the tears of these eyes that predispose to severe inflammation sans mechanical contributory factors. These pro-inflammatory factors could also be the cause for the peri-optic thinning or the laminar resorption noted more commonly among the different types of keratoprostheses in these eyes redirecting research towards more robust prostheses. Identifying and subsequently targeting these with antidotes might be the solution to harnessing sequelae, second only to measures directed towards prevention and the role of amniotic membrane in the acute stage of SJS. Country-specific issues having an impact in the decision-making of implanting a keratoprosthesis include a primarily agrarian population, tropical climate facilitating fungal infections, relative non-compliance with medications, lack of regular follow-up and a low socio-economic background. However despite these diverse hurdles, India has stood united in its battle against these odds and has remained in the forefront of corneal stem cell therapy as well as keratoprosthesis for end- stage ocular surface disorders.

PHARMACOGENETIC MANIPULATION OF NEURONAL ACTIVITY REVEAL A ROLE OF BRAIN SPINAL TRIGEMINAL NUCLEUS IN REFLEX TEARING.

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Purpose: Reflex tearing, marked transient secretion, is physiological reaction against external sensory stimuli to corneal surface. Vc/C1 region of spinal trigeminal nucleus of brain (Vc/C1) is known to relay region of corneal sensation. Designer Receptors Exclusively Activated by Designer Drugs (DREADD) technology enable to manipulate specific neuronal activity in a freely moving animal. In this study, using DREADD system, we investigate the role of the Vc/C1 in reflex tearing.
Methods: Eight weeks, female C57Bl/6J mice were used. Surgeries for Adeno associated virus (AAV) injections were conducted under pentobarbital anesthesia (50 mg/kg, i.p.) using stereotaxic instrument

with a glass micropipette and an air pressure injector system. AAV-CMV-hM3Dq-mCherry (600nl/injection) were unilaterally injected into Vc/C1 (according to mouse brain atlas). Two weeks after the surgery, the changes in tear secretion and eye scratching behavior were analyzed after the firing of hM3Dq expressed neurons by administration of hM3Dq agonist clozapine-N-oxide (CNO, 1mg/kg, i.p.). Saline was used as control.
Results: CNO injection increased tear secretion along with eye scratching behavior ipsilateral to the AAV injected side. Increasing ratio were peaked at 30 min after the CNO injection, approximately 200% (tear secretion) and 3000% (eye scratching) to before CNO injection (n=5). These increase were sustained up to 240 minutes. Administration of saline did not altered these responses. In all mice, the **expression of hM3Dq-mCherry were confirmed in Vc/C1.**
Conclusion: Our results indicate that activation of Vc/C1 involves in reflex tearing.
No commercial relationships

PREVALENCE OF DEMODEX FOLLICULORUM IN PATIENTS WITH KERATOCONJUNCTIVITIS SICCA.

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Purpose: To determine the prevalence of demodex mites in a population of patients with keratoconjunctivitis sicca.
Methods: 73 patients with mild to severe dry eye were included in the study. We compared the ophthalmological examination results of the group with demodex infestation (n=32; demodex group) with the group without any signs of demodex (n=41, control group). The results, the Ocular Surface Disease Index (OSDI)-Scores and the meibography findings were analyzed in two separate age groups. Demodex folliculorum was diagnosed after eyelash epilation by optical microscope evaluation. Anamnesis and examination parameters were tested for a statistical correlation with demodex infestation.
Results: Demodex was found in 43.8% of all patients. The average number of demodex was 0.52 mites per eyelash. Demodex became more frequent with increasing age ($p=0.035$). The OSDI Score in patients with demodex infestation was 52.7 ± 23.9 compared to 42.8 ± 25.1 in the control group. 97.3% of sicca patients suffered from a blepharitis posterior, 41.1 % of these had demodex mites. A significant correlation between a demodex infestation and the occurence of a blepharitis posterior ($p=0.035$) was found. The Schirmer test with anasthesia for patients with demodex infestation (9.42mm) was significantly lower in comparison to the sicca patients without demodex infestation (12.95mm; $p=0.038$). 62 Sicca patients had a meibomian gland dysfunction (MGD). 41.9% of those patients were 'demodex positive'. There was a significant correlation between demodex evidence and both eyelash loss ($p=0.048$) and occurence of asymmetrical cylinders ($p=0.003$).
Conclusions: Demodex folliculorum showed a high prevalence in our patients with dry eye disease, especially in patients with MGD, posterior blepharitis, increased loss of eyelashes or the occurrence of asymmetrical cylinders.

TRANSLATING AN IDEA INTO A THERAPY: ESCAPING THE OCULAR STRESS TRAP.

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Purpose: We determined whether nucleases are deficient in the tear fluid of dry eye disease (DED) patients, and whether this causes extracellular DNA (eDNA) and neutrophil extracellular trap (NET) accumulation in the precorneal tear film, thus causing ocular surface inflammation.
Methods: Exfoliated cells adhered to Schirmer test strips were collected on glass slides, and immunofluorescence confocal microscopy was used to evaluate neutrophils, eDNA, NETs, and their molecular components. Similar experiments were performed with mucoid films collected from the inferior conjunctival fornix or bulbar conjunctiva. We used quantitative PCR to evaluate eDNA signaling pathways and inflammatory cytokine expression. We also determined the amount of ocular surface eDNA and evaluated tear fluid nuclease activity. Two patients with DED having excessive eDNA in tear fluid were treated with DNase I eyedrops.
Results: eDNA, NETs, and neutrophils were present on the ocular surface in DED patients and abundant in mucoid films. NETs consisted of eDNA, histones, cathelicidin, and neutrophil elastase. Tear fluid nuclease activity was decreased significantly in DED patients, whereas the amount of eDNA on the ocular surface was increased significantly. Expression of genes downstream of eDNA signaling, such as TLR9, MyD88, and type I interferon, as well as the inflammatory cytokines interleukin-6 and tumor necrosis factor-α, was significantly increased in DED patients. Treatment of patients having DED with DNase I eyedrops reduced eDNA abundance, abrogated signal increase, and improved comfort.
Conclusions: Extracellular DNA production and clearance mechanisms are dysregulated in DED. Nuclease deficiency in tear fluid allows eDNA and NETs to accumulate in precorneal tear film, and results in ocular surface inflammation. A novel therapeutic approach for managing DED may be to measure eDNA abundance in tear fluid with the PicoGreen dye assay and reduce excessive amounts with DNase I eyedrops. [Supported by NEI R01 EY024966]

A RELATIONSHIP BETWEEN NUTRITION, BODY COMPOSITION AND SIGNS BUT NOT SYMPTOMS OF DRY EYE.

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Purpose: To examine the relationship between nutritional status, body composition and signs and symptoms of dry eye in healthy adults.
Methods: A preliminary single-visit cross-sectional study was conducted. Subjects completed nutrition and lifestyle questionnaires. Body composition was measured using digital scales (weight, height) and bioelectrical impedance analysis (Tanika BC-601). Multiple linear regression analysis was used to examine predictors of signs (tear osmolarity, lipid layer thickness, NIBUT, meniscus height, Phenol Red Thread, TBUT, and staining) and symptoms (OSDI) of dry eye.
Results: Thirty nine (mean age 27 ± 10 years) of 40 subjects were retained for analysis including one pescatarian. Subjects consumed approximately one fifth of their food portions as non-dairy proteins with the remaining portions evenly split between vegetable, fruit, dairy, and snacks. Oily fish consumption ranged from none to 5 serves per week (mean $\pm$ standard deviation 1.5 ± 1.4). Metabolic age and dairy intake were significant predictors of tear lipid layer thickness ($p<0.001$, $R^2adj=0.37$). Age, low cereals, low dairy and low oily fish intake were significant predictors of staining ($p=0.003$, $R^2adj=0.30$). Nutrition, body composition and signs of dry eye were not significant predictors of ocular symptoms in multivariate analysis ($p>0.05$).
Conclusions: Body composition and nutrition appear to be related to signs but not to symptoms of dry eye. [Disclosures: None]

PLASMACYTOID DENDRITIC CELLS ARE CRITICAL FOR THE MAINTENANCE OF CORNEAL ANGIOGENIC PRIVILEDGE.

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Purpose: Resident plasmacytoid dendritic cells (pDCs) have been recently identified in the cornea and around limbal vessels. This study aims to unravel anti-angiogenic properties of pDCs.
Methods: Corneal pDCs were locally depleted by subconjunctival injections of 30ng Diphtheria toxin (DT) in 6-8 weeks male BDCA2-DTR mice. DT treated wild-type C57BL/6 mice and PBS treated BDCA2-DTR mice served as controls. Neovascularization (NV) area was evaluated on confocal micrographs of corneal whole-mounts stained with CD31 via ImageJ. Relative mRNA levels of Endostatin and Thrombospondin-1 (TSP-1) in the corneal stroma were assessed via qPCR. Spleen, naïve and sutured corneas underwent flow cytometry for CD45 (pan-leukocyte marker), Siglec-H, PDCA-1, B220 (pDC markers), Endostatin, and TSP-1. ANOVA with Scheffe post hoc was used to compare groups. Results: 7 days after local pDC depletion, corneal angiogenic privilege was lost, as NV was evident in pDC-depleted corneas (NV area=32.0±3.1%) versus PBS (12.5±1.9%) and DT treated controls (12.7±1.3%; $p<0.001$). 14-day pDC repopulation after initial 7-day depletion, yielded in regression of NV to 23.3±0.9% ($p=0.02$). We observed greater NV on day 7 after suture placement in pDC-depleted corneas (84.7±10.3%) versus PBS (32.3±2.1%) and DT treated controls (29.7±5%; $p=0.001$). Relative Endostatin and TSP-1 mRNA levels were decreased to 45.2% and 56.6% of controls 7 days after pDC depletion ($p<0.01$). Flow cytometry showed co-staining of pDCs with Endostatin and TSP-1 in spleen, naïve and suture-induced inflamed corneas.
Conclusions: Resident corneal pDCs contribute to maintenance of corneal angiogenic privilege by secreting Endostatin and TSP-1 during steady state and inflammation. Funding Support: NIH R21-EY025393-01 (PH), NIH R01-EY022695 (PH), Research to Prevent Blindness Career Development Award (PH), Tufts Medical Center Institutional Support (PH)

ANALYSIS OF FACTORS ASSOCIATED WITH MEIBOMIAN GLAND LOSS AND LIPID LAYER THICKNESS IN PATIENTS WITH DRY EYE SYNDROME.

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Purpose: To determine the effects of clinical variables, including age, sex, ocular surface indexes, and meibomian gland (MG) parameters on the lipid layer thickness (LLT) and loss of MG (MGL) in patients with dry eye syndrome (DES).
Methods: One hundred and seven patients with DES were enrolled. All eyes were evaluated with the ocular surface disease index (OSDI), fluorescence staining score, tear film break-up time (TBUT), Schirmer's score, tear meniscus area (TMA) using optical coherence tomography, and MG dysfunction (MGD) grading. MG images of lower lid and LLT were measured with LipiView II® (TearScience Inc., Morrisville, NC, USA). MGL was determined with ImageJ software. Result: In DES patients, mean LLT was 82.91±21.44 nm and mean MGL was 24.56±21.94 %. MGD grading was 1.91±1.21 (0–4, median 2) and 84.6 % of the subjects was diagnosed with MGD. In a multivariate analysis, decreased TBUT, TMA, and LLT, and increased MGL as well as female sex were significantly related to increased OSDI (β =-3.896, $p<0.001$; β=-0.225, $p=0.003$; β=-0.209, $p<0.003$; β=0.176, $p=0.011$; and β=9.641, $p=0.002$, respectively). In addition, reduced MGL and TBUT, increased age, and female sex were independently associated with increased LLT (β=-0.360, $p<0.001$; β=-1.605, $p=0.03$; β=0.214, $p=0.020$; and β=7.373, $p=0.012$, respectively). Furthermore, increased MGD grading were independently related to increased MGL (β=5.830, $p<0.001$).
Conclusion: Determination of MG status on the function and morphology is important to DE evaluation. Although MGL and LLT are affected by demographic factors such as age and sex, they can be informative for understanding DES patients' symptoms.

IN VIVO VISUALIZATION OF CA2+ DYNAMICS OF MYOEPITHELIAL CELLS IN LACRIMAL GLAND.

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Purpose: Lacrimal gland (LG) myoepithelial cells surround the basolateral membranes of acinar cells. It has been reported that intracellular Ca^{2+}-dependent myoepithelial contraction plays a role in expelling tear components from acinar cells within isolated LG alone. In this study, our goal is to verify the role of the myoepithelial cells in tear secretion using in vivo Ca^{2+} dynamics imaging together with the YC3.60 transgenic mice (a mouse lines expressing Yellow Cameleon 3.60), which is established based on the Cre/loxP system under control of a CAG promoter.
Methods: Eight-week-old female YC3.60 transgenic mice were used. Mice were placed in a prone position, and their LG were exposed by skin incision on the left temporal side of the head under anesthesia. In vivo FRET (fluorescence resonance energy transfer) ratio imaging of LG was performed by two-photon microscopy in order to visualize the Ca^{2+} dynamics. The LG was excited at 840 nm, and the fluorescence emission of CFP and YFP were detected at 460-500 nm and 520-560 nm, respectively. The images were acquired at approximately 1 frame/sec. To calculate the FRET ratio, the fluorescence images of each emission wavelength were analyzed by the software FluoView FV1200MPE. The changes in FRET ratio after intravenous injection of 1 mg/kg pilocarpine, cholinergic agonist, were evaluated. Results: YC3.60 probe was specifically expressed in the LG myoepithelial cells, not in acinar cells, of YC3.60 transgenic mice. Pilocarpine increased the FRET ratio in the myoepithelial cells, and obviously decreased in the area surrounded by the myoepithelial cells.
Conclusions: Our study demonstrated that Ca^{2+} dynamics of LG myoepithelial cells can be visualized in living animal, which will contribute to our further understanding of the physiological role of LG myoepithelial cells in tear secretion.

PRECLINICAL CANDIDATE WITH A NEW MECHANISM OF ACTION AGAINST OCULAR SURFACE DISEASES.

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Purpose: The Protease activated receptors (PARs) are important modulators of inflammation and pain. Multiple serine proteases activate the PAR system irreversibly. Based on our proprietary serine protease inhibitors database containing the inhibition parameters against more than 15 serine proteases, we aimed to identify a multi-target serine protease inhibitor that was able to modulate tissue

damage, inflammation and pain. Additionally, the selected compound must pass an early preclinical data package.
Methods: The compounds were evaluated in a rat ocular surface disease model described by C. Joossen et al.(Exp Eye Res 2016;146:172) The pain component was evaluated in a post-inflammatory rat model for visceral pain described by A Deiteren et al. (Gut 2014;63:1873) The selected compound was evaluated within standard early ADME-T assays and stability of the formulation was evaluated by HPLC-UV-MS.
Results: Our lead candidate exceled Restasis© by generating faster and stronger reduction of the inflammatory and tissue damage parameters in the rat ocular surface disease model. The same compound was also able to reduce pain in the visceral pain model. As such our compound showed a phenotypic readout that can be related to PAR modulation. Additionally the compound showed no red-flags in the early ADME-TOX assays and we were able to develop a stable formulation.
Conclusions: We identified an interesting serine protease inhibition profile to modulate ocular surface diseases and the compound is ready to initiate preclinical development. This research was supported by an IOF-SBO and BOF grant from UAntwepren, an IWT-SBO grant and a FRO grant.

EVALUATION OF INTERFACE REFLECTIVITY AND CORNEAL ABERRATIONS FOLLOWING DESCEMT'S STRIPPING AUTOMATED ENDOTHELIAL KERATOPLASTY (DSAEK)

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Purpose: to evaluate visual outcome after descemet membrane stripping automated endothelial keratoplasty (DSAEK) and relate to interface and corneal Higher-Order Aberrations (HOAs)
Methods: We enrolled 16 eyes of 16 patients (8 males and 8 females) in this interventional case series and followed after DSAEK operation for about 2-20 months. Interface reflectivity and HOAs were examined by OCULUS Pentacam as well as other ophthalmic evaluations in follow up visits. Statistical relations were analyzed.
Results: There was statistically significant correlation between interface reflectivity and Best Corrected Visual Acuity (BCVA) ($r=0.56$, $p=0.021$). Pachymetry (central corneal thickness) and BCVA had a moderate correlation($r=0.6$, $p=0.013$).There was no statistically significant correlation between pachymetry and follow up time($r= -0.36$, $p=0.16$). Negative correlation between follow up and interface reflectivity was also not statistically significant($r= -0.24$, $p=0.35$). Coma had a significant correlation with BCVA in cornea and cornea front maps ($r=0.74$, $p=0.009$ and $r=0.71$, $p=0.013$ respectively).
Conclusions: Significant correlation between interface reflectivity and BSCVA was found and anterior corneal HOAs are significantly higher than posterior HOAs.
[The authors have no financial interest in any materials mentioned.]

THE BLOCKADE OF IL-6 COUNTERPARTS THE OSMOLAR STRESS-INDUCED APOPTOTIC CHANGE AND JUNCTIONAL INSTABILITY IN HUMAN CONJUNCTIVAL EPITHELIAL CELLS.

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Purpose: To determine the effect of osmolar stress on cell survival/apoptosis and intercellular junctions of conjunctival epithelial cells and evaluate the possible role of IL-6.
Methods: Wong-Kilourne-derived human conjunctival epithelial cell line (WK-hC) was used in this study. Confluent cells were incubated under different osmolarity (290 and 500 mOSm) with or without neutralizing IL-6 antibody (50 ng/ml). The expression of IL-6 level was measured in the supernatant of each conditioned medium. Cell viability/apoptosis assay was performed using Annexin V/PI and CCK-8. Western blot was conducted to measure the abundance of apoptic markers, IL-6 related downstream signaling pathway (JAK/STAT/ERK), and junctional markers (ZO-1, Occludin, beta-catenin, E-cadherin). Cellular morphology and expression of junctional molecules were assessed on immunocytochemistry.
Results: The concentration of IL-6 showed time, dose-dependent increase in cells treated with 400 mOsm, 500 mOsm, not in control. Twenty four hours incubation in 400 mOsm, 500 mOsm decreased conjunctival epithelial cell viability and increased apoptosis. IL-6 neutralizing antibody reduced apoptotic change and junctional instability of cells incubated in 400mOsm and 500 mOsm based on the results of TUNEL, CCK assay and flow cytometry with Annexin V/PI. IL-6 neutralizing antibody inhibited the activation of JAK-STAT signaling pathway and loss of junctional molecules (ZO-1, occludin, beta-catenin, and E-cadherin), which were induced by hyperosmolar stress.
Conclusions: Hyperosmolar condition induced apoptosis and junctional instability in conjunctival epithelial cells, along with increase of IL-6 production. IL-6 neutralizing antibody inhibited apoptosis and JAK-STAT signaling and loss of junctional proteins in hyperosmolar condition. These findings suggested that IL-6 may be involved in apoptotic change and desquamation of conjunctival epithelial cells in hyperosmolar stress.

ASSESSMENT OF MEIBOMIAN GLANDS AND TEAR FILM IN POST-REFRACTIVE SURGERY PATIENTS.

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Purpose: To evaluate the long-term effects of corneal refractive surgery on meibomian glands and tear film, we compared ocular surface parameters between post-refractive surgery patients (undergone surgery at least 12 months previously) and controls.
Methods: A total of 80 eyes of 80 controls, 40 eyes of 40 post-laser in-situ keratomileusis (LASIK) patients, and 40 eyes of 40 post-laser epithelial keratomileusis (LASEK)/photo-refractive keratectomy (PRK) patients were enrolled. Tear meniscus height, non-invasive tear film break-up time (TBUT), and meibography using Keratograph® 5M, TBUT, ocular surface staining, and examination of lid margins and meibomian glands, Schirmer's test, and the Ocular Surface Disease Index (OSDI) questionnaire were performed.
Results: In post-LASIK patients, the ocular surface parameters including OSDI scores, TBUT, and staining scores, except Schirmer's scores, were significantly worse than those in controls ($P < 0.050$). Ocular surface staining scores in post-LASEK/PRK patients was higher than that in the control patients ($P = 0.002$). In post-refractive surgery patients, the grade of meibomian gland expressibility and meiboscores were higher than that of controls (all $P < 0.050$). Histories of refractive surgery were associated with the meiboscore ($\beta = 0.882$, $P = 0.017$ for LASIK and $\beta = 1.210$, $P < 0.001$ for LASEK/PRK). The proportions of dry eye disease and/or meibomian gland dysfunction were 26.2%, 60.0%, and 42.5% in control, post-LASIK, and post-LASEK/PRK patients, respectively.
Conclusion: Corneal refractive surgery influences the ocular surface over the long-term. Reductions in the number of functional meibomian glands by refractive surgery may contribute to chronic tear film dysfunction. [The authors have no commercial or proprietary interest in this article. This work was supported by an INHA UNIVERSITY HOSPITAL Research Grant.]

NOVATEARS® AS NEW THERAPY IN DRY EYE – RESULTS FROM THREE PROSPECTIVE, MULTICENTER, NON-INTERVENTIONAL STUDIES IN DIFFERENT PATIENT POPULATIONS.

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Purpose: Dry eye disease (DED) is one of the most common pathological conditions of the eye, affecting millions of patients. Recently the novel eye lubricant perfluorohexyloctane has been certified as a medical device under the name NovaTears® (marketed as EvoTears®). This non-aqueous, non-blurring, preservative-free lubricating agent reduces shearing forces between surfaces, strengthens the lipid layer and thereby prevents evaporation.

Methods: Three different patient populations participated in three post-market clinical follow-up studies. NT-001: 30 patients with mild to moderate evaporative DED. NT-002: 72 patients with DED due to mild to moderate Meibomian Gland Dysfunction (MGD). NT-003: 25 patients with DED due to chronic ocular Graft-versus-Host Disease (ocular cGvHD). Treatment duration was 6-12 weeks. After providing informed consent, patients applied NovaTears® 4 times daily in both eyes.

Results: TFBUT was increased (NT-001: OD $p=0.0026$, OS $p=0.0006$; NT-002: OD&OS $p<0.0001$) and corneal staining was decreased (NT-001: OD $p=0.0013$, OS $p=0.0041$; NT-002: OD&OS $p<0.0001$) in both NT-001 and NT-002, but remained unchanged in NT-003. Studies also showed a consistent picture for symptoms; a questionnaire similar to the OSDI© improved in NT-001 and NT-002 (NT-001&NT-002: $p<0.0001$) but not in NT-003. In all 3 studies only 8 AEs related to NovaTears® were reported, mainly symptoms of mild to moderate ocular irritation, which disappeared quickly after treatment stop.

Conclusions: Parameters measured in the 3 studies with NovaTears® show a coherent picture of the efficacy of the treatment. Patients with mild to moderate evaporative DED and MGD benefited from NovaTears®. Patients with severe DED due to ocular cGvHD did not receive additional benefit from treatment with NovaTears® to the existing therapy. Safety and tolerability was excellent in all 3 studies.

[Supported by Novaliq GmbH]

PROFILE, TREATMENT AND OUTCOMES OF OCULAR SURFACE SQUAMOUS NEOPLASIA (OSSN) IN A RURAL POPULATION OF CENTRAL INDIA.

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Purpose: To evaluate patients of marginalized and economically backward community in rural and tribal Central India, presenting with OSSN on basis of demography, clinical characteristics, treatment methods and outcomes. To assess the post-operative recurrence, complications and histopathological features of these patients.

Methods: The data is a retrospective hospital based case series of patients who underwent treatment from February 2013 to October 2014. Cases that completed 1 year of follow-up were included.

Results: Average age of patients was 56.2+/-16.2 yrs (12-68yrs). Average follow-up time was 20.1+/-7.5 months. All patients were seronegative for HIV. Male: female ratio was 1:1. 8 patients (80%) had unilateral OSSN and 2 (20%) bilateral. Four eyes (33.3%) had diffuse tumors and 8 eyes (66.6%) localized tumor. Of the 2 patients who had bilateral OSSN, 1 patient had localized OSSN in one eye and diffuse OSSN in other eye while a 12 year old boy with xeroderma pigmentosum had bilateral diffuse OSSN. For localized tumors, wide local excision with cryotherapy to conjunctival and/or scleral base was done and intra-op mitomycin-C (0.04%) was applied. All specimens had negative margins and showed presence of squamous cell carcinoma on histopathology. Topical mitomycin-C(0.04%)was used in all cases either as primary modality or post surgery regimen of 2-4 cycles with each cycle consisting of one week treatment and one week gap. Recurrence was seen in 3 eyes (25%) at the end of 1 year follow-up. All recurrences were seen in diffuse OSSN. Mitomycin-C related limbal stem cell deficiency was seen in 4 eyes (33%) and dry eye was seen in 3 cases(25%). These complications were seen in diffuse type OSSN or large tumors.

Conclusion: Diffuse OSSN has a high risk of recurrence and needs long term rigorous follow up. Post-operative mitomycin-C cycles should be used even in margin free cases of localized OSSN to prevent recurrence.

NO FINANCIAL DISCLOSURE

DOES HYPEROSMOLARITY CAUSE AN IRREVERSIBLE PROCESS LEADING TO HUMAN CORNEAL EPITHELIAL CELL DEATH?

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Purpose: Tear film hyperosmolarity leads to increased ocular surface stress, friction, inflammation and damage, as well as to symptoms of discomfort and visual impairment. We hypothesized that (1) short-term exposure to a hyperosmolar environment would alter cell morphology but not necessarily initiate an irreversible process leading to cell death, and (2) extended exposure to the same conditions would be cytotoxic.

Methods: Human corneal epithelial cells (a gift from Dr. James Jester) were cultured in normal (290 mOsm/L) or hyperosmolar (308, 338, 400, 600 mOsm/L) KSFM for up to 24 hours. Cells were examined for appearance, apoptosis and death.

Results: Our results demonstrate that hyperosmolarity causes morphological and cytotoxic effects in human corneal epithelial cells and that these responses are both dose- and time-dependent. Very few cells die after a 24-hour exposure to 290 or 308 mOsm/L solutions. However, cells exposed to 338 mOsm/L medium exhibit membrane blebs (i.e. a sign of impending cell death), the 400 mOsm/L condition kills a large percentage of cells, and the 600 mOsm/L medium causes complete cell death after 3, 6 or 24 hours. Cell death does not seem to be mediated primarily through apoptotic DNA fragmentation. After a 1-hour exposure to the 600 mOsm/L medium, cells were still alive. Limiting this 600 mOsm/L exposure to 1 hour and replacing with 290 mOsm/L medium for 23 hours enhances cell survival.

Conclusions: Our findings indicate that chronic exposure to a hyperosmolar challenge will kill the majority of human corneal epithelial cells, whereas changes in cell morphology due to brief exposures can be largely ameliorated by normalization of the surrounding environment. Our results also suggest that hyperosmolar conditions may induce forms of death other than apoptosis (e.g. necrosis) in these cells. (Supported by a donation from TearLab and the Margaret S. Sinon Scholar in Ocular Surface Research fund)

ILUX SYSTEM FOR MEIBOMIAN GLAND TREATMENT – REPORT OF SAFETY ASSESSMENT ON HEALTHY VOLUNTEERS.

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Purpose: This study evaluated the safety profile of the iLux™ System for treatment of meibomian gland dysfunction (MGD).

Methods: The iLux System is a novel handheld device for treating MGD using light-based heating and manual compression of the eyelids with visual guidance. Healthy volunteers were enrolled from a single center in this non-randomized open-label safety study. Each eye

received four 90-second heating and compression cycles with the iLux System, 2 in the upper and 2 in the lower eyelids. Subjects underwent a thorough ocular exam before and after each session, including visual acuity, slit-lamp, corneal fluorescein staining, IOP measurement and lid margin assessment. A calibrated IR camera was used to measure temperatures of the eyelid, cornea, and surrounding eye tissue before and after each session. Differences between pre- and post-session exams were analyzed. Subjects rated any eye pain (0=no pain; 10=intolerable pain) on the day of the procedure (before and after session) and 1 day later. Adverse events (AEs) were collected throughout the study.

Results: Fifteen subjects were enrolled and participated, with a mean age of 39.9 ± 15.1 years. No AEs were observed during the study. Max eyelid temperature was 40.6°C (mean max temp=38.5±0.8°C), max corneal temperature was 38.8°C (mean max temp=37.7±0.5°C), and max surrounding surface tissue temperature was 39.7°C (mean max temp=38.2±0.7°C). No clinically significant changes in subject vision between pre- and post-session exams were reported (mean increase of 0.1-1.3 letters), nor were there any subject reports of clinically meaningful pain (highest score=1).

Conclusions: This study demonstrated that the iLux System is not associated with clinically significant changes in vision or pain, and does not excessively heat the eyelids, cornea, or surrounding tissue. Therefore, these results suggest that the light-based heating and manual compression associated with the iLux System does not negatively impact subjects' eyes, their vision, or the surrounding tissue. [This study was supported by Tear Film Innovations, Inc.]

RELATIONSHIP BETWEEN OCULAR SURFACE EPITHELIAL DAMAGE, TEAR ABNORMALITIES, AND BLINK IN DRY-EYE PATIENTS.

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Purpose: Considering that tears play the role of a lubricant, it is speculated that in the pathophysiology of dry eye, the increased friction during blinking results in corneal and conjunctival damage, which may in turn affect the blink itself. The purpose of this present study was to investigate the relationship between ocular surface epithelial damage, tear abnormalities, and blink in dry-eye patients.

Methods: This study involved 45 eyes of 45 female dry-eye patients (mean age: 57.6 years). In all eyes, tear meniscus radius (TMR, mm), spread grade (SG) of the tear-film lipid layer (SG 1-5: 1 being the best), fluorescein breakup time (FBUT, seconds), corneal and bulbar conjunctival epithelial damage (CED: 15 points maximum, CjED: 6 points maximum), and the Schirmer 1 test (ST1, mm) were evaluated. Blink rate (BR, per minute), palpebral aperture height (PAH, mm), upper-eyelid opening/closing-phase amplitude (UOA/UCA, mm), upper-eyelid opening/closing-phase duration (UOD/UCD, msec), and upper-eyelid opening/closing-phase maximum velocity (UOMV/UCMV, mm/sec) were measured by use of a custom-made high-speed blink analyzer. Finally, the factors that determine CED and CjED were investigated by multiple regression analysis in which the parameters were chosen using the stepwise procedure.

Results: CED and CjED were demonstrated to be described as: 2.687 + (1.816 x SG) - (0.937 x FBUT) (R^2=0.656, p<.0001), 0.684 + (0.801 x SG) - (0.526 x FBUT) - (0.041 x ST1) + (0.010 x UCMV) (R^2=0.714, p<.0001), respectively.

Conclusions: While CED was significantly related only to tear abnormalities, CjED was significantly related both to tear abnormalities and blinking.

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HAPPINESS AND DRY EYE.

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Happiness is now scientifically revealed to be a crucial component of both physical and mental health. However, in the field of dry eye, it has not been widely reported. First, we investigated the association between subjective happiness and dry eye disease in a cross-sectional study (the Osaka study) and found that the subjective happiness score was inversely correlated with the dry eye symptom score. The level of subjective happiness was the lowest in the group without objective results, but with reported subjective symptoms of dry eyes ($p < 0.05$). Next, for an ongoing project, the experiments on the tear secretion of happy (environmental enrichment) and unhappy mice (stress induced) will be also presented. Findings of these studies reveal a new perspective on dry eye disease.

SELF-REPORTED COMPLIANCE IN SYMPTOMATIC VERSUS ASYMPTOMATIC PATIENTS WITH EVAPORATIVE DRY EYE.

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Purpose: Our goal was to investigate the self-reported compliance of patients with evaporative dry eye who were prescribed home therapy of daily warm compresses and lid scrubs. An additional goal was to compare compliance rates in symptomatic versus asymptomatic patients.

Methods: Consecutive patients diagnosed with evaporative dry eye, over the age of 18 years, and with five or fewer functional meibomian glands per lower eyelid were fully consented and enrolled. Patients were classified as symptomatic (n=50) or asymptomatic (n=50) using the Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire. All patients were prescribed home therapy of daily warm compresses and lid scrubs. Patients were asked to record their average compliance weekly over a period of three months. Self-reporting was divided into the following major categories: 0-19% (non-compliant, therapy performed infrequently if at all), 20-79% (partial compliance), and 80-100% (compliant, therapy was very frequently performed).

Results: Symptomatic patients reported compliance more frequently than the asymptomatic patients (26% vs. 6%, p<0.05). Symptomatic patients reported non-compliance less frequently than the asymptomatic patients (56% vs. 76%, p<0.05). Overall non-compliance was high in both groups, greater than 50%. The frequency of partial compliance did not differ between the two groups (18% vs. 18%, p>0.05)

Conclusions: Symptomatic patients were significantly more compliant with home therapy than asymptomatic patients. However, even the symptomatic patients evidenced 56% non-compliance. This data has implications for the likelihood of treatment success for patients prescribed therapy that requires high levels of compliance.

INCOMPLETE BLINKING AND MEIBOMIAN GLAND FUNCTION IN A GRADUATE STUDENT COHORT.

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Purpose: Dry eye studies have historically focused on older populations. Our goal was to investigate meibomian gland dysfunction (MGD) and partial blinking in a cohort of young adults enrolled in a graduate student program.

Methods: An IRB approved, prospective, cross-sectional pilot study enrolled 81 graduate students (n = 26 males and n = 55 females, median age 24.7 years) from the New England College of Optometry. Partial blink rate was captured using LipiView (TearScience). The number of meibomian glands yielding liquid secretion (MGYLS) was evaluated for each lower eyelid using the Korb Meibomian Gland Evaluator (TearScience).

Results: A total of 144 eyes (86.7%) exhibited at least one partial blink. Of these, 95 eyes (66.0%) had a partial blink rate greater than 50%, including 59 eyes (41.0%) without any complete blinks. The average partial blink rate was 61%. The mean MGYLS was 8 per lower lid (range 0-30). A total of 123 lids (74.1%) showed evidence of MGD (MGYLS<11).
Conclusions: The prevalence of incomplete blinking and MGD was alarmingly high in our cohort of graduate students, and we expect that this will only increase with time. These facts become even more worrisome when we consider that this cohort faces decades of computer use and exposure to desiccating stress. Further socio-economic concerns are raised by these findings being applicable to graduate students of all disciplines and the future of our professional workforce as a whole. [The authors wish to acknowledge the New England College of Optometry and TearScience for use of instrumentation used in this study].

ASSOCIATION BETWEEN OUTDOOR AIR POLLUTION AND DRY EYE DISEASE IN SOUTH KOREA: THE POTENTIAL IMPORTANCE OF OZONE.

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Purpose: We investigated associations between outdoor air pollution and dry eye disease (DED) in Korean population
Methods: A population-based cross-sectional study using Korea National Health and Nutrition Examination Survey data (from January 1, 2010 to December 31, 2012). 16,824 subjects were included in this study. DED was defined as previously diagnosed by an ophthalmologist or the presence of frequent ocular pain and discomfort. Outdoor air pollution factors [mean annual humidity, particulate matter with aerodynamic diameter less than 10um (PM_{10}), ozone (O_3), and nitrogen dioxide (NO_2) concentrations in South Korea] were collected from national monitoring stations. Associations of multiple air pollutants with DED were assessed from multivariate logistic regression analyses. Sociodemographic factors and previously known associated factors with DED were applied as covariates. (model 1: including sociodemographic factors, model 2: including sociodemographic, behavioral and clinical factors)
Results: In model 1 and 2, higher O_3 concentration and lower humidity were significantly associated with DED symptom and diagnosis. [model 1: 0.003ppm increase of O_3-OR=1.16/1.21, p=0.036/0.008 (DED symptom/diagnosis), 5% increase of humidity-OR=0.87/0.86, p=0.027/0.011], [model 2: 0.003ppm increase of O_3 - OR=1.17/1.27, p=0.026/0.002, 5% increase of humidity - OR=0.88/0.86, p=0.045/0.017] NO_2 was associated with DED diagnosis in model 2. (0.003ppm increase of NO_2 - OR=1.12, p=0.018) PM_{10} and SO_2 concentrations were not associated with DED symptom or diagnosis in model 1 and 2. (each p>0.05)
Conclusion: Higher O_3 concentration and lower humidity were associated with DED, while there were no relationships between PM_{10} concentration and DED in the Korean population.

NEWER CLASSIFICATION OF TEAR FILM BREAK PATTERN; CLINICAL AND PATHOPHYSIOLOGICAL ANALYSIS.

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Purpose: To present modified classification of tear breaking pattern and suggest the different pathophygiological mechanisms in patients with dry eye syndrome (DES)
Methods: Sixty-six eyes from 66 subjects were enrolled in this observational study. According to their fluorescent tear breaking pattern, all patients were divided by two major groups according to their tear breaking patterns, which were 'random', and 'dot' group. Clinical records were also reviewed with the severity of DES, tear film break up time, oxford corneal staining score, and ocular surface disease index (OSDI). Of 10 enrolled subjects and 5 normal subjects, tear collection and impression cytology was performed and studied the quantity of inflammatory cytokines; interleukin (IL) 1b, IL-8 and sialic acid, which is one of the marker of mucin family.
Results: 'Dot' group has showed not only higher clinical severity, but subjective symptoms. Inflammatory cytokines were higher in 'dot' group. The amounts of sialic acid were decreased in both groups, when it compared with normal subjects.
Conclusions: The pathophysiological mechanism and clinical severity was different in two different tear breaking patterns. In this study, 'dot' break mainly resulted from Inflammatory condition of ocular surface, while 'random' break pattern might be caused by tear film instability rather than ocular surface inflammation.

TOXICITY OF POVIDONE IODINE TO THE OCULAR SURFACE OF RABBITS.

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Purpose: We evaluated the toxicity of 5% (w/v) povidone iodine (PI) applied to the ocular surface of rabbits for various times.
Methods: Twenty three white rabbits were divided into four groups; these were a control group and three study groups in which the ocular surface was exposed to PI for different times. In the control group, phosphate-buffered saline (PBS) was applied once, for 10 mins. In the PI groups, 5% (w/v) PI was topically administered (once) for 1 min, 3 mins, and 10 mins, and the animals were observed for 7 days. The Schirmer test, Rose Bengal staining, corneal fluorescein staining, and conjunctival impression cytology, were performed on days 0, 3, and 7. After day 7, conjunctiva and cornea were evaluated by microscopy. Immunofluorescence staining was also performed to detect mucin 5AC (MUC5AC).
Results: The decrease in goblet cell density (GCD) and histopathological changes were more prominent in the 5% (w/v) PI groups than the control group (P<0.05). Moreover, these changes were more noticeable when PI was applied for 3 and 10 mins rather than 1 min (both P values <0.05). Reductions in MUC5AC levels, and histopathological and ultrastructural changes in the conjunctiva, were more prominent in study groups exposed to PI for longer times.
Conclusion: PI caused damage to the ocular surface in a time-dependent manner. Therefore, excessive PI exposure during ophthalmic procedures could be a pathogenic factor of dry eye syndrome after surgery. [None of the authors has a financial or proprietary interest in any material or method mentioned.]

COMPARISON OF LONG TERM CLINICAL RESULTS OF LIMBAL CONJUNCTIVAL AUTOGRAFT VERSUS AMNIOTIC MEMBRANE TRANSPLANTATION IN PRIMARY PTERYGIUM SURGERY.

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Purpose: To compare the long term efficacy and the recurrence of limbal conjunctival autograft versus amniotic membrane transplantation in surgically treated pterygium patients.

Methods: A prospective randomized study of 135 eyes of 135 patients older than 50 years undergoing excision of primary pterygium was performed. After pterygium excision, limbal conjunctival autograft was done in 75 eyes (Group 1) and cryopreserved amniotic membrane graft was used in 60 eyes (Group 2). The patients were followed for approximately three years. Mean follow-up period was 36 months. All patients were examined for graft success, recurrence, which was graded from G0 to G3, and complications such as delayed epithelial wound healing and granuloma formation.
Results: In Group 1, 60 out of 75 cases showed no recurrence (grade 0), and 10 cases of grade 1 recurrence and 5 cases of grade 2 were observed. On the contrary, 43 out of 60 cases in Group showed no recurrence, and 12 cases of grade 2 recurrence and 5 cases of grade 3 recurrence were observed. Conjunctival granuloma formation was occurred in 6 cases in amniotic membrane transplantation group and none in limbal conjunctival autograft group. Epithelial wound healing is not delayed in both group.
Conclusions: Both limbal conjunctival autograft and amniotic membrane transplantation can be safe and effective adjunctive treatments for primary pterygium. However, limbal conjunctival autograft has a lower recurrence rate and less complications than amniotic membrane transplantation for long term follow up period. Limbal conjunctival autograft appears to be a more effective technique to reduce the recurrence after pterygium excision. No commercial relationship

ANGIOGENIN AS BIOMARKER OF DRY EYE.

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Purpose: To investigate the properties of angiogenin (ANG) as biomarker for the diagnosis and grading of dry eye syndrome (DES) by analyzing tear protein profiles.
Methods: Tear samples were collected with capillary tubes from 52 DES patients and 29 normal individuals as controls. Tear protein profiles were analyzed with an immunodot blot. To confirm that the tear protein profiles were changed according to the grade of dry eye, the ANG and lactoferrin (LF) tear contents of normal controls and DES patients were analyzed with an enzyme-linked immunosorbent assay (ELISA).
Results: In the immunodot blot assay, the area of ANG was lower than that of normal controls in grade 3 and 4 DES patients. The basic fibroblast growth factor, transforming growth factor β2, and interleukin 10 areas were significantly greater in patients with grade 4 DES than in normal controls. Otherwise, these proteins were not linearly correlated with dry eye severity. Upon ELISA analysis, the mean concentrations of ANG and LF decreased significantly as dry eye severity increased, except between grades 1 and 2. In addition, the ratios of ANG and LF to total tear proteins were correlated significantly with DES severity.
Conclusions: ANG level was significantly lower in DES patients than in normal controls. ANG and LF level was significantly correlated with the severity of DES, except between grades 1 and 2. Therefore, ANG may be a useful biomarker of DES severity.

EFFECTS OF SUBCONJUNCTIVAL ADMINISTRATION OF ANTI-HIGH MOBILITY GROUP BOX 1(HMGB1) ON DRY EYES IN A MOUSE MODEL OF SJÖGREN SYNDROME.

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Purpose: To investigate effects of subconjunctival administration of anti-HMGB1 on dry eyes in a mouse model of Sjögren syndrome.
Methods: 0.02 to 2 μg of anti-HMGB1 antibodies or PBS were injected subconjunctivally into 10 week-old NOD.B10.H2b mice twice a week for 2 consecutive weeks. Tear volume and corneal staining scores were measured 1 or 2 weeks after the treatment. Goblet cell density was measured in PAS stained forniceal conjunctiva and inflammatory foci score was measured in extraorbital glands. The changes of BrdU+ cells, IL17-, IL10- or IFNγ-secreting cells, functional B cells, and IL22 secreting innate lymphoid cells (ILCs) were evaluated in cervical lymph nodes. The level of IL22 was measured in intraorbital glands.
Results: Injection of anti-HMGB1 attenuated corneal epithelial erosions and increased tear secretion and goblet cell density, although the inflammatory foci score and the number of BrdU+ cells, IL17-, IL10-, and IFNγ-secreting cells, and functional B cells were not changed. In addition, the percentages of IL22 secreting ILCs were significantly increased in cervical lymph nodes and the expression of IL22 was significantly increased in intraorbital glands with 2 μg of anti-HMGB1 injection.
Conclusion: This study suggests that subconjunctival administration of anti-HMGB1 attenuate clinical manifestations of dry eye probably by increasing IL-22-secreting ILCs, in a mouse model of Sjögren syndrome.
This work was supported by a grant from the Seoul National University Hospital Research Fund (Project No. 03-2012-0340). All authors have no proprietary interest in methods described in this article.

ROLE OF MTOR SIGNALING IN PTERYGIUM FIBROBLASTS

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Purpose: Epithelial mesenchymal transition (EMT) and myofibroblast differentiation have been known to be related to the pathogenesis of pterygium. In this study, we investigated role of mTOR signaling in human pterygium fibroblasts (hPFs) by inhibiting mTORC1 or mTORC2.
Methods: hPFs were grown in culture and transformed into myofibroblasts using TGF-β (2 ng/ml) and activation of the mTOR pathway was examined by immunoblotting. Cell proliferation was examined by MTT assay after treatment with different concentrations of mTORC inhibitors (rapamycin and torin). The expression of αSMA and fibronectin after mTORC inhibition (rapamycin and torin) and effects of downstream signal pathway were investigated using immunoblotting or immunofluorescence.
Results: The TGF-β treatment activated mTOR pathway and increased the expression of αSMA and fibronectin. Pretreatment with torin, which is inhibiting both mTORC1 and mTORC2, significantly inhibited expression of αSMA and fibronectin, whereas rapamycin showed limited effect of suppressing myofibroblast differentiation. These effects were not related to Smad 2/3 signaling pathway, but seemed to be related to Akt-mTOR pathway. Rapamycin and torin also reduced proliferation of hPFs similarly (20 to 40%).
Conclusions: Akt-mTOR signaling appears to have important roles in myofibroblast differentiation in pterygium fibroblasts. This may provide rationale for targeting specific components of mTORC pathways in pterygium.

AGE-RELATED DIFFERENCES IN CORNEAL EPITHELIAL THICKNESS MEASUREMENTS WITH ANTERIOR SEGMENT OPTICAL COHERENCE TOMOGRAPHY.

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Purpose: To measure corneal epithelial thickness (CET) in normal healthy subjects adults and to investigate its variation with age by use ofing anterior segment optical coherence tomography (OCT).
Methods: A total of 210 healthy individuals normal subjects were enrolled and divided into four 4 groups on the basis of age: Groups groups 1 (18–29 years, 54 individuals), 2 (30–44 years, 52 individuals), 3 (45–59 years, 54 individuals), and 4 (60–80 years, 50 individuals). The CET and total corneal thicknesses in the central area (6.0 mm in diameter) were obtained by a Fourier-domain OCT, and the regional thickness and topographic variability were compared among the age groups. In addition, the correlation between the CET and age, gender, and refractive status was analyzed using partial correlation tests and multiple regression analysis.
Results: The CET of the central segment (2 mm in diameter) in Groups groups 1, 2, 3, and 4 were 53.74 ± 3.82, 54.48 ± 3.33, 53.89 ± 3.73, and 53.30 ± 3.36 μm, respectively, showing no significant change with age ($P = 0.416$). In most of the paracentral and all of the mid-peripheral zones (annuli 2–5 and 5–6 mm from the center), the CET differed significantly among the four 4 groups. Correlation analysis suggested that the CET is greater in men than in women and that that of the paracentral and the mid-peripheral zones are inversely correlated with age. Topographic variability was also inversely correlated with age.
Conclusions: The CET became thinner with aging age in the paracentral and mid-peripheral zones, while the central CET seemed to remain constant. Gender differences should be considered in the assessment of CET. The authors has no commerical relationships.

AUTOMATED MEASUREMENT OF TEAR FILM DYNAMICS AND LIPID LAYER THICKNESS FOR ASSESSMENT OF NON-SJÖGREN DRY EYE SYNDROME WITH MEIBOMIAN GLAND DYSFUNCTION.

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Purpose: To investigate automated values from an advanced corneal topographer with a built-in real keratometer, color camera, and ocular surface interferometer for the evaluation of non-Sjögren dry eye syndrome (NSDES) with meibomian gland dysfunction (MGD).
Methods: Sixty-four patients (128 eyes) diagnosed with NSDES with MGD were enrolled. All eyes were evaluated using the Ocular Surface Disease Index (OSDI), fluorescence staining score, tear film break-up time (TBUT), Schirmer's test, and MGD grade. Non-invasive Keratograph® average TBUT ($NIKBUT_{av}$), tear meniscus height (TMH_k), meibomian gland (MG) dropout grade, and lipid layer thickness (LLT) using LipiView® were measured. Results: Among automated indexes, $NIKBUT_{av}$ and MG dropout grade significantly correlated with the OSDI ($p < 0.05$), as did all conventional indicators, except Schirmer's score ($p < 0.05$). TMH_k had significant relevance to Schirmer's score, the staining score, TBUT, $NIKBUT_{av}$, and LLT, but not any MGD indicator, even MG dropout grade. $NIKBUT_{av}$ showed significant correlations with all clinical parameters and other automated values, except Schirmer's score and LLT ($p < 0.01$). MG dropout grade was highly correlated with all indexes except TMH_k ($p < 0.05$). LLT was significantly associated with TBUT, MGD grade, TMH_k, and MG dropout grade ($p < 0.05$), although it was not related to patient symptoms.
Conclusion: Automated non-invasive measurements using an advanced corneal topographer and LLT measured with an ocular surface interferometer can be alternatives to conventional methods to evaluate tear conditions on the ocular surface; the former device can provide information about conformational MG changes in NSDES with MGD.

TRANSPLANTATION OF SUBSTRATE-FREE CULTURED ORAL MUCOSAL EPITHELIAL CELL SHEETS (COMECS) IN TREATMENT OF LIMBAL STEM CELL DEFICIENCY

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Purpose: To investigate the efficacy and safety of substrate-free Cultured Oral Mucosal Epithelial Cell Sheets (COMECs) transplantation in patients with severe total limbal stem cell deficiency **Methods:** A prospective clinical trial (nct number: NCT02149732) has been conducted in 8 eyes in 8 patients with total limbal stem cell deficiency (Stevens-Johnson syndrome 6, chemical burn 1, phemphigoid 1) after an approval of institutional review board of Seoul National University Hospital (H-0707-043-213)and Korea Food and Drug Administration. COMECs were made without use of any temperature sensitive polymers in culture system and without any carriers. The COMECs were transplanted without any suture fixation after a removal of conjunctivofibrous tissues on the cornea. Penetrating keratoplasty was done in 3 patients after stabilization of COMECs transplantation. Stable epithelialization, change in visual acuity and postoperative complications were evaluated.
Results: During mean 8 months follow-up, COMECs was survived in 75% of the eyes. Complete stable epithelialization was achieved within average of 47.5 days. Visual improvement (≥ 1line) was achieved in 62.5% of the eyes. No infection, local tumor formation and systemic complication were found during the follow-up. Peripheral non-significant vascularization was observed in 100% of the eyes. **Conclusion:** substrate-free COMECs transplantation seems to be efficient and safe procedure to reconstruct ocular surface in patients with limbal stem cell deficiency. This work was supported by a grant from the Korea Healthcare Technology R&D Project, Ministry for Health & Welfare, Republic of Korea (Project No. HI14C1573).
All authors have no proprietary interest in methods described in this article.

TOWARDS A HOLISTIC UP-TO-DATE MODEL OF THE PATHOPHYSIOLOGY IN DRY EYE DISEASE.

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Purpose: Dry Eye Disease (DED) is a complex alteration of the functional anatomy of the ocular surface. Several disease models have been proposed - typically centered around then identified mechanisms and often oversimplified.
Methods: In order to achieve a holistic model of DED - simple enough but still complex to reflect all known important mechanisms, a new model was elaborated based on a review of the existing scientific literature.
Results: Primary CAUSATIVE FACTORS of DED are (1) impairment of aqueous secretion in ´Lacrimal Gland Dysfunction´ (LGD), (2) Meibomian Gland Dysfunction (MGD) with lipid deficiency, and (3) alterations of blinking & lid integrity for which the newly coined term (3) ´Eye Lid & Blinking Dysfunction´ (LBD) is

suggested - leading to tear film deficiency even though gland secretions may be normal. They give rise to Primary PATHOLOGICAL CONSEQUENCES of (A) tear film deficiency and (B) ocular surface damage - both give rise to sequences of downstream SECONDARY PATHOGENETIC FACTORS. These interact and eventually result in the two main secondary factors of chronic mechanical irritation and hyperosmolarity that both induce tissue wounding. Impairment of innervation leads to disturbance of neural reflex arcs for secretion & blink regulation. Their similarity in lacrimal and Meibomian glands offers their cross regulation. The nervous system does not only regulate function but also sensation. Pain is influenced and modulated by higher order mechanism and can lead to chronic pain syndromes that may explain why signs and symptoms can typically be disparate in DED. Vicious circles (VC) act ´back´ in the pathogenetic process and therefore lead to a self-enforcement of the disease. In contrast to conventional thinking, in DED there are several VC that constitute important ´disease carousels´.

Conclusion: We have elaborated a new pathophysiology model of DED that incorporates long established as well as new mechanisms - complex but simple - to please basic scientist & practitioner.

THE RELATIONSHIP BETWEEN CORNEAL NERVE MORPHOLOGY AND SUBJECTIVE SYMPTOM IN DRY EYE DISEASE.

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Purpose: The purpose of this study was to evaluate the relationship between the in vivo confocal microscopic (IVCM) morphology parameters of cornea and subjective symptom in patients with dry eye disease (DED).

Methods: Twenty patients with DED and 23 healthy age- and sex-matched control subjects were included. Each patient underwent an evaluation of ocular surface disease symptoms using the Dry Eye-Related Quality-of-Life Score (DEQS); tear film break-up time (TBUT); corneal fluorescein staining; and corneal subbasal nerve and immune dendritic cell analysis with IVCM. One eye of each subject was included in the study.

Results: DEQS was significantly worse in the DED group as compared with the control group ($p<0.001$). The DED group showed significantly lower corneal subbasal nerve density (16.4 ± 5.3 mm/mm^2) compared to the control group (22.9 ± 4.7 mm/mm^2, $p<0.001$). Dendritic cell density was significantly higher in the DED group than in the controls (52.9 ± 33.5 vs 21.2 ± 11.6 cells/mm2, respectively, $p<0.001$). In the DED group, no statistically significant correlations were found between DEQS and corneal subbasal nerve density ($r=-0.01$, $p=0.98$), and dendritic cell density ($r=0.06$, $p=0.84$).

Conclusions: The relationship between corneal nerve morphology and subjective symptom, as evaluated with IVCM and DEQS, respectively, shows no significant correlation in DED. [The authors have no financial interest in the subject matter of this presentation.]

RECONSTRUCTION OF OCULAR SURFACE BY THE TRANSPLANTATION OF LIMBAL EPITHELIAL CELLS CULTURED IN TRIDIMENSIONAL SYSTEM (SANDWHICH METHOD).

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Purpose: Evaluate immunophenotypes and clinical outcomes of rabbit injured ocular surface treated with limbal epithelial cells (LECs) cultured on denuded human amniotic membrane (dHAM) through a conventional versus a modified protocol (sandwich method, 3D culture).

Methods: Rabbit LECs were cultured on monolayer of dHAM (conventional method, group I) or between double layers of dHAM fragments (sandwich method, group II) for 10 days. The dHAM containing cells were transplanted onto the cornea of the right eye of 20 rabbits with unilateral limbal deficiency. Immunohistochemical expressions of p63 (clone 4A4), K3/K12 (clone AE5) and PCNA (clone PC10) were studied. Clinical data based on the presence of chemosis, blepharospasm, hyperemia, and corneal opacity/edema were collected 14 and 63 days after transplantation. Differences were considered significant when $p\leq.05$.

Results: All samples were positive for expression of p63, K3/K12 and PCNA. On the postoperative day 14, 10% of groups I and II showed mild chemosis ($p>0.05$), 70% of group I and 100% of group II showed mild to severe blepharospasm ($p>0.05$), 20% of the group I and 70% of group II had mild to severe hyperemia ($p<0.05$) and all patients of groups I and II showed mild opacity/edema ($p>0.05$). On the day 63, chemosis was absent for groups I and II, blepharospasm and hyperemia were mild to 10% of groups I and II ($p>0.05$). Opacity/edema was still observed in both groups ($p>0.05$).

Conclusions: The research groups were similar with respect to immunophenotypes and clinical outcomes. [This research was supported by grants from FAPESP (Proc. 2012/17308-5 and 2014/18007-4) and CNPq (467289/2014-0)].

TEAR CYTOKINE ANALYSIS AND IN VIVO CONFOCAL MICROSCOPY IN POST-LASIK ECTASIA.

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Purpose: The pathogenesis of post-LASIK ectasia (PLE) remains poorly understood. We report the tear cytokine profile and in vivo confocal microscopy findings in eyes with PLE.

Methods: This retrospective study included age-matched 7 (14 eyes) post-LASIK controls (PLC) and 6 (12 eyes) post-LASIK ectasia (PLE) subjects. Corneal topography was used to categorize the subjects into PLC and PLE groups. Ocular Surface Disease Index (OSDI) scores obtained were based on standard questionnaire and in vivo confocal microscopy images were used to determine corneal dendritic cells density (DCD). Inflammatory cytokines in the tears were quantified using flow cytometry based cytometric bead array.

Results: Pentacam-based scores, OSDI scores and corneal dendritic cell density were significantly ($P<0.05$) higher in patients with PLE compared to PLC. Total OSDI score and discomfort-related subscale exhibited a positive correlation ($r - 0.807$, $P = 0.005$; $r - 0.817$, $P = 0.004$ respectively) with corneal DCD in post-LASIK ectasia cohort. Inflammatory cytokines were found to be significantly ($P<0.05$) higher in the PLE cohort.

Conclusion: The current study found a significant difference in the tear film cytokine profile between normal and post-LASIK ectasia eyes. Presence of increased corneal dendritic cells and altered tear cytokines suggests an ongoing inflammatory response in post-LASIK ectasia. [The authors extend their sincere gratitude to Dr Abhijit Sinha-Roy, Narayana Nethralaya Foundation, Bangalore for his valuable inputs towards corneal topography and statistical analysis. The authors also acknowledge Narayana Nethralaya Foundation, Bangalore, India for funding this work.]

OCULAR SURFACE, TEAR FILM AND NEURO-MARKERS IN SUBJECTS WITH OCULAR ITCHINESS.

Sailesh Kolanu[1], Blanka Golebiowski[1], Mark Willcox[1], Arthur Ho[1, 2], Isabelle Jalbert[1], [1]School of Optometry and Vision Science, UNSW Australia, [2]Brien Holden Vision Institute, Australia

Purpose: To measure ocular surface, tear film and neuro-markers in subjects with itchy eyes and compare them to allergic and control subjects.

Methods: 50 subjects were classified into three groups based on the presence of itchy eyes and prior diagnosis of allergy (itchy eyes, allergy and control groups). Skin Prick Test (SPT) was conducted. The following were measured: allergy symptoms, tear function, ocular surface signs, ocular surface sensitivity (Cochet-Bonnet), corneal nerve morphology, tear substance P and tear IgE (Allerwatch). Kruskal-Wallis/one-way ANOVA was conducted to compare the variables between the three groups, following which a pairwise comparison was conducted. Exploratory discriminant analysis was performed to understand the relationship of itchy eyes with allergy.

Results: Subjects in the itchy eyes and the allergy groups not only had differences in conjunctival signs (hyperaemia (0.7 grade higher; $p<0.0001$), chemosis (1 grade higher; $p<0.0001$)); lid roughness (0.9 grade higher; $p<0.0001$) and lid margin staining (1 grade higher; $p=0.01$), but also in neuro-markers such as corneal sensitivity threshold (0.12 grams/mm^2 higher; $p=0.006$) and corneal nerve density (4mm/mm^{2}lower; $p<0.0001$), than the control group. Differences in allergy markers (SPT ($p=0.004$) and Allerwatch ($p=0.01$)) and corneal nerve interconnections (1.1 interconnections/mm lower; $p=0.005$) were limited to allergy group. Factors extracted from the discriminant analysis suggested that the itchy eyes and the allergy groups could be distinguished from the control group using a combination of conjunctival and neuro-markers such as hyperaemia, chemosis, corneal sensitivity threshold and corneal nerve density. In addition, the itchy eyes group could be distinguished from the allergy group using a combination of allergy and neuro-markers such as SPT, tear IgE, corneal sensitivity threshold and corneal nerve density.

Conclusion: Ocular surface and neuro-markers indicated that itchy eyes group possibly had either undiagnosed or subclinical allergy.

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Conclusion: Ocular surface and neuro-markers indicated that itchy eyes group possibly had either undiagnosed or subclinical allergy.

INVESTIGATION OF THE CLINICAL FEATURES OF "PATCHY SPK".

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Purpose: Superficial punctate keratopathy (SPK) is the fundamental finding of dry eye. When examining subjects, we sometimes encounter a "patchy pattern" fluorescein staining (what we term "patchy SPK", or pSPK) that is a similar finding to SPK in dry eye patients. The purpose of this present study was to investigate the difference of clinical features between the two types of SPK (pSPK and non-pSPK).

Methods: This study involved 65 eyes of 65 patients (4 males and 61 females; mean age: 65.2 years) with SPK, of which the SPK types were categorized as either pSPK (35 eyes) or non-pSPK (30 eyes). In all 65 eyes, the tear meniscus radius (TMR, mm), spread grade (SG) of the tear-film lipid layer (grades 1-5, 1 being the best), non-invasive breakup time (NIBUT, seconds), fluorescein breakup time (FBUT, seconds), corneal epithelial damage (CED, 15 points maximum), conjunctival epithelial damage (CjED, 6 points maximum), and the Schirmer 1 test (ST1, mm) score were examined. Moreover, the prevalence of Sjögren's syndrome (SS) in each group was evaluated.

Results: In the comparison of each examination (pSPK vs. non-pSPK) between the pSPK and non-pSPK types of SPK, statistically significant difference ($p<0.05$) was found in CjED (3.1 ± 1.9 vs. 1.3 ± 1.6), ST1 (5.6 ± 7.4 vs. 14.8 ± 11.4), and the prevalence of SS (60.0% vs. 16.7%).

Conclusions: The findings of this study revealed significant differences in the clinical features CjED, STI, and the prevalence of SS between pSPK and non-pSPK eyes, and that patients with pSPK may also present clinical characteristics associated with inflammation.

CAN MEIBOGRAPHY FAIL TO REVEAL FUNCTIONAL GLAND STRUCTURE?

Donald R. Korb[1], Caroline A Blackie.[2] Korb Research, Boston MA[1]; TearScience, Inc., Morrisville, NC[2]

Purpose: The purpose of this pilot study was to evaluate if functional meibomian glands can be demonstrated even when infrared surface reflective meibography fails to visualize gland structure in patients diagnosed with dry eye and MGD.

Methods: A retrospective analysis was performed on de-identified data from consecutive eligible, fully consented, patients at a single clinical center. The inclusion criteria for the test group (n = 5) were diagnoses of dry eye, MGD and absence of definitive structural details of the lower lid meibomian glands as observed with the Modi ReSeeVit Topographer with meibography. Consecutive patients without either dry eye or MGD, and with observable lower lid meibomian gland structure, served as controls (n = 5). The nasal third of the eyelids and right eyes only were analyzed. The number of functional glands, using standardized meibomian gland expression, was compared between the expected zero for the test group against

the expected ~ 5 functional glands for the control group
Results: Mean age: Test group = 49.4 ± 13.7 years, (range = 31- 67 years); Control group = 50.2 ± 10.9 years, (range = 35- 64 years). Mean expected number of functional MGs: Test group = 0; Control group ~ 5. Mean actual number of functional glands: Test group = 1.8 ± 1.1 glands, (range = 0 - 2); Control group = 5.0 ± 2.0, (range = 3 - 8).
Conclusions: This pilot study indicates that despite the absence of observable meibomian gland structure in a meibographic image, functional glands can exist. While the number of functional glands is reduced where gland structure is not observable, it may not be zero. These findings contradict the consensus that treatment is futile when glands cannot be visualized. Treatment may indeed be indicated to preserve and possibly enhance the remaining gland function even when gland structure cannot be visualized.

IS DRY EYE THE WRONG DIAGNOSIS FOR MILLIONS?

Donald R. Korb[1], Caroline A. Blackie.[2] Korb Research, Boston MA[1]; TearScience, Inc., Morrisville, NC[2]
Purpose: The purpose of this study was to evaluate if patients with dry eye who were refractory to conventional treatment focused on aqueous production and dry eye sequelae, could improve if treated with a program specifically focused on MGD, the leading cause of dry eye. This is the first study to address this question.
Methods: A retrospective analysis was performed on de-identified data from eligible, fully consented, refractory dry eye patients with MGD at a single clinical center. Subjects: 12 males, 35 females, n = 47. A comprehensive dry eye workup was conducted on all patients. An MGD-first treatment approach was prescribed for all 47 patients. The primary outcome measures were improvement in the number of functional glands and dry eye symptom score.
Results: Mean age = 50.9 ± 16.5 years, range = 18 – 80 years. Mean number of functional MGs: Before Tx: 3.3 ± 2.0 (range 0-9); After Tx: 6.3 ± 2.2 (range 0-12); $p < 0.0001$ (paired t-test). Mean symptom score: Before Tx: 13.9 ± 5.2 (range 5-28); After Tx: 8.4 ± 4.2 (range 2-18); $p < 0.0001$ (paired t-test). Approximately 60% of the patients reported greater than 50% subjective overall improvement post treatment.
Conclusions: This study indicates that in this refractory population, treatment to ameliorate meibomian gland obstruction and rehabilitate gland function achieved significant success. This success was achieved despite the failure of prior conventional treatment focused on treating inadequate tear production and resulting sequelae based on a diagnosis of 'dry eye'. These results demonstrate the importance of diagnosing and implementing specific treatment for MGD. Since MGD is now believed to be the major cause of all dry eye, we recommend MGD be routinely evaluated in all dry eye evaluations, and when present, that specific MGD treatment is the first treatment consideration. This study provokes the statement that 'dry eye' is the wrong diagnosis for millions.

MECHANISMS AND MOLECULAR REGULATION OF LACRIMAL GLAND MORPHOGENESIS AND MAINTENANCE.

Alison Kuony and Frederic Michon, University of Helsinki, Helsinki, Finland.
Purpose: Dry Eye Syndrome (DES) represents one of the most common eye disease (up to 35% of the elderly affected). It can result from different factors such as decrease in tear secretion from the lacrimal gland (LG), and leads to an impaired vision and a severe discomfort.
Ectodermal organs share similar morphological features and molecular mechanisms during development. It gives rise to the formation of functional organs, such as LG, containing stem cell (SC) niches. The existence of LG SCs was suggested, but no SC population has been identified yet.
In my work, I investigate the molecular mechanisms underlying the LG development and maintenance.
Methods: I take advantage of my team expertise in *ex vivo* cultures, using different transgenic mouse lines to decipher the implication of various signaling pathways during LG development, at the molecular and cellular level.
Results: By comparing *in vivo* and *ex vivo* LG development, I showed that LG explants cultures can be used as a reliable model to study the mechanisms and molecular regulations implicated during LG morphogenesis.
Conclusion: While no definitive DES treatment is available so far, I propose to enrich the knowledges on LG SC to develop new clinical strategies, and to propose new alternatives to DES treatment based on SC therapy and bioengineering. Financial supports: University of Helsinki, Academy of Finland, CIMO, Jane and Aatos Erkko Foundation, ILS doctoral program.

THE ASSOCIATION BETWEEN MEIBOMIAN GLAND WIDTH, CLINICAL TESTS, AND PATIENT-REPORTED OUTCOMES IN CONTACT LENS AND NON-CONTACT LENS WEARERS.

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Purpose: To examine the relationship between meibomian gland (MG) width and patient-reported outcomes associated with dry eye, as well as the MG width relationship with clinical tests in contact lens (CL) and non-contact lens (NCL) wearers.
Methods: This was a cross-sectional study open to participants who attended the American Academy of Optometry's 2015 annual meeting. Upper eyelids of 198 subjects (106 CL and 92 NCL wearers) were everted and MGs were imaged using a Keratograph 5M infrared camera (OCULUS). Seven central MGs were selected from the images and processed using custom designed software developed in MATLAB. Regression analysis was used to determine associations between MG width and age, gender, phenol red thread (PRTT), tear meniscus height (TMH), the Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire, and the Contact Lens Dry Eye Questionnaire-8 (CLDEQ-8).
Results: No difference in MG width was observed between CL and NCL wearers (both 0.45±0.07mm, $p>0.05$). Overall, correlation analyses indicated significant correlations between MG width and TMH ($R=-0.16$, $p=0.02$) and PRTT ($R=-0.16$, $p=0.02$). No significant correlations or differences were found between MG width and age, CLDEQ-8, SPEED, and gender. Individual group analysis showed a significant correlation between MG width and PRTT ($R=-0.22$, $p=0.02$) in CL wearers. A significant correlation between the MG width and TMH ($R=-0.28$, $p<0.01$) and SPEED ($R=0.25$, $p=0.02$) was found for NCL wearers, as well as significantly wider MGs in subjects who self-reported MGD (0.49±0.04mm vs 0.43±0.07mm, $p<0.001$) and dry eye (0.46±0.06mm vs 0.43±0.07mm, $p=0.04$).
Conclusions: Meibography has primarily focused on the area of MG dropout; however, the results of this study indicate that the width of the MGs is potentially a better predictor for ocular discomfort. These results suggest that dilation of the MGs negatively impacts ocular comfort in NCL wearers and reduces tear volume in both CL and NCL wear.

21ST CENTURY DIGITAL DEVICE USE AND OSDI.

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Ketchum University,[1] Fullerton, CA; Illinois College of Optometry,[2] Chicago, IL; Private practice,[3] York, PA; Minnesota Eye Consultants,[4] Minneapolis, MN; Private practice,[5] Clarenville, NL, Canada; Omni Eye Services,[6] New York, NY; Private practice,[7] Azusa, CA.
Purpose: The advancement of digital devices in the 21st century has drastically changed the way we spend our time. The goal of this study was to see how digital device use differs in every decade of life. Methods. A two page survey was created and administered at seven clinical sites and online. The Ocular Surface Disease Index (OSDI) was included.
Results: Two hundred ninety-one subjects age 18 to 98 completed the survey. Most subjects (85.2%) reported using at least two out of four possible digital devices (smartphone, tablet, laptop, desktop). There was a significant drop off for those 60 and older in devices used and hours spent on devices. The 18-29 group (n=58) all used smartphones and looked at them the most (11 times/hour) but only nine used tablets (15.5%). The 40-49 group (n=52) had the largest proportion using tablets (48.0%). Of those that reported using computer monitors (n=222), 68.6% used one monitor and 23.6% used two monitors. There were 17 subjects that used three to six monitors. Those that weren't retired work an average of 36.0+14.8 hours per week (range 2 to 70). The most reported number of hours spent in meetings per week were 2 and 10. Subjects aged 30-39 (n=51) spent the most hours on digital devices (10.1+5.9) but had the least symptoms per OSDI (14.0+14.8). However, the OSDI scores were not statistically different than the 18-29 and 40-49 group (p=0.219).
Conclusions: The age of an individual and the generation they grew up in may influence which digital device(s) they gravitate towards. The results of this study begin to shed light on the changing landscape of digital device use and how it may or may impact dry eye symptoms.

DAYTIME TEAR FILM AND CORNEAL THICKNESS VARIATION WITH SEVERAL SCLERAL CONTACT LENS DIAMETERS.

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Purpose: To evaluate the effect of the scleral contact lens diameter on corneal thickness and tear meniscus area with optical coherence tomography (OCT).
Methods: 21 eyes of 21 subjects volunteered for the study. The subjects wore two contact lenses, randomly assigned, with neutral power and different diameters [12.7 mm (L1), 18 mm (L2)] and being equal for the others parameters: material (HS100) and thickness (0.29mm). At 20 minutes margin (t1) and 8 hours margin after insertion (t2), the area of the tear meniscus was evaluated with OCT (SL SCAN-1, Topcon) as well as central corneal thickness (Visante, Carl Zeiss) and tear osmolarity (TearLab Corporation). The contact lens wear has been discontinued for four days between each measurement in order for eyes to recover.
Results: No statistically significant differences between two contact lenses influence were found in the values of tear meniscus area at t1 (p=0.3) and t2 (p=0.2) or in corneal thickness t1 (p=0.2) and t2 (p=0.2). Whereas statistically significant differences were found in the area of tear meniscus throughout the day for L1 (0.020 mm^2 at t1 and 0.016 mm^2 at t2, $p<0.05$) and for L2 (0.018 mm^2 at t1 and 0.013 mm^2 at t2, $p<0.05$). Regarding the central thickness, no statistically significant differences were found between the lenses (t1, p=0.4 y t2, p=0.3) or throughout the day for each lens (L1, p=0.3 and L2,p=0.3). Regarding the osmolarity, mean values do not change significantly throughout the day for the same lens (L1, p=0.5 and L2, p=0.5) or when comparing contact lenses (t1, p=0.4 y t2, p=0.5).
Conclusions: The results obtained in this study allow us to ensure that the selection of the diameter of the scleral lens has no influence on the tear meniscus or central corneal thickness. This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No642760

HA-SULFADIAZINE CONJUGATE FOR THE TREATMENT OF DRY EYE DISEASE.

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Purpose: Dry eye disease (DED) is a multifactorial disease affecting the ocular surface for which there is no putative cure. Hyaluronic acid (HA) is shear thinning, highly lubricious, and can bind enormous amounts of water, relieving DED symptoms. HA also binds CD44, a multifunctional cell surface receptor which can increase goblet and epithelial cell survival while lowering inflammation. Sulfadiazine (SD) has recently been identified as a potent matrix metalloprotease inhibitor (MMPi). Overactivity of MMPs, particularly MMP-9, is so congruent with DED that it has become a de facto marker in the clinic. By conjugating HA to SD, a novel formulation has been developed which synergistically combines the mucoadhesiveness of HA with an active ingredient.
Methods: HA-SDZ materials are prepared by dissolving 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC), Hydroxybenzotriazole (HOBt), and an excess of SD in 70:30 DMSO:water. The solution is heated to 70°C for 24 hours, and excess SDZ is precipitated by increasing the water content. This formulation was tested in New Zealand White (NZW) rabbits which were chemically induced to display DED symptoms by topically administering a 0.1% Benzalkonium Chloride (BAC) solution twice daily for 14 days. These DED rabbits were rescued with HA-SD, and their performance was compared to commercially available eye drop Systane Ultra. This rescue is assessed using fluorescein staining with a slit lamp ophthalmoscopy, Schirmer's testing, conjunctival impression cytology (CIC), and conventional histology.
Results: HA-SD performed at least as well as Systane Ultra at relieving DED symptoms after scoring on a modified Draize test. HA-SD returned all relevant metrics (tear film, CIC, staining) to normal levels much faster than untreated controls.
Conclusions: A novel formulation of HA and SD was created to treat DED.

OCULAR SURFACE INVOLVEMENT ON GVHD PATIENTS.

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Introduction: Graft Versus Host disease (GVHD) is a common and severe complication of allogeneic bone marrow graft, ocular surface is one of the targets of this disease;
Purpose: to identify the different complications of GVHD on ocular surface
Patients and methods: ocular surface examination on patients with GVHD , referred by the center of bone marrow graft of Algiers, all benefited from OSDI questionnary, slit lamp examination, fluorescein coloration and Schirmer test,
Results: 31 patients were assessed, 22 males , tha mean age value were 39,3 years+/_ 7,4; all patients presented different levels of severity of dry eye at slit lamp examination, 5% of them had a very low visual acuity; Mean OSDI score was 76,4+/_10,2 corneal staining was present on 92% of cases (oxford : 6,5+/_ 2,5) and Schirmer value 10+/_5,4).
Conclusion: dry eye is the most common ocular complication on GVHD patients, in most of cases it is a severe dry eye with corneal involvement and visual impairment, an early diagnosis and treatment of ocular manifestations of GVHD is essential to prevent severe complications.

EFFECTS OF MECHANICAL MEIBOMIAN GLAND SQUEEZING ON CLINICAL OUTCOMES AND TEAR FILM LIPID LAYER THICKNESS IN MODERATE AND SEVERE MEIBOMIAN GLAND DYSFUNCTION.

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Purpose: We aim to demonstrate the efficacy of mechanical squeezing of meibomian glands in combination with conventional eyelid scrubs and warm compresses in patients with moderate and severe meibomian gland dysfunction (MGD). Thus, we investigated changes in clinical outcomes and tear film lipid layer thickness (LLT) using interferometer after squeezing of meibomian glands in combination with conventional eyelid scrubs and warm compresses.

Methods: Thirty-five eyes of 35 patients with moderate and severe MGD were treated with mechanical squeezing of meibomian glands in combination with conventional eyelid scrubs and warm compresses and non-preserved artificial tears. We evaluated tear film break-up time (TBUT), corneal and conjunctival fluorescein staining, biomicroscopic examination of lid margins and meibomian glands, the Ocular Surface Disease Index (OSDI) questionnaire, and the LLT before initiating treatment, and 1 month after treatment.

Results: There were significant improvements in TBUT, corneal and conjunctival fluorescein staining, lid margin abnormality, meibum quality, expressibility, the OSDI questionnaire, and the MGD stage after mechanical squeezing of meibomian glands in patients with moderate and severe MGD. However, there were no significant changes in LLT and interferometer- derived parameters between before and 1 month after treatment. All patients reported tolerable discomfort with increased satisfaction.

Conclusions: Mechanical squeezing of meibomian glands in combination with conventional eyelid scrubs and warm compresses can provide clinical benefits without serious adverse events. This research was supported by a grant of the Korean Health Technology R & D Project, Ministry of Health & Welfare, Republic of Korea (HI14C2044).

LANGERIN+ CELLS PREVENT OCULAR SURFACE INFLAMMATION AND FACILITATE SUBBASAL NERVE REGENERATION IN DRY EYE DISEASE.

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Purpose: To investigate the functional role of langerin(CD207)+ cells (LCs) during ocular surface inflammation and loss of subepithelial nerve plexus (SNP) in dry eye (DE) disease.

Methods: All participants completed the Ocular Surface Disease Index (OSDI) questionnaire using visual analog scale (VAS). The tear break-up time (TBUT), Schirmer test, and corneal erosion score were assessed. Ocular surface LCs and SNP was examined by confocal microscopy. LC density, area, and process length were analyzed correlating with SNP changes (e.g., nerve density, beading, and tortuosity grade). After seven days of DE induction in B6 mice, corneal erosion was graded and expression of ocular surface neurotrophic factors, as well as substance P (SP) levels were measured. Inflammatory cytokines and CD3+, CD11b+, and Gr1+ cell numbers were analyzed with fluorescence activated cell sorting (FACS) and compared between WT and CD 207-deleted mice after DE induction.

Results: Mean LC area and process length, but not LC density, was significantly greater in low symptom dry eye (LSDE) than high symptom dry eye (HSDE) patients. SNP damage was negatively correlated with LC area and process length. There were no correlations between LC density and VAS, erosion grade,and TBUT. Corneal erosion and inflammatory cytokine upregulation were found after DE induction in mice. Ocular surface NGF, BDNF, CGRP, and SP levels were significantly higher in LSDE than HSDE patients and control subjects. NGF, CGRP, and SP levels were significantly decreased with depletion of LCs+ in CD207-DTR mice. Induction of neurotrophic factors and neurotransmitters in the WT DE model was not present in CD207depleted mice.

Conclusions: LC is an important negative regulator of ocular surface inflammation, and provides a neuroprotective role in DE disease. LC activation parameters are more valuable parameters for measuring DE severity and predicting DE-induced SNP damage.

COMPARISON OF CYTOTOXICITY AND WOUND HEALING OF DIQUAFOSOL TETRASODIUM AND HYALURONIC ADIS ON HUMAN CORNEAL EPITHELIAL CELLS.

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Purpose: To compare the cellular toxicity of human corneal epithelial cells(HCECs) under the treatment of 3 different clinically used dry eye treatment agents - 3% diquafosol tetrasodium, 0.3% and 0.18 % Hyaluronic acid.

Methods: HCECs were exposed to 3% Diquafosol tetrasodium (Diquas, Santen, Osaka, Japan), 0.3% Hyaluronic acid (HA) (Hyaluni, Taejoon, Seoul, Korea) and 0.18% HA (Kynex-2, Alcon, Seoul, Korea) for the period of 1, 6 and 24 h. Methyl thiazolyltetrazoiun (MTT)-based calorimetric assay was performed to assess the metabolic activity of cellular proliferation and lactate dehydrogenase(LDH) leakage assay to assess the cytotoxicity. Cellular morphology was evaluated by inverted phase-contrast light microscopy and electron microscopy. The wound widths were measured 24h after confluent HCECs were scratch wounded.

Results: The inhibitory effect of human corneal epithelial cell proliferation and cytotoxicity showed a time-dependent response and had a significant effect when exposed only at diquafosol. HCECs treated with diquafosol were more detached from the bottom of the dish and damaged cells show degenerative changes like microvilli disappearance, vacuoles formation, and chromatin of the nuclear remnant condensed along the nuclear periphery. All significantly stimulated reepithehlialization of HCECs scratched, which were less observed in diquafosol.

Conclusion: It should be considered the epithelial toxicity resulting from long term or overdose usage of diquafosol especially in dry eye patients who already have punctated epithelial erosion.

DIFFERENTIAL GENE EXPRESSION OF *RNF182* AND *ITLN1* IN MEIBOMIAN GLAND DYSFUNCTION – A VALIDATION STUDY.

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Purpose: Meibomian gland dysfunction (MGD) is a complex condition contributing to evaporative dry eye for which potential genetic biomarkers have been little explored. Gene expression profiling from whole blood of MGD cases and controls in an Indian population indicated significant downregulation of ring finger protein 182 (*RNF182*) and intelectin-1 (*ITLN1*) in cases (Fold change

[FC] -5.08 and -1.72, respectively). *RNF182* and *ITLN1* have been associated with neuron function and anti-inflammatory properties respectively. As such, downregulation could indicate innervation changes or systemic inflammation associated with MGD. This study aimed to validate differential expression of *RNF182* and *ITLN1* in MGD from an independent Australian cohort.
Methods: RNA extracted from whole blood of moderate to severe MGD (n=15) and healthy age- and gender-matched controls (n=13) was reverse transcribed to cDNA with SuperScript VILO Mastermix. TaqMan gene expression assays for *RNF182* (AJ6ROC9) and *ITLN1* (Hs00914745_m1) genes were used for analysing differential expression on a 7500 Fast Real Time-PCR System with 16S endogenous control used for normalisation. The ΔΔCt method was used for comparative quantification and FC were determined by the corresponding values ($2^{-\Delta\Delta Ct}$).
Results: Mean(SD) age of participants were 47.3(12.8) years with no significant difference of European (11 vs 9) and Asian (4 vs 4) descent in each group ($p = 0.81$). Differential expressions of *RNF182* (FC = +1.06) and *ITLN1* (FC = -1.19) were not significant between MGD cases and controls (both $p > 0.05$).
Conclusions: Although *RNF182* and *ITLN1* genes were significantly downregulated in an Indian population, these could not be replicated in an Australian population. While multiple factors could be attributable to the result, further investigations of *RNF182* and *ITLN1* are required to determine the pathogenic role in MGD. [This research was supported by Australian Postgraduate Award, Brien Holden Vision Institute and Hyderabad Eye Research Foundation]

COMPARISON OF CLINICAL FEATURES, ANTIBIOTICS SUSCEPTIBILITY, AND TREATMENT OUTCOME ACCORDING TO METHICILLIN SENSITIVITY IN STAPHYLOCOCCUS AUREUS KERATITIS.

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Purpose: To investigate epidemiology, clinical manifestation, antibiotics sensitivity (cephalosporin-CP, gentamicin-GM, erythromycin-EM, linezolid-LZ, vancomycin-VM, fluoroquinolone-FQ), clinical outcome and risk factor of Staphylococcus aureus keratitis. This study was designed to compare differences between methicillin-sensitive and methicillin-resistant S. aureus keratitis.
Methods: We performed a retrospective chart review of 46 isolates in 46 eyes with S. aureus keratitis between January 1998 and December 2014. Comparative analysis between MSSA (31 eyes, 67.4%) and MRSA (15 eyes, 32.6%) was done. Risk factor of poor visual outcome was confirmed using logistic regression analysis.
Results: During 17 years study period, isolation rate of S. aureus had a trend of decrease among total Gram positive bacterial keratitis. Epidermiologically, male (1.56:1) and people more than 60 years old (47.8%) were more occurred. Ocular surface disease/ocular surgery history (39.1%) and trauma (37.0%) were more common in predisposing factor. MRSA sensitivity was low in CP(8.3%)/GM(13.3%)/EM(28.6%), and high in LZ(100%)/VM(100%). Sensitivity of FQ to MRSA was 64.3% (less than third generation FQ 50.0%). MRSA was longer in length of stay (p=0.020) than MSSA. There was no difference in early corneal findings and hypopyon. BCVA was improved after treatment in total eyes (p=0.022). Visual outcome did not differ significantly between the MRSA and MSSA groups. Risk factors for poor visual outcomes included the BCVA less than 0.1 at initial evaluation (p=0.014).
Conclusions: Isolation rate of S. aureus was decreased during study period and MRSA occupied 32.6% among total S. aureus. MRSA had no difference than MSSA in early clinical manifestation. BCVA after treatment was improved significantly on total eyes. [The authors have no proprietary or commercial interest in any materials discussed in this research.]

RELIABILITY OF A NEW NON-INVASIVE TEAR FILM BREAK-UP TIME MEASUREMENT USING A KERATOGRAPH.

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Purpose: To evaluate the repeatability of non-invasive tear film break-up time and identify its relationships with dry eye parameters.
Methods: A total of 100 participants (50 with dry eye, and 50 in the control group) were enrolled prospectively. Non-invasive keratograph first (NIKf-BUT) and average (NIKav-BUT) break-up times were evaluated 2 times using Keratograph 4 (Oculus, Wetzler, Germany), and then tear film break-up time with fluorescein (FBUT) was measured. The correlation analyses were performed between non-invasive parameters (NIKf-BUT and NIKav-BUT) and FBUT. Intra-observer agreements of NIKf-BUT and NIKav-BUT were assessed using intraclass correlation coefficients (ICC). The receiver operating characteristic (ROC) curve technique was used to evaluate the non-invasive method in the diagnosis of dry eye.
Results: The correlation analyses revealed positive correlation between NIKav-BUT and FBUT in both groups (dry eye; $r = 0.66$, $p < 0.001$ and control group; $r = 0.77$, $p < 0.001$). The ICCs of NIKf-BUT and NIKav-BUT were 0.72 and 0.94 in the dry eye, respectively, and 0.70 and 0.91 in the control group. NIKav-BUT was not different from FBUT in either group. The areas under the ROC curves of NIKf-BUT and NIKav-BUT were 0.917 and 0.980, respectively.
Conclusions: The high ICCs verified the repeatability of NIKf-BUT and NIKav-BUT. NIKav-BUT showed no difference from FBUT and positive correlation with FBUT. NIK-BUT showed high diagnostic power and can be considered a new parameter to evaluate dry eye syndrome.
[The authors have no proprietary or commercial interest in any materials discussed in this research.]

DEVELOPMENT OF AN AUTOMATIZED METHOD FOR ANALYZING TEAR FILM LIPID LAYER THICKNESS AND CORRELATION ANALYSIS AMONG CLINICAL FINDINGS OF DRY EYE DISEASE.

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Purpose: A novel, cheap interferometry using a piece of copy paper was introduced by the authors, which can estimate the tear film lipid layer thickness (LLT). This study was designed to develop a new automatized quantification method using the macro function of ImageJ and to apply this new method to patients' data, analyzing the correlation of the LLT with other clinical findings of dry eye as a preliminary study.
Methods: The macro function was developed following the algorithm of deciding area to analyze, obtaining RGB color codes for each pixel, assigning the appropriate color and the LLT for each pixel, and calculating the representative LLT of the photo automatically. Fourteen normal subjects, 44 patients with dry eye disease were enrolled in this study. After obtaining the photos using the interferometry, other clinical findings were evaluated - tear film break up time, corneal fluorescein staining, lid margin photograph, and infrared meibography.
Results: The mean LLT of 14 normal eyes were 59.9+-10.6 nm (thickest) and 55.3+-11.2 nm (average). The mean LLT of 44 dry eyes were 73.2+-28.8 nm (thickest) and 62.3+-24.9 nm (average). Total and lower lid meiboscore analyzed from the meibography showed significant correlation with average LLT (rho=0.320, P=0.034; rho=0.313, P=0.039, respectively, Spearman correlation analysis). The LLT of the higher meiboscore group (total score ≥3) was significantly

thicker than that of the lower meiboscore group (71.6+-26.7 nm vs 55.2+-21.4 nm, P=0.021, Mann–Whitney U test).
Conclusions: We successfully developed a free automatized method of analyzing LLT from the images of paper interferometry. The LLT was correlated with the structural changes of the Meibomian gland. [This research was supported by grants from Hallym University Research Fund (HURF-2016-05)]

CORRELATION BETWEEN TEAR PROSTAGLANDIN E2 LEVELS AND SEVERITY OF DRY EYE.

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Purpose: Prostaglandin E2 (PGE2) levels have been shown to be elevated in dry eye patients and correlated with patient symptoms. Nonetheless, clinical signs of dry eye can be inconsistent with symptomatology and the relationship between PGE2 levels in tears and other dry eye parameters has not been reported. We conducted a cross-sectional study to investigate the correlation between tear PGE2 levels and dry eye disease severity based on both clinical signs and symptoms.
Methods: Tear samples were collected prospectively from 16 *non-Sjögren* syndrome dry eye patients (4 men and 12 women, mean age 48.50 ± 13.45 years). All participants were submitted to the administration of the Ocular Surface Disease Index (OSDI) questionnaire, slit-lamp examination, estimation of fluorescein tear break-up time (fTBUT), cornea and conjunctiva fluorescein staining, Schirmer test without anesthesia, and meibomian gland evaluation. The levels of PGE2 in tears were measured using enzyme-linked immunosorbent assay (ELISA). Statistical analysis was performed using Spearman's correlation coefficients.
Results: The levels of PGE2 were positively correlated with the disease severity (R = 0.665, *P* = 0.005). An increase in tear PGE2 levels was significantly associated with an increase in OSDI score (R = 0.564, *P* < 0.05). There was no significant correlation between PGE2 levels and fTBUT (R = 0.108, P = 0.692), Schirmer test (R = -0.072, P = 0.790), ocular surface staining (R = 0.416, P = 0.109), or meibomian gland dysfunction grading (R = 0.031, P = 0.909).
Conclusions: The levels of PGE2 in tears are strongly correlated with disease severity, as detected by OSDI. However, no significant correlation was found between PGE2 levels and the results of other common diagnostic tests. [This work was supported by a Research Grant from the Faculty of Medicine, Ramathibodi Hospital, Mahidol University.]

BILATERALITY IN DRY EYE DISEASE: IMPLICATIONS FOR CLINICAL TRIALS.

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Purpose: Dry eye usually presents as a bilateral disease although there can be differences in degree of severity in some cases and a small number of cases present with predominantly unilateral disease. Recent studies have demonstrated that eyes do not function as independent units but rather communicate and affect one another, yet many clinical studies report data for only one eye. We report on effects of this practice.
Methods: Subjects with a diagnosis of DED within the last two years were measured for bilateral tear osmolarity, Schirmers, TBUT, corneal staining, conjunctival staining, and meibomian gland dysfunction over three consecutive months. The percentage of subjects for whom the score of the worse eye switched from one eye to the other on subsequent visits were noted either between visit 1–2 and 2–3.
Results: We have previously reported that there is eye-to-eye variability in tear osmolarity readings in DED patients that is not seen in normal subjects, suggesting that it is important to test both eyes and take the higher number of the two, with an inter-eye difference greater than 8 mOsm/L being indicative of pathological tear instability. Similarly, in this study, the maximum tear osmolarity switched between eyes on average 42.3%, TBUT 22.1%, Schirmers 16.3%, corneal staining 14.6% (although a majority of subjects were disqualified having no apparent corneal staining, being a late stage sign), conjunctival staining 22.0%, and meibomian gland grading 14.4%.
Conclusions: In the course of a three month period there is a significant movement from one eye to the other in objective measures of disease severity. This is a reflection of the instability of the tear film in DED and supports the clinical utility of capturing these shifts, many of which would have gone unnoticed in studies in which only one study eye was utilized. This study demonstrates the validity and clinical utility of testing both eyes to capture the dynamic range of values in both diagnosis and response to treatment.
This research was supported by TearLab. Corp.

INTENSE PULSED LIGHT THERAPY FOR MEIBOMIAN GLAND DYSFUNCTION.

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Purpose: To investigate the effect of intense pulsed light (IPL) for meibomian gland dysfunction (MGD) in a multicenter prospective study.
Methods: Ninety-two eyes with 46 MGD patients who underwent IPL treatment to the periocular area were enrolled. Every patient received two sessions of IPL treatment with a 3-week intervals and follow-up evaluation was conducted at 3 weeks after the treatment. Meibomian gland morphology (MGD grade with meibography) and function (meibum quality and expressibility) were evaluated. Lid margin alterations (lid margin telangiectasia, irregularity, orifice plugging and mucocutaneous junction [MCJ] displacement), tear film breakup time (TBUT), corneal fluorescein staining with Oxford scheme and symptoms (Ocular Surface Disease Index [OSDI] and Standard Patient Evaluation of Eye Dryness [SPEED] questionnaires) were analyzed.
Results: MGD grades were significantly improved in 2 secessions of IPL from baseline (baseline = 2.67 ± 1.05; post-1st = 1.75 ± 0.61, $p<0.05$; post-2nd = 1.25 ± 0.84, $p<0.05$). Mebium expressibility was significantly improved ($p<0.05$), but there was no difference in mebium quality. Lid margin telangiectasia and orifice plugging were improved from baseline (all, $p<0.05$) but there was no significant change in lid margin irregularity and MCJ displacement. TBUT, OSDI and SPEED questionnaires gradually improved significantly at post-1st and -2nd IPL from baseline (all, $p<0.01$). However, there was no difference in corneal staining.
Conclusion. Two sessions of consecutive IPL treatment for MGD is effective in the subjective symptom of patients as well as objective indices. We suggest IPL treatment could be promising therapeutic option for MGD. [None of the authors has a financial or proprietary interest in any material or method mentioned.]

A FRACTAL DIMENSION APPROACH TO TEAR FILM DYNAMICS CHARACTERIZATION IN HIGH SPEED VIDEOKERATOSCOPY.

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Purpose: To develop a new methodology for characterizing tear film (TF) dynamics in Placido disk based high speed videokeratoscopy (HSV) utilizing a Fractal Dimension approach.
Methods: Fractal Dimension (FD) is a measure of texture roughness that highly correlates with human perception of texture and it is relatively insensitive to changes in image intensity and to multiplicative noise. FD is characterized by a fractional number that describes how an object fills the space, and therefore how complex it is. The regularity of the reflected Placido disk pattern in HSV depends on TF stability. A disruption of the TF will cause either irregularity (which corresponds to a high FD) or fading (which corresponds to a low FD) of the reflected rings. Recorded raw images from videokeratoscopy (Medmont E300) were analyzed offline and FD was computed using custom-built software for 10 healthy young subjects. Two features of the reflected rings pattern were extracted from this analysis: distortions and breaks of the TF.
Results: Time series of FD were estimated for HSV recordings in suppressed blinking conditions. Dynamic quality of TF has been described by means of the normalized relationship between irregularity and fading. The new proposed TF quality estimator was contrasted against previous method of TF analysis based on image homogeneity. The FD method is able to identify up to 3 phases of TF dynamics: the build-up, stability and break-up (when applies). More importantly, in contrast to its predecessor, the FD method provides information about the nature of TF instability (distortion and/or breaks).
Conclusions: The proposed method has the potential to characterize TF dynamics in more detail compared to previous methods and it is less affected by eye movements and image background (changes in pupil size) than other techniques. In addition, it showed good correlation with subjective (manual) assessment of TF. Disclosure: This study was supported by Marie Skłodowska-Curie Innovative Training Networks grant, EDEN (European Dry Eye Network), ID 642760.

VASCULAR ENDOTHELIUM: ITS MORE THAN JUST A MONOLAYER.

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Three decades of study tells us that the endothelium plays an active and crucial role in maintaining vascular homeostasis. At baseline, the endothelium is non-adhesive, selective and semi-permeable barrier that maintains a non-thrombogenic surface. Recent studies show that the vascular endothelium can rapidly alter its phenotype in response to a broad spectrum of physiological and pathological stimuli. Upon exposure to proinflammatory cytokines, endotoxins or after injury, the vascular endothelium becomes hyper-adhesive, prothrombotic, and loses barrier function and becomes leaky. The mechanisms underlying certain of these changes are now under stood at the cellular and molecular level. Our laboratory has focused on the endothelial cell dependent mechanisms that mediate leukocyte recruitment using in vivo and in vitro models. This lecture will give an overview of the vascular endothelial responses to proinflamamtory stimuli, and examine current concepts regarding how the endothelium alters its phenotype to recruit leukocytes to its surface, and promote their passage to extravascular space. Our lab is supported by postdoctoral and grant-in-aid awards from the American Heart Association, and award HL125780 from the National Heart Lung and Blood Institute.

HYDROGEL SURFACE COATING OF RGP LENSES IMPROVES WETTABILITY AND LUBRICITY.

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Purpose: Comfort is a leading cause for discontinuing contact lens wear. Both wettability and lubricity have been associated with patient comfort yet are difficult to control over longer time scales with conventional materials. The goal of this study was to determine whether Hydra-PEG treatment improves wettability and lubricity of rigid gas permeable (RGP) lenses.
Methods: RGP lenses were coated with Hydra-PEG, a hydrogel that is covalently attached to the lens surface. Advancing contact angles were measured using the captive bubble technique and coating thickness was measured by ellipsometry. Water break-up time was assessed after dipping lenses in saline by measuring the amount of time during which the water film remained intact. Tear film stability was also assessed using the interfacial dewetting and drainage optical platform (iDDROP) to visualize film thickness and water break-up. Lubricity was scored on a scale of 1 to 6.
Results: Hydra-PEG treatment reduced the advancing contact angle from 94° to 24°. The hydrogel coating also improved the ability of the lens to support the tear film, as evidenced by an increase in the water break-up time from <1s to >20s. Lubricity was also improved from 2 to 6. Film thickness was 21 nm after initial coating and reduced to 8 nm after 12 months of wear. At this time, the advancing contact angle was 64°, which represents a significant improvement over the untreated lenses.
Conclusions: Hydra-PEG improves both wettability and lubricity of RGP lenses. Unlike temporary surface treatments such as plasma, the hydrophilicity of the lens was maintained for 12 months of simulated use. These surface properties have been associated with increased patient comfort, both in past studies and in clinical studies performed with Hydra-PEG materials, which will be reported separately. In addition, this coating stabilized the tear film, which could improve visual acuity.
The authors acknowledge the Fuller Lab for iDDROP measurements. Funded by NSF (Grant #IIP-1059286 to ASEE; SBIR Grant #1330975).

PRO-INFLAMMATORY CYTOKINES ASSOCIATED WITH CLINICAL SEVERITY OF DRY EYE DISEASE OF PATIENTS WITH DEPRESSION.

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Purpose: The relationship between immune system and nervous disorders plays an important role in the pathomechanism of depression. The pathogenesis of ocular changes in depression is still unknown but the involvement of inflammation and immunological processes in depressed patients has been studied in recent years. The aim of this study was to assess cytokine concentrations in the tears of patients with depression and analyze the relationships with the clinical severity of dry eye disease.
Methods: Tear fluid samples were collected from 32 patients with depressive disorder treated with antidepressant drugs, and 34 healthy subjects. Pro-inflammatory cytokines, including interleukin-6 (IL-6), interleukin-17 (IL-17) and tumor necrosis factor alfa (TNF-α) were assessed by enzyme-linked immunosorbent assays. All the subjects completed self-rating scales of the Beck Depression Inventory. The ophthalmic examination including the tests for dry eye were used to study the ocular surface.

TOPICAL LOW-DOSE PRESERVATIVE FREE DEXAMETHASONE (PFD) FOR CHRONIC OCULAR SURFACE DISEASE REFRACTORY TO CONVENTIONAL THERAPY.

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Purpose: To evaluate the short-term safety and efficacy of topical PFD 0.01% and 0.05% for the treatment of ocular surface disease and/or tearing refractory to conventional treatments. Patient diagnoses included but were not limited to dry eye, blepharitis, rosacea, GVHD, Sjogrens Syndrome, Steven-Johnson Syndrome, Allergic conjunctivitis, Superior Limbic Keratoconjunctivitis, and Limbal stem cell deficiency.

Methods: Retrospective chart review of patients who received topical PFD 0.01% and 0.05% (Leiters Pharmacy, San Jose, CA) from 9/2011 to 5/2016. Follow-up visits were reviewed for subjective responses to the formulation, development of visually significant cataract, and intraocular pressure (IOP). Responses were graded as significant/complete resolution of symptoms (50%–100% improvement), mild (25%–50% improvement), or no improvement.

Results: 301 eyes of 157 patients received topical PFD for the treatment of ocular surface disease. Of these patients, 141 received 0.01% and 16 patients received 0.05% formulations. Follow up ranged from 1 to 49 months. 110 patients (70%) reported moderate-complete resolution of ocular symptoms. 28 (18%) had mild improvement, and 19 patients (12%) had no change in ocular symptoms. Three patients in our series developed IOP elevation greater than 5 mm Hg above baseline. Of these patients, two were initially given 0.05% with subsequent reduction of IOP when switched to 0.01%. One patient developed IOP elevation on 0.01%, however had a history of end stage glaucoma. No patients in our series developed progression of cataract requiring surgery. Of the 66 patients previously treated with commercially available steroids, 53 patients (80%) reported moderate or complete resolution of symptoms, 11 patients mild improvement (17%), and 2 patients (3%) reported no improvement with use of PFD.

Conclusion: Topical PFD may be an effective therapy for recalcitrant chronic ocular surface disease. Minimal risk exists of IOP elevation or formation of visually significant cataract.

CORNEAL SENSITIVITY AND TEAR COMPONENTS IN KERATOCONUS.

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Purpose: To evaluate corneal sensitivity and levels of tear proteins and neuropeptides; Substance P(SP) and Calcitonin gene related peptide(CGRP), and their associations with other clinical parameters in keratoconus(KC).

Methods: A pilot study of 27 KC subjects aged between 18-65 years. The concentration of total tear protein (TTP), lactoferrin, the neuropeptides SP and CGRP in basal tear samples was determined. The concentration of lactoferrin and neuropeptides was normalised by dividing by TTP. Corneal sensitivity (CS) was measured using the Cochet-Bonnet aesthesiometer. Data from the more severe eye were included in the analyses. The association of CS and tear components with ocular symptoms, tear variables,ocular surface staining and nerve density were evaluated using Spearman correlation. Partial correlation was performed to control the effect of confounding factors. For this pilot study, significance was set at $p \leq 0.1$.

Results: There were significant associations between concentrations of SP and CGRP, ϱ=0.532,p=0.041, and CGRP and lactoferrin, ϱ=0.624,p=0.054. The TTP was associated with age of the subjects, severity of KC, DEQ score, corneal staining (ϱ,*p*-values =-0.512, 0.051; -0.536, 0.059; 0.949, 0.051; -0.636, 0.019 respectively). After adjusting for CL wear, CS was associated with age, duration of the disease, OSDI score, corneal staining and lactoferrin concentration (ϱ,*p*-values =0.369, 0.064; 0.380, 0.056; -0.338, 0.098; 0.517, 0.010; 0.706, 0.034 respectively); lactoferrin was associated with corneal staining, ϱ=0.679,p=0.064; TTP was associated with corneal staining and OSDI score (ϱ,*p*-values: -0.567,0.054; 0.679, 0.064 respectively).

Conclusions: Whilst CS was associated with age, duration of the disease, symptoms, corneal staining and tear lactoferrin concentration, there was no association between these parameters and the concentration of the tear neuropeptides. However, association of levels of CGRP with levels of SP and lactoferrin suggest some relationship between neuropeptides and the ocular surface changes in KC.

LOW POWER NARROWBAND UVC EFFECTIVELY INHIBITS BACTERIAL PROLIFERATION IN A GEL-LIKE MEDIUM.

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Purpose: To determine the minimum effective dose of narrowband low power 265nm UVC, required to inhibit bacterial proliferation on and beneath the surface of a medium designed to mimic the infected human cornea, across a range of bacterial growth phases. Methods. Bioluminescent *Pseudomonas aeruginosa* was cultured overnight in an orbital shaker incubator (37°C, 200 rpm). Around 10^8 bacterial cells within 100µl of overnight culture was used to innoculate 3ml molten top agar (0.75% w/v granulated agar in Tryptic Soy Broth (TSB)), and was spread over an agar base (TSB with 1.5% w/v agar) to form a uniform thickness of approximately 1mm. Two experiments were conducted (i) a single UVC exposure (1.93mW/cm^2), (4.5mm spot size), was delivered to different areas corresponding to treatment durations of 1s, 5s, 10s and 15s. (ii), a single 5s UVC exposure was delivered at the zero, first and the third hour during incubation. For both experiments, relative luciferase activity, as a measure of bacterial proliferation, was quantified at different time points for 2mm^2 areas (The *Xenogen IVIS*).

Results: (i) Exposure to UVC resulted in a dose-dependent reduction in bacterial luminescence, most notably at the sixth hour for the exposures of 5s, 10s and 15s ($p<0.0001$) but not for one-second ($p>0.05$), compared to untreated areas that showed a consistent rise in luminescence. There was no difference between 5s, 10s and 15s exposure (all $p>0.05$). (ii) Exposure at the first hour was more effective ($p<0.0001$) than that at zero hour ($p<0.001$) and third hour ($p<0.01$) demonstrating a temporal variation in luminescence as a function of the growth phase. Overall, a single 5s UVC (9.65mW/cm^2) inhibited bacterial proliferation by approximately 60%.

Conclusion: Low power UVC in a 5s dose inhibits bacterial proliferation within and below the surface of a gel-like structure, warranting further investigation of this technique as a possible treatment or adjunct treatment for superficial corneal infection.

CHANGING PATTERNS OF MICROBIAL KERATITIS.

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Purpose: To explore risk factors, hospital resource utilisation and clinical outcomes of severe microbial keratitis (MK) in Auckland, New Zealand (NZ).

Methods: Cases of MK admitted to hospital over a 2-year period (2013 and 2014) were retrospectively analysed. Visual outcome, hospital presentation time (HPT), hospital bed days (HBD), healing time, and factors influencing these outcomes were studied. Results were compared to published data for the same population from 1999 to 2000.

Results: Of recent cases (n=196), over 80% were associated with ocular

risk factors including contact lens (CL) wear (33.1%), ocular surface disease (OSD) (29.6%), ocular surgery (18.6%) and trauma (14.8%). MK incidence secondary to steroid use or multiple causes decreased over the decade ($p<0.05$). The coagulase-negative *Staphylococci* infection rate decreased ($p<0.001$) while that of *Pseudomonas*, *Corynebacterium* and herpetic disease increased ($p<0.05$). Antibiotics including ciprofloxacin 0.3% (21%), or combined cefuroxime 5% and tobramycin 1.35% (62%) were typically prescribed as the first-line treatments. *In vitro* testing of bacterial isolates showed high sensitivity to most antibiotics (95-100%) except for cefuroxime (33%). In terms of outcomes, median initial and final VA were 20/130 (IQR, 20/400 to CF) and 20/30 (IQR, 20/32 to 20/80), respectively, with poorer outcomes associated with culture-proven ulcers ($p<0.0001$). Median HPT was 3 days (IQR, 2 to 7), less than a decade ago ($p<0.001$). HBD was 3 (IQR 1 to 5) and lesions healed in 9 days (IQR 5 to 21). CL-keratitis ranked as the least severe cause of MK ($p=0.0043$).
Conclusion: CL wear and OSD are currently the major risk factors for MK in NZ, although CL-related infections show the best outcomes. Current therapeutic strategies are successful but alternatives to cefuroxime might be warranted in light of increasing resistance. Improvements in diagnostic speed and accuracy over the last decade are reflected in more rapid presentation for treatment and improved outcomes with shorter hospital stays.

PREVALENCE OF DRY EYE SYNDROME IN SÃO PAULO – BRAZIL.

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Purpose: To determine the prevalence of Dry Eye Syndrome (DES) in São Paulo, Brazil, using the Short Questionnaire for DES, development by Schaumberg et al.
Pacient and Methods: This is a cross-sectional study, with the population participant of São Paulo Eye Study (SPES) by Salomão et al., who lives in three low-income districts localized in east of the São Paulo. It was made an adaptation and validation of the "Short Questionnaire for DES" to brazilian Portuguese. We applied by telephone. The content of this included two symptom questions: (1) How often do your eyes feel dry (not wet enough)? and (2) How often do your eyes feel irritated? The patient was given four choices as to the frequency of the symptoms, which were scored as follows: never 1; sometimes 2; often 3; and constantly 4. Responses were recorded on a standardized form. The third question was as follows: Have you ever been diagnosed (by a clinician) as having dry eye syndrome? For this question, the participant's answer was recorded as "Yes" or "No." On the basis of this short questionnaire, a subject was considered as having DES if there was the presence of both dryness and irritation either constantly or often (that is, severe symptoms) or a report of a previous clinical diagnosis of DES.
Results: 607 interviews ; 71.5% Female : 28.5% Male ; Mean Age: 61 years old ; DES prevalence: 22.57%.
Conclusions: Our result is closer to the others in the world for DES. This is the first study in Brazil to have epidemiological rates for DES.

ANTI-INFLAMMATORY EFFECTS OF REBAMIPIDE EYEDROPS ON SUPERIOR LIMBIC KERATOCONJUNTIVITIS

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Purpose: Rebamipide is a quinolone derivative that increases mucin-like substances production. It also increases the number of conjunctival goblet cells by promoting proliferation and increasing the secretion of Muc5ac. Rebamipide increases the production of transmembrane mucin: MUC1 and MUC4, without modification of MUC 16. It has anti-inflammatory action , suppresses cytokine expression and decreases tumor necrosis factor alpha improving the barrier function of the corneal epithelium and promoting wound healing. The purpose of this study was to evalute therapeutic clinical effect of rebamipide eye drops for patient with recurrent superior limbic keratoconjuntivitis (SLK).
Methods: Retrospective, observational case series. Four patient (8 eyes) with recurrent severe SLK were included who received rebamipide 2% eye drops 4 times daily for varying periods. All patient suffered at least 1 previos event treated without surgical procedures. The following ítems were evaluated before and 4 week after the start of the tratment: presence of SKL, conjuntival and cornea staining (SICCA score), Schirmers Test I (without anesthesia), tear film break-up time and presence or abscence of blefarospasmo. Presence or abscence of thyroid disease.
Results: Two patients with severe SLK received rebamipide 2% drops associated to local application of 0.5% silver nitrate solution. Attenuation of symptoms in all patients. One patient showed complete disapaerance of SLK and the other patient demonstrated significant improvement, but had minimal residual punctate rose bengal and fluorescein staining. No modifications on Schimer test results. Tear film break-up time increased sigificantly post-treatment. All 4 eye showed complete disapearance of blepharospasm. No patient presented thyroid disease. No adverse side effects were observed.
Conclusions: Rebamipide 2% eye drops may be useful for the treatment and management of the inflammation in SLK as adyuvante therapy to silver nitrate application and might be a good option as monotherapy.
[The authors have no financial disclosures]

NEW ADVANCES IN THE UNDERSTANDING OF THE ROLE OF THE OCULAR SURFACE AND TEAR FILM IN CONTACT LENS DISCOMFORT.

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Purpose: Despite the investment into contact lens technology, 10-50% of wearers drop out of lens wear within three years of commencement, the most common reason cited being discomfort. In order to understand this conundrum, the TFOS commissioned the 2013 Contact Lens Discomfort (CLD) workshop to conduct an evidence-based evaluation and establish a consensus regarding the definition of CLD, its aetiology and management. Since the publication of the report, research into the mechanisms of CLD has grown significantly. The new advances in the understanding of the role of the ocular surface and tear film in CLD will be discussed.
Methods: An evidence-based review of the literature published since 2013 was conducted.
Results: The 2013 report highlighted the link between CLD and friction and the clinical signs of lid wiper epitheliopathy. Since then, lid wiper epitheliopathy and has been found to be a useful clinical sign for differentiating clinical performance and has been shown to reduce in conjunction with symptoms in the presence of an oil-in-water emulsion. Biochemical markers of CLD have received attention, with degraded lipids and wax esters associated with a lower non-invasive surface drying time, while albumin and cholesterol have been found to increase friction in vivo. Cytokine changes in tears and their relationship with CLD have been explored, with one study identifying prolactin-induced protein as an indicator of CLD, while other studies have not identified any factors that are significantly associated with

CLD. A difference in tear film kinetics between symptomatic and asymptomatic contact lens wearers has also been reported.
Conclusions: Research into CLD has increased significantly over the last three years. Lid wiper epitheliopathy has been highlighted as a potential new area of research to address CLD. Identification of a biochemical marker of CLD is ongoing with significant advances in the field anticipated as a result of this workshop.

TEAR FILM MMP-9 AND TIMP-1 IN TOPICAL FLUOROQUINOLONE USE.

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Purpose: Topical fluoroquinolones are commonly used for treating infections such as bacterial keratitis. There have, however, been reports of corneal ulcer progression and corneal perforation with their use. Studies conducted in rats have shown that fluoroquinolone use leads to an upregulation of collagen-degrading enzymes known as matrix metalloproteinases (MMPs). This study aimed to evaluate the impact of topical fluoroquinolones on tear film MMP-9, tissue inhibitor of matrix metalloproteinase-1 (TIMP-1), the MMP-9:TIMP-1 ratio and corneal thickness in humans.
Methods: This was a prospective, contralateral study where thirty-five participants were instructed to instil Ciprofloxacin 0.3% eye drops into their right eye (treatment eye) and unit dose sterile saline 0.9% into their left eye (control eye) for 2 days. Drops were instilled upon awakening on the first day and every 10 minutes for the first hour, followed by one drop every 2 hours until the hour before sleep when drops were instilled every 10 minutes for 1 hour. On day 2, the drops were instilled every 10 minutes for the first hour and then every 2 hours until the scheduled visit. Tear samples were collected and central corneal thickness was measured using anterior optical coherence tomography before and after treatment. The concentrations of total MMP-9 and TIMP-1 were analysed using enzyme-linked immunosorbent assay (ELISA).
Results: Total MMP-9 levels and central corneal thickness were not altered as a result of topical fluoroquinolone therapy. However, there was a significant increase in TIMP-1 concentration in the treatment eye compared to the control eye, post-treatment. There was also a decrease in the MMP-9:TIMP-1 ratio in the treatment eye compared to the control eye post-treatment, indicating an upregulation of TIMP-1 as a result of topical fluoroquinolone therapy.
Conclusions: These findings indicate a possible anti-inflammatory effect of topical fluoroquinolones in the tear fluid rather than a collagen-degrading effect.

TEAR BIOMARKER ANALYSIS AS A DIAGNOSTIC TOOL FOR DRY EYE DISEASE.

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Purpose: To determine if tear biomarker analysis could be utilized as an objective diagnostic test for dry eye disease (DED).
Methods: Normal (n=18) and DED (n=60) subjects were recruited. DED status was established using a validated symptom questionnaire (OSDI), non-invasive tear break-up time and Schirmer test. A tear sample (1μl) was collected from each subject and analyzed for 7 inflammatory markers using a multiplex immunoassay. Receiver operator characteristic (ROC) curves were used to establish sensitivity and specificity values and the most appropriate diagnostic cut-off for DED for each biomarker. ROC curves were also used for established clinical tests (tear osmolarity, evaporation rate, tear turnover rate (TTR) and assessment of corneal staining) for comparison to tear biomarker analysis.
Results: The results show that, in terms of sensitivity and specificity (and when considered individually) the 7 biomarkers are not as accurate at diagnosing symptomatic DED, as the established clinical tests. The most promising biomarker, tumour necrosis factor alpha, showed sensitivity of 61% and specificity of 61%, at a point of 2930 pg/ml. The other 6 biomarkers showed lower predictive power. However when considered together as a panel of 7, the biomarkers sensitivity was 70% and specificity 67%. This indicated a better predictive power for DED than clinical tests, e.g. tear evaporation rate (56% sensitivity, 50% specificity) and tear osmolarity (62% sensitivity, 56% specificity), and a similar result to TTR (73% sensitivity, 67% specificity). Assessment of corneal staining was the best predictor for DED, with sensitivity of 85% and specificity of 94%. However, corneal staining is a subjective test and vulnerable to intra/inter-examiner variability.
Conclusions: A panel of tear biomarkers have proven to be comparable to established clinical tests for predictive power of DED. However, no individual biomarker indicative of DED has been determined. Thus, further research investigating other potential biomarkers is required. With thanks to GCU for financial support of this research.

LACRIMAL GLAND EPITHELIAL CELL METABOLIC ACTIVITY AND FUNCTION ON A DECELLULARISED SCAFFOLD IS INCREASED USING A DYNAMIC CULTURE FORMAT.

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Purpose: Dry eye syndrome (DES) can cause painful blindness but only palliative treatments exist. *In vitro* reconstruction of lacrimal gland (LG) tissue may provide a curative treatment but a suitable scaffold to enable efficient delivery needs to be identified, and culture methods require optimisation. We sought to evaluate decellularised porcine jejunum (SIS-Muc) as a scaffold, and the benefit of dynamic culture.
Methods: LG epithelial cell cultures were initiated from porcine LG explants. Immunocytochemistry was used to confirm cell phenotype. $2x10^5$ cells were seeded onto the former lumen of SIS-Muc and left to adhere for 2 days. Culture was then continued under either static or dynamic (3.8ml/min in a perfusion chamber) conditions for 1 week. Histology and immunohistochemistry (IHC) were used to characterise cells on SIS-Muc. Metabolic and secretory activities were quantified using MTT and the β-hexosaminidase assays respectively.
Results: LG explants yielded cells that expressed Rab3D, HexA and pan-cytokeratin, whilst lysozyme expression was limited to a few cells. On day 2 on SIS-Muc, H&E staining revealed a monolayer of cells on the mucosal surface. On day 6, mucosal crypts were filled with cells. On day 9, epithelial cells in dynamic cultures had remodelled the mucosa to form a cell layer 6-8 cells deep. In static cultures, the cell layer was only 1-2 layers deep. IHC revealed continued expression of pan-cytokeratin and Rab3D, but also of lactoferrin and lysozyme. Cells also stained for mucins (PAS alcian blue). On day 9, metabolic and secretory activities in dynamic cultures were increased 2- and 3-fold respectively cf. static ($p<0.05$).
Conclusions: SIS-Muc supports LG epithelial cell growth, and dynamic culture promotes metabolic activity and function. This is useful towards *in vitro* reconstruction of LG tissue for curative DES treatments. [No commercial relationships. This work was supported by The Volkswagen Foundation.]

VARIATION OF TEAR OSMOLARITY AND ASSOCIATION WITH OCULAR SURFACE MEASUREMENTS IN PATIENTS WITH DRY EYE SYNDROME

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Purpose: To analyze the distribution of tear film osmolarity and its association with ocular surface parameters in patients with dry eye.
Methods: Subjective and objective metrics of dry eye were assessed in 199 patients. Patients were classified in three categories: 1) clinically significant dry eye [OSDI>12 and total ocular surface staining score (cornea and conjunctiva combined)(OSS)≥3)] (n=124), 2) symptomatic dry eye (OSDI>12 and OSS<3) (n=43), and 3) control patients (OSDI≤12 and OSS<3) (n=32).
Results: Clinically significant and symptomatic dry eye patients had a higher mean tear osmolarity and higher standard deviation (311 ±15 and 314±48 mOsm/L respectively) compared to control patients (310±9)(p=0.41). Dry eye patients (both groups combined) had a higher proportion of abnormal tear osmolarity (either <300 or >312) compared to controls (49% vs 37%, p=0.22). Importantly, dry eye patients tended to have a greater average difference in osmolarity between eyes than controls (2.0 vs 0.1 mOsm/L, p=0.50). Average osmolarity was significantly associated with greater OSDI score (+0.1 mOsm/L for every 1 point increase in OSDI score, p=0.01) and total OSS (+1.1 mOsm/L for every 1 point increase in total OSS, p=0.03).
Conclusions: Tear film osmolarity seems to be greater with more variability in dry eye patients compared to normals. Symptomatic dry eye patients appear to have the highest and most variable osmolarity values, potentially indicating that osmolarity precedes the worsening of clinical findings of more severe disease. Our findings demonstrate that tear osmolarity should be considered in the diagnostic workup and therapeutic management of dry eye patients. Commercial relationships and grant support: Supported in part by a research grant from Allergan, Inc. and Jerome L. Greene Sjögren's Center, Johns Hopkins University. Osmolarity cards were donated by Tearlab and TMS-4 videokeratoscopy was provided by TOMEY.

TEAR FILM BARRIER TO INFLAMMATION

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The tear film is essential to the health of the ocular surface. It provides a smooth surface for refraction of light, supplies essential nutrients, helps dilute and wash away waste products, protects against mechanical forces generated during blinking and protects the eye from environmental insults. These activities arise from the ability of the tear film to interact strongly with the underlying cells of the cornea and conjunctiva and from the vast array of molecules that comprise the tear film. Lipids form the outermost component of the tear film and lie above an aqueous component that harbours a large number of active proteins. A mucin layer serves to anchor the tears to the glycocalyx and hydrophobic membranes of the ocular surface cells. As is the case elsewhere in the body, inflammation at the ocular surface is both a blessing and a curse. While inflammation is necessary to defend against pathogen challenge it can also be destructive and cause harm. Inflammation at the ocular surface may lead to severe irritation and discomfort, visual disturbances and result in unsightly redness of the conjunctiva. Thus it is essential that there are ways to limit and terminate inflammation to prevent unwanted damage. In this presentation mechanisms by which the tear film can help prevent, reduce and resolve inflammation will be discussed. These mechanisms encompass simple physical effects such as the dilution of inflammatory mediators to levels below their effective concentration. More sophisticated mechanisms include the presence of a variety of molecules with known anti-inflammatory activity for example tissue inhibitors of metalloproteinases (TIMPs) that can inactivate matrix metalloproteinase 9 a pro-inflammatory molecule implicated in the pathogenesis of dry eye. Differences in tear components in the closed eye environment, which compared to the open-eye, represents a sub-clinical inflammatory environment, will also be discussed.

THE INFLUENCE OF EYE CLOSURE ON DRY EYE SYNDROME SYMPTOMS.

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PURPOSE: Scleral lenses instantly and completely block corneal surface evaporation thereby avoiding the activation of dryness detecting sensitized low-threshold C-mechanoreceptors.[1] These observations suggest that the symptoms that scleral lenses suppress represent corneal evaporative hyperalgesia[1] This study examines if eye closure could also suppress symptoms related to evaporative dry eye.
Methods: Prior to any invasive procedures the level of symptoms for 75 subjects were assessed using a visual analogue scale (VAS). They were then instructed to close their eyes gently for 10 seconds and record 'eyes closed' symptoms using the same VAS (Figure 1). Oculus Keratograph, (Wetzlar, Germany) tear break up time testing was used to compare two contrasted groups as described in the results.
Results: Group A: A suspect evaporative dry eye group (N=11) whose 'eyes open' score was higher (mean 74.5, range 100 to 60) and who recorded greater symptom relief with eye closure (a 79.9% reduction to a mean score of 15.0). Group B: A suspect non-evaporative dry eye group (N=9) whose 'eyes open' score was higher (mean 55.8, range 43 to 95) but who recorded no symptomatic relief with eye closure (actually no change for 4 patients but an overall mean 6.6% increase to a mean score symptom of 59.5. Mean right eye non-invasive tear break times were: group A: 2.8 +/-3.4secs (range 0 to 10.5) and group B: 6.5+/-3.9secs (range 0 to 12.6 and significantly higher than group A, p<0.046).
Conclusions: These findings appear to support the hypothesis that evaporative dry eye patients would record greater symptom improvement with eyes closed compared to patients with non-evaporative dry eye such as, for example, those whose symptoms may include neuropathic mechanisms. There is no commercial relationship or grant support relevant to this study for either author.

EVALUATION OF RADIO FREQUENCY THERMISTOR FOR USE IN MGD DRY EYE TREATMENT.

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Purpose: ThermiSmooth® device is FDA approved for reducing facial wrinkles. It is hypothesized that the energy produced by the thermistor regulated handpiece could also have a positive effect on meibomian gland function and dry eye symptoms through localized heating or neural stimulation.
Materials and Methods: 31subjects with significant periorbital wrinkles were screened using a variety of subjective and objective dry eye measures and 18 qualified and completed the study. The OSDI and SPEED questionnaires were completed at each visit. A masked investigator evaluated both eyes on Days 1, 15, 30 and 45. Treatment of the randomized test eye was done by an unmasked investigator after the eye exams on Days 1, 15 and 30. Treatments lasted approximately 12 minutes at temperatures of 42-45^{0}C in regions around the eye but not on the lids. Transient localized redness was usually observed. Tear Meniscus Height, NITBUT, LLT and meibography were evaluated along with TFBUT with D.E.T and corneal staining (NEI scale).
Results: Between Visit 1 and the Exit visit on Day 45 rather dramatic reductions in dry eye symptoms were achieved: 87% of patients improved in OSDI (avg=14.3) and 80% improved in SPEED (avg=5.2 points). Some dry eye signs improved: 60% had modest improvement in Lipid Layer Thickness and 66.7% improved with DET TFBUT. 80% showed modest improvement in Corneal staining. No changes occurred in tear meniscus height, NITBUT, lissamine green staining.

The contralateral eye also improved in LLT, DET TFBUT and NaFl corneal staining.
Conclusions: This study demonstrated that improvements can occur in dry eye symptoms and signs using the ThermiSmooth® device. Further studies must be performed to optimize the reduction in dry eye signs and symptoms and achieve consistent wrinkle reduction. The mechanism of action is not well established and may be linked to neurostimulation of the nerves supporting the meibomian glands.

TOWARD AN UNDERSTANDING OF THE ROLES OF MEIBUM LIPIDS AND DIETARY FAT IN DRY EYE DISEASES.
Jillian Meadows,[1] Jianzhong Chen,[1] Kari Green,[2] Jason Nichols,[1] Kelly Nichols[1] [1]University of Alabama at Birmingham, School of Optometry[2] University of Florida, Department of Chemistry
Purpose: Little is known about the molecular differences in meibum across dry eye (DE) diseases and in response to the types of dietary fat consumed. We aimed to test the hypotheses that meibum lipids are differentially expressed across DE subtypes and across varying intake ratios of saturated-to-unsaturated fat (fat_s/fat_u).
Methods: Eighty-one subjects with sufficient meibum samples were included. All subjects completed a Vio Food Frequency Questionnaire that estimated their dietary intakes of fat_s and fat_u. Subjects were categorized as normal or aqueous-deficient, evaporative, or combined DE (ADDE, EDE, and CDE, respectively). Extracted meibum lipids in solution were directly infused into a maXis 4G UHR-QTOF mass spectrometer. The resultant peaks were analyzed by volcano plots that compared (1) DE subtypes and (2) fat_s/fat_u tertiles. One-way ANOVA and logistic regression were used to compare the mean fat_s/fat_u ratios and to estimate the odds ratios (OR) associated with each tertile.
Results: Differential expression was detected across DE subtypes at thresholds of $p<0.05$ and fold-change (FC) >1.05. Many very long chain fatty acids were increased in ADDE, while triacylglycerols were increased in EDE. For both subtypes, many very long chain wax esters were decreased. For CDE, several phosphatidylcholines, sphingomyelins, and triacylglycerols were increased. Regardless of disease status, however, the largest tertile of fat_s/fat_u was associated with a decrease in many wax esters (mean FC = 0.89 ± 0.04, $p<0.05$) and an increase in many diesters (mean FC = 1.17 ± 0.03, $p<0.04$). There was a significant difference in the mean fat_s/fat_u ratios among the DE subtypes ($p=0.02$), the mean being larger for ADDE than others. Women in the highest tertile of fat_s/fat_u had an increased risk of ADDE (OR=3.61, $p=0.048$).
Conclusions: For normals and DE subjects, meibum composition varies with dietary fat_s/fat_u. Even within DE subtypes, there are further differences in meibum composition. A better understanding of dietary fats in DE is needed.

RECENT INNOVATIONS IN OCULAR SURFACE SURGERY.
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The ocular surface comprises of an area encompassing the tarsal and palepebral lids, the bublar conjunctival surface as well as the cornea. Due to the intimate relationship between all the components of the ocular surface, surgerical management will often involve correcting more than one component of the ocular surface. Innovations in the management of the ocular surface have seen newer developments in the area of conjunctival reconstruction with stem cell therapy and various forms of amniotic membrane, the use of lasers in conjunctival surgery, lid reconstruction with the use of mucous membrane surface. For the cornea the control of the innate bacterial ocular surface is vital to control ocular surface inflammation. For corneal epithelial reconstruction, the use of cultivated limbal epithelial transplantation, cultivated conjunctival and oral mucosa and simple limbal epithelial transplantation are becoming increasingly popular with variable results. The corneal procedure of choice is still lamellar transplantation and the use of integrated OCT has helped accomplish this more consistently. The limitation to stem cell reconstruction is the cost and the availability of labs. GMP regulation has become a gold standard but is not widely available and has increased the cost substantially. In centres where it is not available the use of keratoprosthesis is used. The two most widely used are the Boston Keratoprosthsis and the OOKP. However, they can be associated with substantial complications that require careful follow up and longterm supervision.

TOWARDS A NOVEL IN-VITRO ANTERIOR EYE MODEL FOR OCULAR SURFACE EVALUATION.
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Purpose: Previous research has established the viability of maintaining, independently, either corneal or crystalline lens tissue physiologically stable for a period of ~10 days. This study aimed to design and evaluate a novel complete anterior eye model that combines these two structures, allowing ocular surface evaluation.
Methods: Eight porcine eyes were sectioned at the equator and mounted in a perfusion chamber specially designed in SOLIDWORKS and 3D printed. Artificial anterior chambers were perfused with saline at a flow rate of 2.5 µl/min under an intraocular pressure of 18 mmHg. The epithelium was exposed to air, and its anterior surface was separately irrigated with saline. "Normal" and "evaporative dry eye" conditions were simulated over 40 minutes using two "lacrimation" intervals (20 s and 60 s). Corneal and conjunctival damage were observed with fluorescein and lissamine green, respectively, and quantified using ImageJ software. Morphometric data from four porcine eyes were obtained using Optical Coherence Tomography before and after dissection / mounting.
Results: There was no significant ($p>0.05$) difference in corneal thickness (by 0.02 ± 0.02 mm) and anterior chamber depth (by 0.08 ± 0.16 mm) calculated before and after the mounting procedure. Lissamine green and fluorescein staining area were significantly ($p<0.05$) larger in eyes under "evaporative dry eye" condition than in anterior chambers under "normal" condition (by 55.86 ± 13.32 mm^2; 28.79 ± 11.37 mm^2 respectively). Lissamine green staining intensity was significantly ($p<0.05$) more intense (by 45.94 ± 15.89) in corneas under "evaporative dry eye" condition than in corneas under "normal" condition.
Conclusions: The porcine eyes could be dissected and mounted without causing structural changes and the expected corneal and conjunctival damage with reduced surface lacrimation was evident. Therefore, this novel complete porcine anterior eye model may form a reliable tool for the testing and evaluation, in a controlled experimental fashion, of novel pharmaceutical approaches to Dry Eye Disease and medical device application.

ARE THERE GOOD ANIMAL MODELS FOR HUMAN DRY EYE DISEASE?
NO. Austin K. Mircheff. Keck School of Medicine, University of Southern California, Los Angeles, CA, USA
Animal dry eye disease (DED) models have yielded wondrous knowledge. The task here is to review gaps concerning DED pathogenesis and phenotypes. The commonest diagnosis is mild- to moderate disease DED presumably due to primary Meibomian gland dysfunction (1°MGD). More severe phenotypes involve lacrimal gland (LG) dysfunction. 2°LGD phenotypes may arise secondarily to MGD. Atrophy, infections, 1° and 2° Sjögren's syndrome (SjS), graft-versus-host disease (GVHD), and chronic immune-mediated inflammatory

processes (CIMIP) cause 1°LGD. 1°SjS manifests multiple phenotypes: T cell- or B cell-predominant, germinal center (GC)-positive or -negative. 2°SjS phenotype diversity is little studied. MG orifice cautery induces DED in rabbits; ocular surface CIMIP are little characterized, 2°LG CIMIP even less so. Animal models have yielded conflicting results concerning to LG atrophy. Mutations and autoantigen immunization determine several murine models mimicking features of 1°SjS. How closely any maps to a 1°SjS phenotype is unknown, and genetic factors increase risk but are not determinative for SjS. Epstein-Barr (EBV) gene expression correlates strongly with GC-positive 1°SjS. Viral infections induce LGD in animals, but whether that any mimics EBV-associated 1°SjS is unknown. LG CIMIP are much more prevalent than SjS, and they manifest diverse phenotypes. LG CIMIP are unremarkable in murine DED induced by physical desiccating stress (pDS). pDS is associated with T cell infiltration of rabbit LG; mechanisms and pathophysiology are not known. Systemic scopolamine causes severe DED and LG atrophy in mice. Scopolamine-induced DED has not been adoptively transferred to immunocompetent mice, while autoreactive lymphocytes readily transfer diverse phenotypes to rabbits. Immunological differences between mice and humans are known. How well local immunoregulation, pathogenesis, and phenotype diversity in rabbits mimic the human can scarcely be addressed, as few reagents exist for identifying rabbit immune system cells and proteins. However, the major conundrum is that we do not understand human DED well enough to recognize a good model. [No support]

MADCAM-1 AND ITS RECEPTORS AS NOVEL BIOLOGICAL TARGETS TO ENHANCE CORNEAL GRAFT SURVIVAL.

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Purpose: To investigate the expression and function of mucosal addressin cell adhesion molecule (MAdCAM)-1 and its cognate receptors (alpha 4 integrins) in corneal transplantation.

Methods: The murine models of corneal transplantation were performed. Gene expression of MAdCAM-1 in the cornea was assessed by real-time PCR and confirmed by immunohistochemistry of whole mount corneas. In vivo rolling and sticking of adoptively transferred fluorescently-labeled conventional dendritic cells (cDCs) were studied in limbal vessels utilizing epi-fluorescent intravital microscope with either anti-MAdCAM-1 blocking antibody or isotype before cDC injection. Corneal graft survival was assessed in anti-α4 (MAdCAM-1 receptor) blocking antibody or isotype treated mice.

Results: MAdCAM-1 mRNA level increased in rejected corneal grafts as compared to steady state and accepted grafts ($p<0.05$). MAdCAM-1 protein was upregulated on corneal blood and lymphatic vessels of rejected corneal grafts. Rolling fraction (RF) and sticking efficacy (SE) of cDCs increased significantly in rejected grafts (1.7 and 2.5-fold) compared to naïve mice, respectively ($p<0.05$). Blockade of MAdCAM-1 decreased RF compared to isotype blockade (10% vs.14%; $p=0.04$). MAdCAM-1 blockade decreased SE in rejected grafts as compared with controls (0.5% vs. 3%; $p<0.03$). Corneal graft survival rate at 6 weeks follow-up was 62.4% in α4 blocking antibody and 23.2% in isotype treated mice ($p=0.04$).

Conclusion: MAdCAM-1 up-regulates after corneal inflammation and mediates cDC recruitment to the inflamed cornea. MAdCAM-1 receptors blockade increased corneal graft survival. MAdCAM-1 and its receptors may provide new pharmacological targets to enhance corneal allograft survival and decrease ocular surface inflammation. Funding supports: NIH KO8 -EY020575 (PH), NIH-RO1-EY022695 (PH), MEEI Foundation (PH), Research to Prevent Blindness (PH), Richard Lindstrom/Eye Bank of America (HM)

CORRELATION OF MEIBOMIAN GLAND DROPOUT WITH DRY EYE EVALUATION IN PRIMARY SJÖGREN'S SYNDROME.

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Purpose: To correlate Meibomian gland (MG) dropout with Schirmer´s test, Ocular Surface Staining (OSS), and tear break-up time (TBUT) in patients with primary Sjögren's syndrome (SS1).

Methods: Prospective, consecutive, transversal, case series study of patients with SS1 confirmed by salivary gland biopsy, serology, and/or SICCA Ocular Staining Score (SICCA OSS) according to 2012 classification criteria. Ophthalmic and dry eye evaluations included, TBUT, Schirmer-I test with and without anesthesia, OSS (Oxford, NEI-CLEK and SICCA OSS) and meibography. Meibography was performed with Keratograph 5M® and MG dropout was subjectively graded 0-3 (0: 0%, 1: <33%, 2: 33-66%, 3: >99% of MG dropout) by 2-blinded evaluators. Correlation between MG dropout and the other dry eye variables was analyzed using Spearman´s correlation.

Results: We evaluated 79 eyes of 40 patients, 97.5% were female. Mean ± Standard Deviation, SD) age was 53.78 ± 12.13 years. The mean ± SD (min - max) MG dropout grade was 1.47 ± 0.50 (0-3). We found no significant correlation ($p > 0.50$) between MG dropout grade and the evaluated dry eye parameters: TBUT, Schirmer-I test with and without anesthesia, and OSS (Oxford, NEI-CLEK and SICCA OSS).

Conclusions: Meibomian gland dropout grade does not correlate significantly with any of the evaluated dry eye parameters. [All authors declare no conflict of interests and no commercial relationships. No grant support]

COMPARISON OF KERATOGRAPH 5M® TEAR MENISCUS HEIGHT WITH DRY EYE EVALUATION IN PRIMARY SJÖGREN'S SYNDROME.

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Purpose: To correlate tear meniscus height (TMH) with non-invasive Keratograph 5M® tear break-up time (NIK-TBUT), invasive tear break-up time (TBUT), Schirmer's-I test, and Ocular Surface Staining (OSS) in patients with primary Sjögren's syndrome (SS1) dry eye disease.

Methods: Prospective, consecutive, transversal, case series of patients with SS1 confirmed by salivary gland biopsy, serology and/or SICCA Ocular Staining Score (SICCA OSS) according to 2012 classification criteria. Ophthalmic and dry eye evaluations included TBUT, Schirmer's-I test with and without anesthesia, OSS (Oxford, NEI-CLEK, and SICCA OSS scores), and Keratograph 5M® (NIK-TBUT, and TMH). Correlation between TMH and the other variables was analyzed using Spearman´s correlation. Results. We evaluated 79 eyes of 40 patients. 97.5% were female. Mean +/- standard deviation (SD) age was 53.78 +/- 12.13 years. Mean +/- SD (Min-Max) TMH was 240µm +/- 109µm (90-610µm). The following were significantly correlated with TMH: Schirmer's-I without anesthesia ($p=0.049$, $r=0.224$), Schirmer's I with anesthesia ($p=0.009$, $r= 0.294$), TBUT ($p=0.039$, $r=0.223$), Oxford ($p<0.000$, $r=-0.447$), NEI-CLEK

(p<0.000, r=-0.462), and SICCA OSS (p<0.000, r=0.554).
Conclusions: TMH correlated significantly with most variables. SICCA OSS, NEI-CLEK, and Oxford scores showed a moderate correlation. Schirmer's-I with and without anesthesia, and TBUT had a weak correlation.
[All authors declare no conflict of interests and no commercial relationships. No grant support]

CORRELATION OF OCULAR SYMPTOMS QUESTIONNAIRES WITH DRY EYE EVALUATION IN PRIMARY SJÖGREN'S SYNDROME.

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Purpose: To correlate Ocular Surface Disease Index (OSDI), Dry Eye Questionnaire (DEQ5), and National Eye Institute Visual Functioning Questionnaire 25 (NEI-VFQ25) scores with Schirmer´s test, Ocular Surface Staining (OSS), and tear break-up time (TBUT) in patients with primary Sjögren's syndrome (SS1).
Methods: Prospective, consecutive, transversal, case series/cohort study of patients with SS1 confirmed by salivary gland biopsy, serology and/or SICCA Ocular Staining Score (SICCA OSS) according to 2012 classification criteria. Ophthalmic and dry eye evaluations included questionnaires (OSDI, DEQ5, NEI-VFQ52), TBUT, Schirmer-I test with and without anesthesia, and OSS (Oxford, NEI-CLEK and SICCA OSS). Correlation between variables was analyzed using Spearman´s correlation. Results. We evaluated 68 eyes of 34 females, mean age +/- standard deviation was 54.16 +/- 10.95 years. Only the following correlations where statistically significant: OSDI and DEQ5 (p<0.000, r=0.605), OSDI and NEI-VFQ25 (p<0.000, r=-0.761), DEQ5 and NEI-VFQ25 (p<0.000, r= -0.557), OSDI and Oxford (p=0.014, r=0.296), OSDI and NEI-CLEK (p=0.003, r=0.351).
Conclusions: The only statistically significant, although weak, correlations found between questionnaires and clinical evaluation was between OSDI and OSS (NEI-CLECK and Oxford). The remaining tests did not correlate with questionnaire scores. All questionnaires showed a moderate to strong correlation amongst them.
[All authors declare no conflict of interests and no commercial relationships. No grant support]

EFFECTS OF THREE DIFFERENT DAILY DISPOSABLE CONTACT LENSES ON TEAR FILM.

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Purpose: To evaluate changes induced by three different daily disposable contact lenses on tear osmolarity (TFO), tear meniscus height (TMH), pre lens tear film stability (PLTFS) and objective quality of vision.
Methods: Forty-six subjects (new or contact lens wearers after a wash out period of three days) were enrolled for this open label randomized cross-over study. Their tear film characteristics were: NIBUT >18sec, TMH >18mm and TFO <316mOsmol/L. Subjects were asked to wear for the first week of the study a contact lens in nesofilcon A (Biotrue ONEDay) always on the same eye and another one in delefilcon A (Total1) on the fellow one. After three days of wash out it started the second week of the study with lenses in nesofilcon A again and lenses in stenofilcon A (MyDay). Exams were performed at day 0 and for each contact lens combination at day 1 after 20min and at day 7 after a minimum of 8h of lens wear. At each examination were evaluated TMH with a slit lamp-adapted Fourier-Domain OCT, TFO with Tearlab, NIBUT and PLTFS with Easytearsview+ and objective quality of vision by means of Objective Scatter Index (OSI) for a period of 20sec between blinks measured with HD Analyzer.
Results: Nesofilcon A lenses demonstrated a greater TMH after 20min and 8h of wear (respectively 206.73±48.2μm and 196.13±42.4μm) than delefilcon A (171.73±42.4μm and 162.93±42.36μm; p<0.05) and stenofilcon A (153.46±49.7μm and 148.34±53.64μm; p<0.05). Nesofilcon A lenses demonstrated also a longer PLTFS (12.53±6.27sec and 12.08 ±5.53sec) than delefilcon A (8.33±3.63sec and 9.06±3.51sec; p<0.05) and stenfilcon A (8.40±3.37sec and 7.80±5.26sec; p<0.05). TFO were not significant different after 20min and 8h of wear with all lenses tested. Nesofilcon A lenses in respect to the other lenses tested presented also a more stable OSI over time.
Conclusion: These results could be attributable to the characteristics of nesofilcon A material that allows a better water retention and wettability in comparison to the other materials tested.

ASSESSMENT OF COMFORT AND PRE-LENS TEAR FILM SURFACE QUALITY.

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Purpose: To evaluate pre-lens tear film surface quality (TFSQ) in five distinct regions of the cornea (Central, Inferior, Superior, Nasal, Temporal, CISNT) and to assess whether there is a link between TFSQ and comfort.
Methods: Eleven subjects (3M/8F, aged <40) participated in a one-day contact lens (CL) study wearing two pairs of hydrogel (LA) and Si-Hy (LB). One 40-second measurement was taken in natural blinking conditions after 6 hours of wear using high speed videokeratoscopy. The subjective comfort was evaluated (scale 1-10). Subjects were neophytes and occasional CL wearers. The quality of Placido disc reflections in CISNT regions were analysed and graded from 1 (best) to 5 (worst) by an operator precisely before each blink. All regions were analysed and correlated. Statistical significance level was set to 0.05.
Results: Statistical differences were noted in TFSQ and comfort between LA and LB. LB was assessed as a better lens due to its effect on TFSQ and better comfort score. The analysis showed no correlation between neither of the regions and comfort with LA. However, for LB, correlation was found between comfort and the percentage of grade1 in C area as well as the percentage of grade 5 in I area.
Conclusions: The results for LA were inconclusive. However, for LB, a new generation lens, TFSQ is scored as best in region C, and the subject was able to distinguish between different levels of comfort, suggesting a visual component in decision making whilst when TFSQ is scored as worst in region I, the subject was able to distinguish between different levels of comfort, suggesting a mechanical (possibly lid wiper) component in decision making. The study highlights the importance of assessing comfort with more than one question as there are several factors contributing to comfort and good vision during CL wear.
[This research was supported by Marie Sklodowska Curie ITN grant, EDEN (European Dry Eye Network), ID 642760]

PHENYLBORONIC ACID BASED POLYMERIC MICELLES FOR MUCOADHESIVE OCULAR DRUG DELIVERY.

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Purpose: Despite poor performance, topical drops are by far the most widely used therapy for many ocular diseases. Physical and dynamic barriers including tight junctions and rapid tear turnover ensure the majority of topically applied drug is unavailable and must be frequently reapplied. We propose the use of mucoadhesive self-assembling

micelles as a drug delivery platform designed to solubilise drug and bind to the mucin layer of the tear flim, providing unable, controlled, and sustained release of a therapeutic.
Methods: pLA-b-p(MAA-PBA) copolymers were synthesized by RAFT polymerization. Copolymer composition and molecular weight were determined using proton nuclear magnetic resonance. Mucoadhesion was determined using Surface Plasmon Resonance (SPR). An in vivo assay was also performed to corroborate these results. Cyclosporin release from micelles was determined using high performance liquid chromatography (HPLC). Nanosep 10K Omega centrifugal units were used to determine entrapment efficiency. Micelles were dissolved at 5mg/ml in sterile PBS for all in vivo work. This system was compared with Restasis to rescue rodent dry eye (DED) models from a disease state. Results We have shown that these nanoparticles work as expected. They can entrap and release a hydrophobic drug (cyclosporin) for over 14 days in in vitro sink conditions. Mucoadhesion has been confirmed both by SPR and an in vivo assay. The particles cause no pathological response in vivo, and are immunologically benign. Disease models for DED were created in rats using [a] benzalkonium chloride to model a mixed evaporative/aqueous deficient disease state and [b] scopolamine and aridity to model a purely aqueous deficient DED. Both of these disease states were more effectively treated using our micelle platform to deliver cyclosporin when compared with Restasis - currently the only approved treatment for DED in North America.
Conclusions: poly lactic acid -co- methacrylic acid micelles were synthesised using RAFT polymerisation, and functionalised with phenylborinic acid granting mucoadhesivity to improve ocular drug delivery.

OCULAR SURFACE AND MEIBOMIAN GLANDS CHANGES AFTER ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION.

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Purpose: We evaluated the changes of an ocular surface meibomian glands after HSCT associated with symptoms for the dry eye.
Method: Thirty nine patients who were able to follow up for at least 1-year underwent Ocular Surface Disease Index (OSDI) questionnaire, Schirmer test without anesthesia, slit-lamp examination to assess TBUT and corneal fluorescein staining, infrared meibography, and lid score.
Results: There was significant increase of OSDI score ($p<0.001$) and fluorescein stain score ($p=0.024$). And meiboscore of total, upper and lower eyelid showed significant increase ($p<0.0001$, $p=0.001$, $p=0.011$, respectively).
Conclusions: There was no difference in the severity of ocular GVHD grading and ocular surface parameters during the follow-up period, and subjective symptoms of ocular GVHD was worsen over time, although proper GVHD management was done. Also, this study presented first evidence of morphological changes of meibomian glands in patients with cGVHD following HSCT.

UNIQUE CHALLENGES AND UNMET NEEDS FOR THE TREATMENT OF OCULAR SURFACE DISEASE IN AFRICA.

Professor Kovin S Naidoo. Brien Holden Vision Institute (CEO)
Ocular surface disease in Africa has received limited attention from the eye care fraternity, especially in terms of understanding the prevalence and management. The competing health priorities of HIV/AIDS and ocular priorities of cataracts and refractive error have exceeded any attention that could be given to the understanding of ocular surface disease in Africa. Furthermore, Africa's human resource limitations places significant burden on existing personnel who deal with the more visually debilitating conditions like cataracts, refractive error, trachoma, glaucoma, etc. The prohibitive costs associated with newer generation, less toxic ocular disease medical therapy, like that for glaucoma, also places further pressure on the need for ocular surface disease research. Currently, fragmented efforts are made to understand ocular surface disease and in most cases are restricted to the topic of dry eyes. The majority of the African continent is made up of hyper-arid to dry sub-humid climatic conditions and currently certain parts are in a drought state, making the majority of the continent prone to inflammatory and non-inflammatory eye conditions which predominate in dry climates. Poverty on the continent has resulted in the highest prevalence of vitamin A deficiency and therefore a higher likelihood of potentially blinding dry eye disease as a result.
Therapies currently employed for ocular surface disease have limited availability in many countries on the continent. Vitamin A supplementation has posed a significant public health problem and the increased efforts in this area has seen improvements, however, there are still children in many parts of the continent who still go without. Other dietary supplementation like omega-3 fatty acids can be limited and where available, quite expensive. In most cases, treatment is palliative because of the prohibitive costs and limited availability of drugs which target the cause directly and therefore usually limited to the basic range of tear supplements. Research has shown that evidence-based approaches to therapy is ideal, however, the lack of equipment and diagnostic dyes make it difficult to identify the exact nature of the dry eye. In recent years, the advent of digital devices and mobile technology has also opened up a new area of enquiry for ocular surface abnormalities.

ESTABLISHMENT OF RAT DRY EYE MODEL WITH OCULAR DISCOMFORT BEHAVIOR.

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Purpose: Ocular discomfort is the most frequent patient complaint in dry eye. Variety of murine dry models have been developed and characterized that display certain features of dry eye patients. Though the symptoms have characterized by ocular surface damage or changes in tear film status alone. The purpose of this study was to verify the ocular discomfort behaviors in rat blink suppressed dry eye model (IOVS 2005).
Methods: Eight-weeks-old female Sprague-Dawley rats were used for this study. Bilateral Harderian glands were surgically removed under deep anesthesia. After 1-week surgery, rats were placed on a swing made of a plastic pipe for 7.5 h/d, and for 16.5 hours, they were placed in individual cages without swing treatment. This dry eye treatment was repeated for up to 6 days under continuous exposure to low-humidity airflow ($25 \pm 5\%$, 2 - 4 m/s). Change in spontaneous blink rate was measured before (day 0) and 1 day after end of dry eye (day 7) treatment under normal condition. Sham operated rats were used as control.
Results: Spontaneous blink rate was not changed in control group during experiment. A significant increase in blink rate was observed in Harderian glands removed group. Increasing ratio were approximately 200% ($p < 0.05$) to control and before dry eye treatment respectively.
Conclusions: Increase in blinking is the characteristic behavior of eye irritation. Harderian glands excision in combination with dry eye treatment induced ocular discomfort behaviors in rat. No commercial relationships.

TFOS DRY EYE WORKSHOP II.

J Daniel Nelson, Jennifer P Craig and David A Sullivan, on behalf of the TFOS DEWS II members.

The mission of the Tear Film & Ocular Surface Society (TFOS; www.tearfilm.org), a non-profit organization, is to advance the research, literacy, and educational aspects of the scientific field of the tear film and ocular surface. To help achieve that mission, TFOS launched the Dry Eye WorkShop II (DEWS II; www.tfosdewsreport.org) in March 2015. The goal of the TFOS DEWS II is to achieve a global consensus concerning multiple aspects of dry eye disease (DED). This initiative involves the efforts of more than 150 clinical and basic research experts, who are using an evidence-based approach and a process of open communication, dialogue and transparency to increase our understanding of DED. The TFOS DEWS II is updating the definition, classification and diagnosis of DED, critically assessing the epidemiology, pathophysiology, mechanism, and impact of this disorder, addressing its management and therapy, and developing recommendations for the design of clinical trials to evaluate pharmaceutical interventions for DED treatment. We anticipate that the TFOS DEWS II Report will be published in The Ocular Surface in the Spring of 2017. Scientific and lay Executive Summaries will then be translated into multiple languages and distributed to eye care practitioners and DED patients throughout the world. At this TFOS Montpellier 2016 Conference, TFOS DEWS II members will provide progress reports from ten Subcommittees, including Definition and Classification; Sex, Hormones & Gender; Epidemiology; Pathophysiology; Iatrogenic; Pain & Sensation; Tear Film; Diagnosis; Management & Therapy; Clinical Trials; and Public Awareness & Education.

SURFACE INTERACTION OF LACRITIN C-TERMINAL SYNTHETIC PEPTIDES WITH HUMAN MEIBUM FILMS.

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Purpose: ^{125}I-labeled N-94 and N-94/C-6, representing the active C-terminal domain of tear protein lacritin, are retained in rabbit tears and on meibomian glands 24 hr after topical application. Here we ask whether tear retention is a consequence of association with the tear lipid layer by assay of surface chemistry interactions with human meibum films (hMGS).

Methods: Lacritin synthetic peptides N-94/C-6 and N-94 were synthesized with an added C-terminal tyrosine, radiolabeled with ^{125}I and topically added (4 μM) to rabbit eyes twice daily for 5 days. Tears, eye tissues, blood and serum were then assessed for TCA precipitable radioactivity. For Langmuir surface balance studies, unlabeled peptides were added (6 μM) to the hMGS films subphase. Surface pressure (π)-area (A) isocycles were used to assess the sample's performance at dynamic area changes. The dilatational rheology of the layers was probed by stress-relaxation technique. Film morphology was monitored by Brewster Angle microscopy.

Results: ^{125}I-labeled peptides are at baseline in blood, serum and other eye tissues. Both peptides rapidly inserted in hMGS films pre-equilibrated at π = 15 mN/m. The peptide penetration kinetics was well described ($R^2 \geq 0.96$) by a sequential reaction model assuming a faster "docking" and slower "incorporation" step. Both peptides shift π/A isotherms to higher π values, and are not squeezed out of the layer at compression, reflecting stable incorporation into hMGS film. Peptide insertion results in a thicker and more uniform meibum layer structure with higher elasticity in the frequency range of 10^{-5}-1 Hz.

Conclusions: N-94 and N-94/C-6 lacritin strongly interact with hMGS films thereby enhancing film structure and surface properties– in keeping with a long tear residence time in vivo. [G.W. Laurie: F; TearSolutions Inc. P; UVa Patent Foundation. Supported by TearSolutions Inc. and EY024327 (to GWL).]

ABOUT THE INFLUENCE OF THE VEGETATIVE ACTIVITY ON DRY EYE SYNDROMES.

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Purpose: Dry eye has many etiologic backgrounds. one main problem may be psychologic complaints like stress, depression or anxiety. The lacrimal glands are regulated by parasympathetic nerval pathways, which may be inhibited by psychological problems noticed in dry eyes. For the question if psychological problems are in relation with dry eyes a study was performed with a test of stress reaction in dry eye patients DE compared with a non dry eye patients who served as a controll group CG .

Methods: 10 DE were compared with 10 CG patients without dry eye symptoms in a prospective study. For the stress reaction a fingersensor for the adrenerg hydrosis (skin contact level SCL) induced swearting reaction was used. The patients had to do calculation exercites, after this they had to relax. Subjectiv stress was asked in 5 steps (emotional tension: ET). For the dryness Lipid layer-thickness, Fluorescein of the cornea, fluorscein-break up time (fBUT), high of tear meniscus and lissamin green staining and the feeling of dry eye symptoms by visual analogue scale (VAS) was used. A dryness score with mean values of these parameters served for severness of dry eye. Results. There was no difference of SCL between DE and CG in stress reaction ($p>0,05$), but a significant difference between both goups in the relaxation time($p>0,05$); there was a significant difference of ET between both groups ($p>0,001$). There was a positive correlation between SCL-stress reaction and dryness score in DE (R: 44,3) but no correlation in CG.

Conclusions: Emotional burden and any psychological complaints are in relation with dry eye symptoms, the different reactions of SCL in both groups may be a visible sign of vegetative tension to influence the tear film function. Conflict of interests: The authors have no commercial relationships in materials of this article.

WHICH IS THE BIGGER RISK FACTOR FOR DRY EYE DISEASE: MEIBOMIAN GLAND DYSFUNCTION (MGD) OR CONTACT LENS DISCOMFORT (CLD)?

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In 2011 the TFOS International Meibomian Gland Dysfunction (MGD) was published, followed two years later by the TFOS International Contact Lens Discomfort (CLD) workshop, both in *Investigative Ophthalmology and Visual Science*. While MGD has been described as "leading cause of dry eye disease throughout the world," contact lens discomfort has long been touted as "the leading cause of contact lens discontinuation worldwide."

It is estimated that there currently are more than 140 million contact lens wearers worldwide, and while many wear contact lenses without any discomfort, most contact lens wearers report the presence of symptoms at least occasionally. In addition, it remains difficult difficult to estimate the number of individuals who previously have worn contact lenses and then abandoned lens wear as a result of CLD. It is reported that 12% and 51% of lens wearers "drop out" of contact lens wear, with CLD the primary reason for discontinuation. Two major contributors of CLD are the contact lens and the environment, with the contact lens category divided further into four subcategories: material, design, fit and wear, and lens care. The environment category also was broken down further into four subcategories: inherent patient factors, modifiable patient factors, ocular environment, and external

environment, all of which could be targets for improving comfort. With millions of contact lens wearers across the globe, eye care providers and researchers alike strive for clarity in diagnosis, management, and emerging trends. In this session, key updates since publication from both reports will be presented in a back-and-forth debate, including pathophysiology, epidemiology, diagnosis, management, and clinical trials. Which will it be—MGD or CLD?

WHICH IS THE BIGGER RISK FACTOR FOR DRY EYE DISEASE: MEIBOMIAN GLAND DYSFUNCTION (MGD) OR CONTACT LENS DISCOMFORT (CLD)?

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In 2011 the TFOS International Meibomian Gland Dysfunction (MGD) was published, followed two years later by the TFOS International Contact Lens Discomfort (CLD) workshop, both in *Investigative Ophthalmology and Visual Science*. While MGD has been described as "leading cause of dry eye disease throughout the world," contact lens discomfort has long been touted as "the leading cause of contact lens discontinuation worldwide."

In recent years, the disparity in MGD prevalence has been reported across the globe, ranging from 3.5 – 60%, and the question remains whether MGD pathophysiology is different across ethnicity, or if the design of the studies has been different, thus impacting findings. Currently, meibomian gland dysfunction is thought to be caused primarily by terminal duct obstruction, hyperkeratinization of the ductal epithelium, and thickened opaque meibum, which containing keratinized cell material. It is thought that the he obstructive process is influenced by endogenous factors, such as age, sex, and hormonal disturbances, as well as by exogenous factors such as topical medication, some of which can be modified, while others may not. These associated factors may indeed be on the rise in our changing internal (medications, hormones) and external (digital device use, pollution) environment. With recent focus on MGD as a significant contributor to dry eye, eye care providers and researchers alike strive for clarity in diagnosis, management, and emerging trends. In this session, key updates since publication from both reports will be presented in a back-and-forth debate, including pathophysiology, epidemiology, diagnosis, management, and clinical trials. Which will it be—MGD or CLD?

ENDOGENOUS OPIOIDS AND CHEMOKINES EXPRESSION IN PATIENTS SUFFERING FROM OCULAR PAIN ASSOCIATED WITH DRY EYE DISEASE.

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Purpose: To analyze the expression of pro-inflammatory and endogenous opioid markers in dry eye disease (DED) in order to investigate the decorrelation often observed between symptoms and signs in this pathology.

Patients and methods: 32 patients with symptomatic dry eye with (group 1) or without keratitis (group 2), and 11 age-matched control subjects were included. Each patient underwent an evaluation of ocular surface disease symptoms using the Ocular Surface Disease Index (OSDI), tear film break-up time (TBUT), corneal and conjunctival staining (Oxford scale), Schirmer test, corneal sensation using the Cochet-Bonnet esthesiometer and in vivo confocal microscopy (IVCM) analysis of corneal subbasal nerves and epithelial cells. The level of pro-inflammatory cytokine / chemokine expression (HLA- DR, IL-6, CCL2, CCR2, CXCR4 and CXCL12) and the precursors of endogenous opioids (POMC, P-ENK) were evaluated by RT-qPCR on conjunctival impression cytology specimens.

Results: Except Oxford score, no significant difference was found between groups 1 and 2 for clinical tests. Subbasal nerves density quantified by IVCM was lower in group 1 than in group 2 ($P = 0.002$). HLA-DR ($P < 0.01$) and IL-6 ($P < 0.02$) expression increased in patients with DED as compared to control subjects. CXCR4 ($P < 0.01$) and its ligand, the chemokine CXCL12 ($P < 0.01$) were also significantly increased exclusively in patients with keratitis (group 2). Finally, POMC expression significantly increased ($P < 0.02$) whereas levels of P- ENK mRNA decreased ($P < 0.05$) in patients suffering from DED as compared to controls.

Conclusion: Endogenous opioids and chemokines might be involved in the pathophysiology of ocular pain associated with DED.

GRAFT-VERSUS-HOST DISEASE.

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Graft-versus-host disease (GVHD) is a major complication after allogeneic hematopoietic stem cell transplantation (HSCT). Dry eye disease represents ocular GVHD and is a most frequent complication after HSCT in ophthalmic field. The number of ocular GVHD patients has increased, attracting greater attention with more papers are being published. However, precise clinical features and pathogenic processes of ocular GVHD remains not well understood at present time. The clinical features and underlying mechanism of ocular GVHD should be explained further. Points should be clarified and resolved. This presentation will be highlightened on the significance of dry eye in diagnosis of systemic GVHD and as well as a better understanding of underlying mechanism of dry eye related to chronic GVHD. In clinical setting, diagnostic criteria and findings of consensus group will be covered to apply in clinical practices. In basic research, the pathogenic processes of tear film, conjunctival mucosal membrane, lacrimal gland, and meibomian gland and also ocular surface immunity in GVHD will be discussed. Ocular cGVHD resembles autoimmune disease such as Sjögren's syndrome involving exocrine glands. It has been reported that immune cell migration, activation, and aging including hematopoietic stem cells or mesenchymal stem cells may be related to the onset, development and perpetuating of ocular GVHD. Recent advances on ocular GVHD in both clinical and basic researches will be explained. Collaborations worldwide are taking advantage of developing a standardized diagnostic criteria and proposing the significance of dry eye disease as ocular GVHD to the transplant community as well as in the field of ophthalmology. Creating a new therapy for ocular GVHD is necessary. Newly discovered findings of GVHD related to both clinical and basic research areas will be discussed. Chronic graft-versus-host disease (cGVHD) is a complication after minor antigen mismatched bone marrow transplantation. Ocular cGVHD resembles autoimmune disease such as Sjögren's syndrome involving exocrine glands. However, the precise source and roles of bone marrow derived cells in the pathogenesis of cGVHD are unknown. Here we show using a minor antigen mismatched cGVHD model that mismatched donor MSCs. These results were supported by clinical data where the number of residual host T cells was significantly higher in cGVHD patients compared to non-cGVHD patients. Our results show that donor MSCs trigger immune responses in residual host T cells during cGVHD, challenging current paradigms on the pathogenesis of the disease.

IMPACT OF HYALURONIC ACID CONTAINING ARTIFICIAL TEAR PRODUCTS ON RE-EPITHELIALIZATION IN AN *IN VIVO* CORNEAL WOUND MODEL.

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Purpose: The role of hyaluronic acid (HA) in the extracellular matrix structure is well documented, while its action on cells involved in tissue repair has been partly clarified. The use of artificial tear products (ATP) containing HA may impact corneal re-epithelialization; however the physicochemical properties of the formulation can facilitate HA retention. This experiment describes preclinical work to evaluate the impact of various ATPs on re-epithelialization of a corneal debridement wound following topical ocular administration.

Methods: Ninety-six C57Bl mice (16 per treatment group; 1:1 ratio of males & females per group) were anesthetized and epithelial debridement on one cornea per animal was performed. Following debridement procedure, each debrided eye was imaged and then 30µl of masked test solution containing one of 6 ATPs (Optive FUSION, VISMED, Thealoz Duo, HYABAK, Hylo-Comod and Systane HYDRATION [a dual polymer containing HA and HP-Guar]) was instilled immediately on the debrided eye of each animal and then every 2 hours afterwards, for a total of 4 administrations. After 24 hours post-debridement, corneas were stained with fluorescein and imaged to calculate the number of corneas completely re-epithelialized (fluorescein negative).

Results: At the time of this abstract, only results on the percentage of corneas in each treatment group with 0% epithelial defects after 24 hours post-debridement was available. The percentage of corneas per group with 0% epithelial defects after 24 hours post-debridement were as follows: 12.5% (Optive FUSION), 26.67% (VISMED), 31.25% (Thealoz Duo), 6.25% (Hyabak), 43.75% (Hylo-Comod) and 53.33% (Systane HYDRATION).

Conclusion: Systane HYDRATION showed better complete corneal re-epithelialization rates, 24 hours following debridement than other HA containing ATPs tested. This experiment provides some supporting evidence of the ocular surface healing properties of Systane HYDRATION. (This research was supported by Alcon Research, Ltd., Fort Worth, TX.)

CHANGES IN CORNEAL ENDOTHELIAL MORPHOLOGY AND CORNEAL THICKNESS IN PATIENTS WITH DRY EYE DISEASE AND SJÖGREN'S SYNDROME.

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Purpose. To assess corneal endothelial cell morphology and central corneal thickness in patients with dry eye disease (DED) and Sjögren's syndrome. Design. Cross-sectional study.

Methods: We observed the corneal endothelial morphology and corneal thickness in patients with non-dry eye disease (non-DED: 64 eyes of 36 patients), dry eye disease (DED: 120 eyes of 69 patients), suspicious dry eye disease (sDED: 72 eyes of 36 patients) and Sjögren's syndrome (SS: 16 eyes of 8 patients). We diagnosed DED using the "Definition and Diagnosis of Dry Eye 2006" by the Japan Dry Eye Society. The corneal endothelial morphology was examined by specular microscopy. We measured corneal endothelial cell density (ECD), coefficient of variation (CV) of endothelial cells and percentage of hexagonal cells (6A). The central corneal thickness was examined by Pentacam® (Oculus). The associations with ECD, CV, 6A and corneal thickness were determined using multiple linear regression analysis adjusted for age and gender.

Results: The mean ECD were 2691±179 cells/mm^2 in non-DED, 2590±355 cells/mm^2 in DED, 2702±338 cells/mm^2 in sDED, 2458±343 cells/mm^2 in SS. The mean CV were 36±4.5% in non-DED, 39±6.6% in DED, 38±6.0% in sDED, and 40±5.0% in SS. The mean 6A were 48%±7.0 in non-DED, 43%±6.7 in DED, 45%±7.3 in sDED and 42%±6.1 in SS. The mean corneal thicknesses were 564±31μm in non-DED, 554±30μm in DED, 557±31μm in sDED and 551±32μm in SS. In multiple linear regression analysis adjusted for age and gender, the DED group (p=0.045) and the SS group (p=0.027) had a significantly lower percentage of ECD compared to the non-DED group. CV was significantly higher in the DED group (p=0.015). The DED group (p=0.014) and the SS group (p=0.009) had a significantly lower percentage of 6A. The corneal thickness was not significantly different between groups.

Conclusions: DED and SS may change corneal endothelial cell morphology.

NANOSCALE ORGANIZATION OF TEAR FILM WAX ESTERS: A VIEW FROM MOLECULAR DYNAMICS SIMULATIONS.

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Purpose: Wax esters (WEs) are a major component of the tear film lipid layer (TFLL), but their properties have not been well characterized. Pioneering studies on wax esters proposed that WEs orient in a hairpin conformation at the air-water interface, with the ester group facing the water phase. More recent studies, however, have suggested that evaporation retarding WE monolayers contain solid regions with an extended molecular conformation. In the current study, molecular dynamics simulations were used to study the nanoscale organization of WE films and their evaporation retarding properties.

Methods: Based on a combination of the OPLS and L-OPLS force fields, we developed an all-atom molecular dynamics model for the WEs. The simulation model was validated by comparing simulated densities, melting points, and crystal structures to the values reported in the literature. Behenyl oleate (BO) films were simulated at the air-water interface using the OPC water model and their organization, surface potential and evaporation resistance were compared with Langmuir monolayer experiments.

Results: The simulation model was in good agreement with all bulk properties available in the literature. Simulations of BO at the air-water interface showed a transition from an ordered, extended conformation to a disordered, hairpin-like conformation close to the melting point of BO. Qualitatively similar surface potential was obtained from simulations and experiments. Simulated water permeation resistance of ordered BO films was higher compared to fluid films.

Conclusions: The simulation model was found to be in good agreement with experimental results and suitable for further simulations of the TFLL. Comparison of simulations with experimental data supports the proposed extended molecular conformation of evaporation retarding WE films.

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HYPERALGESIA IN DRY EYE DISEASE IS ASSOCIATED WITH LOW VIATMIN D.

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Purpose: To study the association of serum Vitamin D with clinical features of dry eye disease (DED) including corneal dendritic cell density (DCD), corneal sub-basal nerve plexus (SBNP) features and tear inflammatory proteins. Methods. A total of 40 patients and 30 healthy volunteers were included in this cross-sectional study. Routine dry eye investigations including TBUT, Schirmer's Test 1 and ocular discomfort grading using ocular surface disease index (OSDI)

questionnaire was performed. The sub-basal nerve plexus (SBNP) features in central cornea was assessed by confocal imaging (Heidelberg Engineering GmbH) using a 400x400 microns^2 frame followed by quantitation (CCMetrics, UK). Corneal dendritic cell density (DCD) was also estimated using Cell Count^R (Heidelberg) from the confocal images. Total vitamin D was measured in the serum and tears. Furthermore, tear inflammatory factors were quantified by cytometric bead array.
Results: The mean total OSDI score (total and discomfort subscale) was significantly higher in the DED patients compared to controls. TBUT and Schirmer's Test 1 values was significantly lower in DED patients than in controls. A significantly higher corneal DCD and a decreased nerve fiber density and branching was observed in DED. A positive correlation was observed between OSDI discomfort subscale scores and DCD in DED patients. In addition, vitamin D was observed to exhibit an inverse association with OSDI scores and DCD. Interestingly, higher vitamin D was observed in tears compared to serum in study cohort. Furthermore, an increased level of tear inflammatory cytokines including IL-17A/F, IFNγ and MCP1 was also observed in DED patients compared to controls.
Conclusions: Vitamin D levels appears to be linked to DED disease parameters. Hence, factoring in vitamin D levels would be beneficial in the diagnosis and management of DED.
[The study was supported by Narayana Nethralaya Foundation, Bangalore, India]

A LIQUID CHROMATOGRAPHY MASS SPECTROMETRY METHOD FOR DETECTION OF LIPID MEDIATORS OF INFLAMMATION IN THE HUMAN TEAR FILM.

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Purpose: Prostaglandins and isoprostanes may be responsible for ocular surface inflammation during dry eye disease and contact lens discomfort (CLD). We have identified a novel method of extraction and mass spectrometry for prostaglandins and isoprostanes in tears.
Methods: Tears (40 µl) were collected from both eyes of non-contact lens wearers and those with CLD using glass microcapillaries and stored at -80°C. A polymeric weak anion solid phase extraction cartridge was used for rapid extraction of prostaglandins (PGs) and F2-isoprostanes (F2-IsoPs). Liquid chromatography- electrospray ionization- tandem mass spectrometry (LC-ESI- MS/MS) was performed using a system consisting of an Eksigent Ekspert MicroLC 200, and a Sciex 6500 Qtrap mass spectrometer. A base-line separation of 8-iso-PGF2α, 8-iso-15(R)-PGF2α, PGF2α, 15(R)-PGF2α, 2,3-dinor-8-iso-PGF2α, and PGE2 was carried out on a 3C18-AQ column using a linear gradient of methanol:acetonitrile (1:1 v/v) in 0.1% formic acid. LC-ESI/MS/MS was operated in multiple reaction monitoring (MRM) mode with suitable precursor ion to product ion m/z transitions.
Results: PGs and F2-IsoPs were identified in the tears of both non-contact lens wearers and those with CLD. The lower limit of detection for the standards, 8-iso-15(R)-PGF2α, 8-iso-PGF2α, 15(R)-PGF2α, 2,3-dinor-8-iso-PGF2α, PGF2α and PGE2 were estimated to be 5 pg/ml, 5 pg/ml, 5 pg/ml, 5 pg/ml, 100 pg/ml, 5 pg/ml, and 10 pg/ml respectively. 2,3-dinor-8-iso-PGF2α was found in highest concentration in both groups.
Conclusions: Solid phase extraction and LC-ESI-MS/MS is a novel method for extraction and quantification of prostaglandins and isoprostanes in the human tear film. Larger sample size will be necessary to confirm the quantitative results of prostaglandins and F2-isoprostanes in tears between groups with and without ocular surface disease. (Commercial relationship/Grant support: None)

CONTACT LENS INDUCED MEIBOMIAN GLAND CHANGES: ARE THEY OF CLINICAL SIGNIFICANCE?

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Purpose: To explore the possibility that reported changes to meibomian gland morphology attributed to the wearing of contact lenses are clinically benign.
Methods: Critical literature review.
Results: Several reports indicate that contact lens wear is associated with changes to meibomian gland morphology. Those proposing links between such changes and functional changes to the ocular surface fall into two categories: A) those reporting effects of insignificant magnitude, in a beneficial direction or of a self-limiting nature; B) those where methodological or analytical errors confounded data interpretation. No evidence was found for a detrimental impact on subjective symptoms.
Conclusion: A convincing evidential basis for ascribing clinically significant reductions in ocular surface behavior to the influence of contact lens wear on meibomian glands is currently lacking.

THE ASSOCIATION BETWEEN SYMPTOMS OF DRY EYE SYNDROME AND METABOLIC OUTCOME IN A GENERAL POPULATION IN KOREA.

Jong Woon Park. National Health Insuranse Service Ilsan Hoapital
Purpose: We investigated the association between Dry eye syndrome(DES) symptoms and metabolic syndrome (MetS) and its components among adults aged >19 years using populatin-based data from the Korean National Health and Nutrition Examination Survey V.
Methods: A sample group of 15,294 adults completed household interviews in which they provided blood and anthropometric measurements to define metabolic syndrome. We also collected information regarding sociodemographic and behavioral risk factors.
Results: The survey results showed that 11.50% of men and 22.35% of women experienced DES and 5.30% of patients had both DES and diagnosis of MetS, including 204 men and 606 women.
Conclusions: No significant difference was observed between DES and the diagnosis of MetS according to sex. however, a significant association was observed between DES and hypertriglyceridemia in women (OR,1.13;95%CI,1.01-1.29) .Therefore, hypertriglyceridemia might be and important factor in the association between DES and MetS.

CHANGE OF TEAR LIPID LAYER THICKNESS AND MEIBOMIAN GLAND STRUCTURES AFTER CATARACT SURGERY.

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Purpose: To evaluate the tear film lipid layer thickness(LLT) and meibomian gland structure after cataract surgery.
Methods: Evaluation was performed before and 1 and 3 months after cataract surgery including LLT and meibomian gland structure measurements using Lipiview interferometer(TearScience® Morrisville, NC, USA) and Image J program, tear break-up time(TBUT), Schirmer's tests, Oxford staining score, and lid margin and meibomian gland examinations(Lid margin abnormality, Meibomian quality, expressibility) and Ocular Surface Disease Index (OSDI) questionnaire.
Results: Sixty-eye eye(43 subjects) were included. LLT was significant thinner 1 and 3 months after surgery than at baseline (P=0.011,0.019),

but there was no significant change in meibomian glands structure (P=0.956,0.228). TBUT, Schirmer's tests, OSDI score were showed no significant change at 1 and 3 months after surgery than at baseline (P=0.416 and 0.632, P=0.671 and 0.300, P=0.767 and 0.067). Oxford staining scores were improved at 1 and 3 months after surgery(P=0.003 and 0.002).
Conclusions: The tear film LLT was significantly thinner after cataract surgery, but the change of meibominal glands structure was not showed. These results suggest that cataract surgery induced the change of meibomian gland function, not meibomian gland structure.
[No author has any conflict of interest to declare, financial or otherwise.]

TEAR MENISCUS VOLUME AFTER CONJUNCTIVOCHALASIS SURGERY USING FOURIER-DOMAIN AS-OCT

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Purpose: To evaluate the tear meniscus and conjunctivochalasis volume before and after conjunctivochalasis surgery using Fourier-Domain AS-OCT.
Methods: A prospective study was included in 32 conjunctivochalasis patients who was performed excisional biopsy with amniotic membrane graft from Jun. 2013 to Sep. 2015. Tear break-up time and cross-sectional areas of tear meniscus and conjunctivochalasis were evaluated at 7 points of low lid at pre and postop. 3 months using RTVue-100.
Results: Tears were multiple separated by several conjunctival folds before surgery. BUT was change from 2.30 to 3.73 sec (<0.05). Conjunctivochalasis volume summation of 7 points were change from 2.85 to 0.05 mm2 (<0.05). Tear meniscus volume summation of 7 points were change from 0.22 to 0.27 mm2 (>0.05).
Conclusions: Conjunctivochalasis patients have dry eye symptoms because of redundant conjunctival folds and short BUT. Short BUT seems to be segmented tears by multiple folds even though normal tear volume. The authors have no commercial relationships.

EFFECTS OF TOPICAL CYCLOSPORINE 0.05% AFTER CATARACT SURGERY IN PATIENTS WITH DRY EYE.

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Purpose: To evaluate the effectiveness of topically administered 0.05% cyclosporine after cataract surgery in patients with dry eye.
Methods: Two hundreds eight patients who underwent unilateral cataract surgery without prior history of topical treatment were enrolled. The control group comprised non-dry eye patients who did not receive postoperative topical cyclosporine. Patients who received postoperative topical cyclosporine were categorized into three groups according to the preoperative dry eye severity as follows: G0 group, non-dry eye; G1 group, level I dry eye; and G2 group, level II dry eye. Disease severity was measured postoperatively using the tear film break-up time(TBUT), Schirmer test-I(STI), and dry eye symptom questionnaire.
Results: The G0, G1, and G2 groups showed significant improvement in the TBUT compared with the control group at 1-week, 1-month, and 2-months postoperatively. Postoperative STI deterioration shown in control group was not found in the G0, G1, and G2 groups. Significant improvement in the dry eye symptom compared to the control group was achieved at postoperative 2-months in G0 group, 1-month in G1 group, and 1-week in G2 group. Symptomatic improvements were greatest in the G2 group throughout the follow-up period. The preoperative TBUT significantly improved at 1-month postoperatively in the G1 and G2 groups, and improved further at 2-months postoperatively. The preoperative STI significantly improved only at 1-month postoperatively in the G1 and G2 groups. Preoperative dry eye symptoms improved significantly at 1- and 2-months postoperatively in the G1 group.
Conclusions: Topical cyclosporine is more effective after cataract surgery in level I and II dry eye patients than in non-dry eye patients. The ocular symptoms and signs improved most in the level II dry eyes.

SEX & THE EYE: A POTENTIALLY BLINDING IMPACT

Louis R. Pasquale, MD[1,2] [1]Mass Eye & Ear. [2]Channing Division of Network Medicine, Brigham & Women's Hospital. Harvard Medical School, Boston, MA, USA.
Purpose: Primary open-angle glaucoma (POAG) is a common cause of blindness. Many of its treatments disrupt the ocular surface, contributing to an unfavorable mismatch between disease-related and treatment-related symptoms. Since POAG is a strongly age-related disease and declining sex hormones are integral to aging, we explored approaches to identify sex hormone targets that might favorably alter disease management.
Methods: We employed various cohorts (National Health and Nutrition Examination Survey (NHANES); Nurses Health Study (NHS); Women's Health Initiative (WHI); and the Mayo Clinic Cohort Study of Oopherectomy and Aging (MCCSOA)) to explore attributes of female reproductive health in relation to POAG. We used a POAG case (n=3,853) – control (n=33,480) group with high throughput genotypes, to explore estrogen and testosterone metabolism in relation to POAG in an unbiased fashion.
Results: We reported adverse relations between later age at menarche (NHANES) and oral contraceptive use (NHANES, NHS) in POAG, supporting a role for reduced estrogen exposure in this disease. Among women older than 65, later age of menopause was associated with a decreased risk of the high-tension (HT) variant of POAG (NHS), which was consistent with the adverse relation between early oophorectomy and OAG noted in the MCCSOA. A randomized clinical trial embedded in the WHI showed that post-menopausal estrogen use was associated with a 0.5 mm Hg reduction in intraocular pressure, consistent with a 42% reduced risk of HT-POAG in the NHS. Estrogen metabolism gene variants were associated with POAG in women, while testosterone metabolism gene variants were associated with POAG in men. Gene-based analyses highlight 17-beta hydroxysteroid dehydrogenase activity and the intracrine generation of estradiol as a key metabolic focus for POAG in men and women.
Conclusions: Current evidence suggests that the eye requires constant estrogenic input to prevent glaucoma and our work points to alternative drug targets in both sexes to achieve that objective. This work is supportd by various NIH grants.

TEST EFFICACY OF THE MODIFIED SCHEIN QUESTIONNAIRE.

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Purpose: Although widely employed, the copyright held on the OSDI symptom questionnaire limits its broader application in research. The purpose of this study was to undertake a preliminary evaluation of test efficacy of an alternative, the modified Schein survey.
Methods: The six-question instrument validated by Schein et al. was modified by adding a category of "never" and giving each of the five possible frequency responses a numerical value of 0-4 for a total scale response of 0 – 24. A battery of clinical tests was used to screen

normals and dry eye subjects that included TBUT, fluorescein and rose bengal staining, meibomian secretion and atrophy via meiboscopy, and the Schirmer I test without anesthesia. Diagnostic criteria to determine whether "dry" or "normal" were: TBUT < 7 secs, ocular surface damage using either fluorescein staining > 4 (0-20 scale, modified NEI system) OR rose bengal staining > 4 (0-24 scale), or Schirmer I test without anesthesia < 5 mm in 5 minutes. Results: Forty seven normals and 125 drys completed the study. The mean Schein scores for normals and dry subjects were 7.98 (+/- 4.0) and 11.2 (+/- 3.7), respectively; p < 0.001. Dunnetts pairwise tests were significant at the 0.05 level for normals vs. 1) obstructive MGD (n = 73), 2) anterior blepharitis (n = 30), and 3) unspecified drys (n = 10). ROC analysis suggested a cut-point of 8.5 (0 – 24 scale) for sensitivity of 0.74 and specificity of 0.62. AUC was 0.73, indicating acceptable discrimination. Repeatability data were available for 69 subjects one week apart. The initial and second scores were 11.1 (+/- 3.7) and 10.2 (+/- 3.4). The intraclass correlation coefficient was 0.70, indicating fair repeatability.
Conclusions: The modified Schein questionnaire is efficient and discriminates normal patients from those with clinically diagnosed dry eye. Moreover, the questionnaire appears to yield repeatable scores, suggesting usefulness as a measure of treatment effectiveness.
Commercial Relationships: JR Paugh: IIT funding from Alcon laboratories AL Nguyen: None

CORNEAL BARRIER TO INFLAMMATION.

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Purpose: The cornea is constantly being exposed to different signals that induce an inflammatory response. In this presentation we will discuss how the cornea utilizes innate and adaptive mechanisms of immunity as a barrier to inflammation.
Methods: Our laboratory have developed in vivo animal models to study in real time corneal immune responses to exogenous and auto antigens utilizing infectious keratitis and ocular graft versus host disease (oGVHD) diseases.
Results: In both pre-clinical models of corneal inflammation, mechanisms of immune cells recruitment are significantly regulated in order to prevent or regulate immune responses. Furthermore, epigenetic regulators of mediators of inflammation are critical in this process. Dysregulation of these signals result in corneal opacity and damage. Topical application of small molecules can be used to regulate immune corneal responses.
Conclusion: Considering the fact that the cornea is exposed to many inflammatory insults, it is fascinating how effective is in regulating these and remain clear. Understanding these pathways is critical in the developing of novel therapies that can be locally delivered to promote the barrier function of the cornea to inflammation to prevent or treat corneal blindness. Grant Support: NIH-NEI: R01 EY024484, NIH Center Core Grant P30EY014801, RPB Unrestricted Award and Walter G. Ross Distinguished Chair in Ophthalmic Research.
Commercial Disclosures: Bausch & Lomb, Capricor, EyeGate Pharm, OBTears LLC, OccuRx and Shire.

IMPACT OF MICROBIOTA ON ADAPTIVE IMMUNE EFFECTORS ON THE OCULAR SURFACE.

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Purpose: To evaluate molecular and cellular mechanisms responsible for protection against *Pseudomonas aeruginosa, Staphylococcus aureus* and fungal keratitis and characterize the influence of the microbiota on anti-microbial immunity.
Methods: Responses to *P. aeruginosa, S. aureus* and fungal pathogens were evaluated either in germ free (GF) mice, specific pathogen free (SPF) mice, or mice colonized with different gastrointestinal (GI) ecosystems. Data were generated using antibody to surface capsules, alginate for *P. aeruginosa* and poly-N-acetyl glucosamine (PNAG) for *S. aureus* and fungal pathogens, that are highly protective against infection and corneal pathology.
Results: In the absence of effective PMN recruitment, as well as lack of a microbiota-driven production of IL-17 and IL-22, antibody-mediated immunity to keratitis is lost, as demonstrated by studies in GF and cytokine-deficient mice. Additionally, GF mice had significantly reduced levels of sIgA at the ocular surface compared to conventionally maintained, SPF mice harboring an indigenous microbiota. Three weeks after colonization with normal GI commensals, previously GF mice developed sIgA at the ocular surface. Similarly, exposure of conventionally-colonized young Swiss-Webster mice to oral antibiotics delayed the appearance of sIgA. Obtaining wild-type levels of tear film IgA was dependent on IL-1ß production, as antibody blockade of this cytokine in conventional SW mice reduced both ocular surface sIgA levels and IgA mRNA transcripts in the lacrimal glands. Tear film sIgA was found to have microbiota-dependent reactivity against *P. aeruginosa*. sIgA was associated with improved resolution of *P. aeruginosa*-induced infection in BALB/C mice as sIgA deficient mice showed delayed recovery from infection.
Conclusions: Overall, protection against ocular pathogens requires a microbiota-driven maturation of humoral and cellular responses, showing that even the immune-privileged status of ocular tissues depends on microbes for generating maximal immune resistance to infection. This research was supported by NIH NEI 016144 (GP) and EY022054 (MG).

DRY EYE DISEASE EXPERIMENTAL MODELLING.

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Introduction. Botulinum toxin A(BT-A) blocks the release of acetylcholine from presynaptic terminals of cholinergic nerve endings, including lacrimal glands.
Objective: The aim was to work out a dry eye disease (DED) model based on lacrimal production in rabbits.
Material and methods: 10 rabbits (20 eyes) weighing 2.5-3.0 kg were given transconjunctival 5ED BT-A (Botox, Allergan, USA) injections into the main lacrimal gland, Garder gland and suborbital gland under anesthesia, using a 29G needle. Estimation of functional parameters, namely, precorneal tear film stability by M. Norn sampling, total lacrimal production according to O. Shirmer as well as the intensity of eye surface epithelium staining by Bengal rose solution according to van Bijsterveld scale during biomicroscopy was made on the 1st, 3rd, 7th, 14th and 21st day of the investigation. The quantity of cytokines IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, IL-17A, IL-1Ra,TNF-α, INF-α, INF-γ in the tear fluid was determined, using solid-phase ELISA at the beginning of the investigation and on the 21st day. The precorneal tear film osmolarity was determined using TearLabOsmolarity System.
Results. On the 7th day of the experiment all the animals showed functional characteristics of precorneal and conjunctival xerosis intensifying by the 21st day: the statistically valid decrease of the precorneal tear film stability, total lacrimal production decrease and the increase of the area of eye surface epithelium staining ($p<0.05$-0.001). The reliable increase of the level of the cytokines under investigation by 1.5 and more times in combination with the increase of the precorneal tear film osmolarity ($p<0.05$-0.001) was recorded in the tear film on the 21st day, which is characteristic of the development of a marked inflammatory process in the eye surface epithelium.
Conclusion. A DED model based on lacrimal production decrease in rabbits that is based on transconjunctival BT-A injections into lacrimal glands and may be used in a wide range of experimental research has been worked out.

THE EFFICIENCY OF 0.01% DEXAMETHAZONE SOLUTION IN COMPLEX THERAPY FOR PATIENTS WITH DRY EYE DISEASE OF DIFFERENT ETIOLOGY.

Brzheskiy V.V.[1], Popov V. Yu.[1], Kalinina I.V.[2]. [1]Saint Petersburg State Medical Pediatric University, Russia[2] Mariinsky Hospital, Russia

Introduction. A wide use of dexamethazone in the officinal dose (0.1) has substantial limitations. Taking this circumstance into account, we have worked out a medicine containing 0.01% dexamethazone phosphate solution in combination with 6% polyvinylpyrrolidone and 1.5-5.5% dextrose.

Objective: The aim was to study the influence of the worked our medicine on the inflammatory process dynamics in eye surface tissues.

Material and methods: 25 volunteers (50 eyes) with dry eye disease (DED) of different etiology were investigated. On the background of tear replacement therapy the frequency of instillations of the medicine under investigation was 3-4 times a day. OSDI, tear meniscus index, production, stability, precorneal tear film osmolarity, eye surface epithelium staining by sodium fluorescein solution and Bengal rose were determined before the treatment and on the 28th day of the investigation. The quantity of cytokines IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, IL-17A, IL-1Ra, TNF-α, TNF-γ was determined in the tear fluid and blood plasma, using solid-phase ELISA.

Results: Statistically valid increase of a tear meniscus index, precorneal tear film stability, basic and total lacrimal production and tear film osmolarity decrease were recorded by the 28th day of the investigation. At the same time the intensity of eye surface epithelium staining by vital dye solutions according to van Bijsterveld and Oxford scales decreased. In addition, the change of immunologicindices, namely, the decrease of the pro-inflammatory cytokines and the increase of the anti-inflammatory ones, was recorded in the tear fluid and blood plasma on the background of the applied therapy. Under these conditions the positive dynamics of functional, objective and biochemical indices was followed by the increase of the patients' life quality according to OSDI scale.

Conclusion. The worked out medicine is characterized by a high clinical efficiency shown by a marked local anti-inflammatory and tear replacement effect in treating DED of different etiology.

PRECLINICAL MOUSE MODEL TO MONITOR LIVE CONJUNCTIVAL GOBLET CELL DIFFERENTIATION UNDER PHARMACOLOGICAL TREATMENTS.

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Purpose: Dry eye (DE) is one of the most widespread ophthalmic diseases that results of multifactorial mechanism including a defect of mucus production by goblet cells of the conjunctiva. Amongst the gelling mucins expressed by the conjunctiva, MUC5AC has received much attention while little is known about MUC5B.

Methods: The mouse *Muc5b* gene product has been GFP-tagged by homologous recombination. Expression profile of Muc5b-GFP was investigated using complementary approaches: probe-based confocal laser endomicroscopy (pCLE, Cellvizio, Mauna Kea Technologies) on living mice, epifluorescent microscopy on fresh tissues and immunohistochemistry. DE was mimicked in mouse eye by topical application of 5µL of 0.2% benzalkonium chloride (BAK) twice daily for 10 days. Five ng of rIL13 were also administered topically twice daily for 4 days. Conjunctival goblet cell clusters (CGCc) and Muc5b expression were investigated by pCLE followed by image analysis. All data were analyzed using nonparametric tests.

Results: Expression pattern of Muc5b-GFP mice is identical to its human counterpart. GFP$^+$ CGCc number is correlated to the total CGCc number (n=8 mice; P=.007) and represents almost 50% of them. BAK induces a 64% and 70% decrease of AB-PAS and GFP$^+$ CGCc number, respectively. Analysis of GFP$^+$ CGCc by pCLE shows a -21.1%(±26.9) decrease of GFP$^+$ CGCc density compared to paired-eye PBS control (n=12 mice; P=.001). A -18.3%(±25.6) decrease of GFP$^+$ CGCc density induced by BAK treatment is reversed by rIL13 topical application for 4 days (increase of 28.6%; n=44 and n=39 mice for PBS and rIL13 after BAK treatment, respectively; P<.0001).

Conclusions: Topical application of rIL13 induces conjunctival goblet cell differentiation in a mouse DE model. Our powerful model is unique and allows a better understanding of the mechanisms that regulate gelling mucin production/secretion and mucous cell differentiation in the conjunctiva of living mice and can be used to test treatment compounds in mucosal disease models.

EXACERBATION OF CLOSED EYE LEUKOCYTE INFLAMMATION IN DRY EYE DISEASE.

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Purpose: The closed eye is known to be inflammatory, and is characterized by an influx of hundreds of thousands of leukocytes, predominantly neutrophils. The purpose of this pilot investigation was to determine if neutrophil hyperactivity or increased T cell infiltration could be observed as part of the closed eye leukocyte population in dry eye disease.

Methods: Six normals and six dry eye subjects were recruited and were trained to wash the ocular surface with phosphate buffered saline for at-home self-collection of tear film leukocytes following a full night of sleep. Cells were isolated and counted, and were incubated with fluorescently-labeled antibodies against CD45, CD14, CD15, CD16, CD11b, and CD66b to identify neutrophils. Antibodies against CD45, CD3, CD4, CD8, CD196, and CD161 were used to identify T cells. A Becton Dickinson (BD; San Jose, CA) proprietary fixable viability stain was used to exclude dead cells from analysis. A BD LSR II flow cytometer was used for all analyses.

Results: Neutrophils isolated from dry eye subjects demonstrated increased expression of CD11b, CD66b, and CD16 as compared to normals, indicating a hyperactive neutrophil phenotype. Similarly, there were more CD4+ T cells and more Th17 cells (as identified as being CD196+CD161+) in the closed eye leukocyte populations as compared to normals. Combined, the results demonstrate increased inflammation in the dry eye closed eye.

Conclusions: In a small cohort, the closed eye leukocyte population in dry eye disease appeared to have increased presence of Th17 cells and an associated neutrophil hyperactivity. The normal, homeostatic, closed eye is in an inflammatory state, and this investigation suggests that this state may be exacerbated in dry eye disease.

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BLINKING FROM A TRIBOLOGICAL VIEWPOINT.

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The mechanical forces between the lid wiper and the ocular surface, and between a contact lens and the lid wiper, are reported to be related to dry eye symptoms. Furthermore, the mechanical forces between these sliding partners are assumed to be related to the ocular signs of lid-wiper epitheliopathy (LWE) and lid-parallel conjunctival folds (LIPCOF). Recent literature provides some evidence that a contact lens with a low coefficient of friction (CoF) improves wearing comfort by reducing the mechanical forces between the contact lens surface and the lid wiper. This lecture discusses the mechanical forces during spontaneous blinks from a tribological perspective, at both low and high sliding velocities, in a healthy subject. It concludes that the coefficient of friction of the ocular surfaces appears to be strongly comparable to that of hydrophilic polymer brushes at low sliding

velocity, and that, with increased sliding velocity, there is no wear at the sliding partners` surfaces thanks to the presence of a fluid film between the two sliding partners. In contrast, in the case of dry eye, collapsed brushed at low velocity and increased tear film viscosity at high velocity are the main factors resulting in deformation and wear of the sliding pairs.

FACTORS IMPACTING THE POST-LENS TEAR FILM MIXING.

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Purpose: Tear film replenishment rate beneath soft contact lenses lens is commonly assumed to be related to lens mobility. However, reported post-lens tear film exchange was almost analyzed with methods measuring the expulsion of fluorescein from beneath the lens. This study aimed to measure the solely effect of the contact lens movement compared to the "pumping effect" in an in-vitro model.

Methods: A glass plate was lubricated by 40 drops of saline solution and a 45mm diameter PMMA disc (PM) was then put on top, representing a contact lens. Then the saline solution around was colored by fluorescein to obtain an uncolored post-disc 'tear film' (PDTF) and a stained 'tear film' around this glass disc. This model was illuminated by UV light. A contact lens movement after blink was simulated by moving this glass disc forward (=inferior) and backward (=superior) by 10mm or 5mm. This setup was photographed before (B_0) the simulated blinks and every 5th of 100 consecutive simulated blinks. Experiment was repeated and lid-wiping was simulated by a weight controlled roller, rolling over the plate backwards and forwards, every simulated blink was photographed. Additionally, combinations of movement + lens rotation, rolling + rotation and all was performed and photographed. This experiments were repeated 5 times. Every image was analysed in terms of post lens tear film mixing.

Results: The plot profile revealed peripheral tear film mixing behind the plate but not centrally. This mixing happened after 10 blinks in the 10mm set-up and 30 blinks in the 5mm set-up. This area did not change after 100 blinks. Tear film under the disk was completely mixed after 26.6 ±5.9 blinks using the roller. Based on a mean blink rate of 15 blinks/min. the tear film would consequently mix after 1:46 min. Lens twisting or combination of all did not remarkable improved the effect of tear film exchange behind the lens.

Conclusions: Lens movement and / or rotation does not appear to have a remarkable effect on post lens tear film mixing but the pumping effect does.

ANALYSIS OF TH17-ASSOCIATED CYTOKINES AND CLINICAL CORRELATIONS IN PATIENTS WITH DRY EYE DISEASE.

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Purpose: To investigate the expressions of three Th17-associated cytokines, interleukin (IL)-17A, IL-6 and IL-23, in protein and mRNA levels and their correlations with ocular surface parameters in patients with dry eye disease (DED).

Methods: A total of 45 subjects were divided into Sjögren's syndrome (SS) DED group, non-Sjögren's syndrome (non-SS) DED group and control group. Ocular surface disease index (OSDI) was self-answered and clinical tests including tear-film breakup time (BUT), Schirmer*I*test, cornea fluorescein staining (CFS) were performed. The conjunctival mRNA expressions of IL-17A, IL-6 and IL-23 were investigated by real-time polymerase chain reaction and the levels of protein in tears were measured by mutiplex bead analysis. The correlations between the expressions of three cytokines and ocular surface parameters were analyzed.

Results: The expressions of IL-17A and IL-6 in protein and mRNA levels were both significantly increased in the DED group comparing to the control group ($P<0.05$), and also higher in SS group comparing to the non-SS group ($P<0.05$). Moreover, the expressions of IL-17A and IL-6 highly correlated with BUT, Schirmer test and CFS (all $P<0.05$, R values over 0.8), and moderately correlated with OSDI (all $P<0.05$, R values range from 0.5-0.8). Despite the expression of IL-23 in protein and mRNA levels was significantly increased in the DED group ($P<0.05$), there was no significant difference found between the expressions of IL-23 in SS group and non-SS group ($P>0.05$) and no correlation found between the expression of IL-23 and any ocular surface parameter ($P>0.05$).

Conclusions: Three Th17-associated cytokines, IL-17A, IL-6 and IL-23, play roles in the pathogenesis of DED and the expressions of IL-17A and IL-6 in ocular surface have potential to be possible diagnostic biomarkers for DED. [This study is supported by National Nature Science Foundation of China (30872813)]

EFFECTS OF AUTOLOGOUS SERUM EYE DROPS FOR THE TREATMENT OF DRY EYE SYDROME AND ASSOCIATED OCULAR SURFACE DISEASES.

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Purpose: To evaluate how standardized ocular surface tests are modulated by the use of autologous serum (AS) eye drops.

Methods: A prospective clinical study was performed in patients with Dry Eye Syndrome (DES) and associated ocular surface diseases. The standardized examination consisted of the ocular surface disease index (OSDI) questioner, tear film osmolarity (TearLab®), Schirmer's test, tear break-up time (TBUT), corneal staining with fluorescein and detection of ocular surface matrix metalloproteinase-9 (MMP-9) before and after treatment. 20% to 50% AS eye drops was the only treatment added after the initial evaluation.

Results: 58 eyes of 31 patients were included in the study. There were 24 females and 7 males with a mean age of 64 ± 10 years. Mean follow up period was 4 ± 2 months. OSDI total score improved from 62 ± 23 to 43 ± 25 ($p<0.001$). TBUT improved from 6 ± 4 to 8 ± 4 seconds ($p<0.001$). Corneal Staining improved from 5 ± 6 to 2 ± 4 ($p<0.001$). Tear osmolarity was analyzed separately for each eye as well as the inter eye osmolarity difference. Osmolarity improved from 314 ± 26 to 305 ± 11mOsm/L ($p=0.027$). Inter eye osmolarity difference also improved from 11 ± 9 to 5 ± 3mOsm/L ($p=0.015$). MMP-9 positivity decreased from 57% to 47% after treatment. Schirmer's was the only test without improvement or significance. No complications or adverse effects were reported during the study period.

Conclusions: Standardized ocular surface tests can be used to assess the effects of therapies targeted to treat ocular surface diseases. Corneal staining had the most significant improvement and interestingly inter eye osmolarity values were also representative of treatment response. Moreover, AS eye drops are a safe and effective treatment, which stabilizes the tear film and significantly reduce symptomatology in DES and associated ocular surface diseases.

OCULAR SURFACE AND TEAR FILM FUNCTION FOLLOWING MODIFIED HUGHES TARSOCONJUNCTIVAL FLAP PROCEDURE.

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Purpose: To evaluate the ocular surface and tear film function in patients who underwent a modified Hughes tarsoconjunctival flap for reconstruction of the lower eyelid's posterior lamella in one eye due to large malignant or semi-malignant lid tumors.

Methods: Patients who underwent a tarsoconjunctival flap procedure between 2005 and 2010 were included into the study. Data for subjective symptoms (OSDI© questionnaire), lid margin morphology, fluorescein tear film break-up time (F-BUT), vital staining, Schirmer test, impression cytology, tear film osmolarity, lipid layer interference patterns, meibography and the size of the tumor and flap were recorded and compared with the contralateral side.

Results: This clinical study comprised 18 patients, 12 were female. The median age of the patients was 72 (49-93) years at the time of surgery and 77 (51-97) years at the time of evaluation. The median follow-up was 34 (9-69) months. There was a statistically significant difference between the surgically treated versus the untreated side in terms of a reduction of meibomian glands, increased lid margin abnormalities and a higher fluorescein staining of the cornea. In comparison the median OSDI© score was higher and the median F-BUT was shorter in the treated eye.

Conclusion: The Hughes tarsoconjunctival flap leads to a favorable cosmetic and functional outcome. Nevertheless, this reconstruction of the lower eyelid's posterior lamella affects the ocular surface and tear film function in the treated eyes. [There are no funding sources to declare. There are no conflicts of interest.]

DYNAMIC INSTABILITY – A PATHWAY FOR NUCLEAR TRANSPORT OF ADENOVIRUS.

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Human adenoviruses within species D (HAdV-D) cause epidemic keratoconjunctivitis (EKC), manifest by severe, acute, ocular surface inflammation, and in up to one-third of infected patients a chronic, relapsing, stromal keratitis. We have earlier shown that human adenovirus type D37 (HAdV-D37) uses a lipid raft mediated caveolin-1 pathway to infect human corneal fibroblasts (HCF). Dynamin 2 was originally identified as a microtubule binding protein, and regulates the stability of microtubules. Dynamin 2 is also associated with fission and endocytosis of various endocytic vesicles, and has been shown to be important to the entry of viruses. Remarkably, dynamin 2 knock down in HCF increases entry of HAdV-D37 by 4-fold, while overexpression of dynamin 2 reduces entry by 50%. In contrast, in tert-immortalized corneal epithelial (THE) cells, dynamin 2 knock down does not alter adenoviral entry. Treatment with the endosomal acidification inhibitor, bafilomycin A1, has no effect on viral entry in either cell type, indicating that adenoviral entry in corneal epithelial cells and fibroblasts is pH independent. The actin polymerization inhibitor cytochalasin D, inhibits adenoviral entry in both HCF and THE cells. The microtubule inhibitor, nocodazole, represses viral gene expression in a dose dependent manner in HCF, but only partially inhibits viral entry in THE cells. In HCF, dynamin 2 knock down increases acetylated tubulin and expression of the motor protein dynein. Microtubule organizing centers (MTOCs), earlier reported to facilitate viral entry, move adjacent to nuclear membranes after dynamin 2 knock down in HCF, likely facilitating viral nuclear entry and increased replication. These studies challenge a previously reported role for dynamin 2 in viral entry, and show that dynamin 2 can negatively regulate viral entry in a cell type specific fashion.

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WHY EX-VIVO EXPANSION OF LIMBAL STEM CELLS IS NECESSARY FOR THE TREATMENT OF LIMBAL STEM CELL DEFICIENCY.

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Purpose: To present why ex-vivo expansion of limbal stem cells is necessary for the treatment of limbal stem cell deficiency (LSCD). Methods. 152 patients (77.6% males), mean age 46.5 ± 14.6 (14 to 80) years - suffering from LSCD secondary to ocular burn were treated with departments in Italy. Patients had unilateral (86.6%) or bilateral (13.4%) burn. The mean follow-up was 8.4 ± 2.5 (5,1 to 14.5) years. Stem cells were obtained from a 2X2 mm limbal biopsy and cultivated on a feeder layer of lethally irradiated 3T3-J2 cells and a fibrin substrate.

Results: Success was attained in 66.5% of the patients at 1-year follow-up. Twelve eyes scored as failure were re-grafted. Nine/12 of these eyes regenerated a normal epithelium after re-grafting. Thus, the final clinical outcome was scored as success in 76.6%. Cultures containing >3.0% of p63bright holoclone-forming stem cells allowed corneal regeneration in nearly 80% of patients. Failures occurred within the first year, whilst restored eyes remained stable overtime, up to 10 years follow-up.

Conclusions: Autologous ex-vivo expansion of limbal stem cells is a new procedure that holds out fresh possibilities for the treatment of LSCD. This procedure has a very low risk for the donor eye and allows repeating the biopsy in case of need. The cells can be stored frozen thus permitting to schedule the surgery and banking. It allows also treating bilateral diseases when there is a spared limbal area, even small. A defined number of stem cells is necessary to assure a good clinical result and p63 expression (p63bright cells) correlates well with the number of stem cells in the culture: based on these data, only cultures possessing more than 3.5% of p63bright cells are currently used to prepare grafts. The handiness and ease of long-distance transportation of the fibrin-cultured epithelial sheets suggest that this method can now be widely applied.

CRISPR/CAS9: EDITING THE MAMMALIAN GENOME *IN VIVO*.

Fei Ann Ran, The Broad Institute, Cambridge, MA.

The ability to precisely manipulate the genome can transform both basic science research and therapeutic development. Cas9, a programmable DNA nuclease from the bacterial CRISPR/Cas system, has emerged as a versatile tool for facilitating targeted genome and epigenome modification in eukaryotes. For *in vivo* gene editing, Cas9 and its guide RNA can be delivered to tissues of interest via viral vectors. We have identified a small Cas9 nuclease from *Staphylococcus aureus* and its associated RNA components that can be packaged into a single adeno-associated virus (AAV) vector. This system can effectively and precisely modify genes in specific tissues in adult animals, opening up new possibilities for *in vivo* therapeutic gene editing.

NEW ADVANCES IN THE UNDERSTANDING OF THE DEFINITION, CLASSIFICATION AND EPIDEMIOLOGY OF CONTACT LENS DISCOMFORT.

Rachel Redfern. The University of Houston, College of Optometry, The Ocular Surface Institute

In 2013, The Tear Film and Ocular Surface Society (TFOS) published the International Workshop on Contact Lens Discomfort (CLD) that included various subcommittees including the CLD definition and classification report and the CLD epidemiology report which will be reviewed in this presentation. The definition and classification subcommittee defined CLD, terminology associated with the

definition, and various contact lens related (e.g. material, design, fit and wear and lens care) and environmental factors (e.g. inherent and modifiable patient factors and ocular and external environment factors) associated with CLD. The report also described five stages of progression of CLD that eventually leads to permanent contact lens drop out. Unfortunately there are still many challenges in understanding CLD epidemiology including that lack of correlation between signs and symptoms and few validated instrumentation. This presentation will discuss the clinical context of CLD (symptoms and signs and association with dry eye), frequency and methods of assessment of CLD, factors associated with CLD, the quality of life and financial burden associated with CLD. Further, the impact and new advances of these two reports (CLD definition/classification and CLD epidemiology) will be examined by determining the number of citations and by performing a systematic literature review since their publication in October 2013. The presentation will also discuss areas of conflict and future studies needed to advance our understanding of the definition, classification and epidemiology of CLD.

SEX, TEARS AND CONTACT LENSES.

Kathryn Richdale,[1] Cecilia Chao,[1,2] Moneisha Gokhale, [2,3] Kim Duong,[1] Michele Madigan,[2] Isabelle Jalbert,[2] Blanka Golebiowski,[2] Mark Willcox[2.] State University of New York Optometry (SUNY),[1] School of Optometry and Vision Science, University of New South Wales (UNSW),[2] Deakin Optometry, Deakin University, Australia[3]

Purpose: There are known sex differences with dry eye/contact lens (CL) discomfort (females higher), and risk of CL related corneal infiltrative events (males higher). CL wear and sex may have an effect on ocular inflammatory modulators. We conducted a secondary analysis to explore differences in tear cytokine concentrations between CL wearers and non-CL wearers, and males and females.

Methods: Basal tears were collected from 137 subjects aged 18-49 years across 4 studies at the SUNY (n=68) and 1 study at UNSW (n=69). All tears were analysed using multiplex assays (Bio Rad Labs). Generalized linear models, with the best fit based on Akaike's Information Criterion, were used to analyze the concentration of tear cytokines evaluated in all studies (IL-6, IL-10, TNF-a) by sex, CL wear and study.

Results: No subjects from SUNY and 11 subjects from UNSW were excluded due to unrecorded CL history (n=7), gas permeable lens wear (n=3) or extended wear (n=1). There were 41 males (CL:NCL 27:14) and 85 females (CL:NCL 68:17), with mean age of 37±7 years. Cytokine levels across the 5 studies were significantly different ($p<0.001$) and the effect of studies were included in all models. For IL-10, sex was not a significant factor, but NCL wearers had 57% higher concentrations than CL wearers (91pg/ml, adjusted 95% CI: 64-117pg/ml; 58pg/ml, adj95%CI: 47-68pg/ml, p=0.02). The concentration of TNF-α was 18% higher in males (265pg/ml, adj95%CI: 225-304pg/ml) than females (225pg/ml, adj95%CI: 198-253pg/ml) and this approached statistical significance (p=0.08), but there was no significant difference with CL wear (p=0.4). There were no effects of CL wear or sex on IL-6 concentration (all p>0.4).

Conclusions: This secondary analysis suggests that CL and sex differences may differentially affect certain inflammatory tear mediators. Future studies should consider potential sex and CL effects.

Support: Blackmores Limited (UNSW), NEI-T35 (SUNY)

EFFECTS OF CONTACT LENS WEARING ON TEAR FILM AND OCULAR SURFACE OF PRESBYOPES POPULATION.

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Purpose: To assess the effect of daily disposable contact lens (CL) on tear film and the ocular surface in a presbyopic population.

Methods: Seventeen presbyopic CL neophytes participated in this study. All of them were fitted Biotrue® ONEday For Presbyopia (nesofilcon A, 78% water content, Bausch & Lomb) CL. Tear meniscus height (TMH), non-invasive tear break-up time (NIKBUT), conjunctival and limbal redness were performed with Keratograph 5M (K5M; Oculus Optikgeräte GmbH, Wetzlar, Germany) before CL insertion, 20 minutes after and 8 hours after multifocal CL wear. In addition, the tear film osmolarity (TFO) was performed with TearLab (TearLab; TearLab Corporation, San Diego, CA). All the measurements were taken for the right eye only.

Results: The age of the participants was 53.9 ± 7.5 years. There was no statistically significant difference in NIKBUT and TFO (p>0,005). Regarding TMH, there was a statistically significant reduction at baseline, 20 minutes and 8 hours of wear (p<0,005). There was a statistically significant increase in nasal, temporal and total conjunctival redness at baseline and 8 hours (p<0,005). Furthermore, limbal redness showed a statistically significant increase at baseline and without CL after 8 hours of wear (p<0,005).

Conclusions: This study showed how CL alters various parameters of the tear film and the ocular surface of presbyopic population which could affect the comfort of the CL. [This study was supported by the EDEN project (642760; MSCA-ITN-2014-EJD: Horizon 2020), granted by the European Commission.]

IMPACT ON THE OCULAR SURFACE OF A NEW DAILY HYDROGEL CONTACT LENS WITH HIGH WATER CONTENT.

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Purpose: To asses the impact on the ocular surface of a new daily hydrogel contact lens with high water content (CL), and to compare the results with two silicone hydrogel lenses of lower water content rates.

Methods: The hydrogel CL fitted and analysed in this study was made of nesofilcon A. The silicone hydrogel lenses were made of delefilcon A and stenfilcon A. CL thickness was measured to assess material stability during daily wear, and ocular surface parameters such as tear film osmolarity (TFO), tear meniscus area (TMA) and central corneal thickness (CCT) were also assessed. Finally, optical quality was analysed for all cases by means of wavefront aberrations. Results: The nesofilcon A was shown to be the thinnest lens ($p<0.001$), while no differences in lens thickness were found between the two silicone hydrogel lenses (p=0.495). No significant differences were found in TFO, TMA, CCT or corneal aberrations, both as a function of the lens measured and the time of use (p>0.05).

Conclusion: In spite of having the thinnest lens and the highest water content, this new hydrogel does not significantly impact on tear film and ocular surface after one day of use in first time users.

[This study was supported by UV-INV-PRECOMP14-206161 entitled "BIOMARKERS TRENDS FOR EARLY DIAGNOSIS OF DRY EYE DISEASE]

LACRITIN C-TERMINAL PROMOTION OF OCULAR SURFACE HEALTH, CORNEAL NERVE ACTIVATION AND TEARING.

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San Francisco, CA [4]Department of Cell and Tissue Biology, UCSF School of Dentistry, San Francisco, CA[5]Department of Integrated Science and Technology, James Madison University, Harrisonburg VA
Purpose: Lacritin lacking C-terminal 25 amino acids (C-25) is inactive. Here we ask whether the C-terminus is necessary or sufficient for lacritin activity.
Methods: HCET cells were stressed overnight with interferon gamma and then for 15 min with TNF-alpha in the presence of C-25, lacritin, or lacritin C-terminal synthetic peptides N-94 (lacking 94 N-terminal amino acids) or N-94/C-6 (also lacking 6 C-terminal amino acids) followed by immunostaining for FOXO3. Normal rats were topically treated with C-25, lacritin or N-94 followed by extracellular recording of single trigeminal ganglion neurons that were responsive to slight cooling (<1° C) and ocular surface drying, and thus were likely decorated with TRPM8. Specificity of cell targeting was tested by inclusion of inhibitory single chain anti-3-O-sulfated heparan sulfate antibody HS4C3 vs negative control MPB49. Dry eye Aire-deficient mice (6 wks) were treated three times daily for two weeks with vehicle (PBS), lacritin, N-94 or N-94/C-6.
Results: N-94 and N-94/C-6 restored HCET health at a level equivalent to lacritin. Ocular instillation for 1 hr with lacritin and N-94, but not C-25, augmented the dry response by ~25% vs the pre-lacritin or pre–N-94 level. This benefit was lost following an artificial tear wash, or by prior incubation with HS4C3 that blocks lacritin targeting of its coreceptor syndecan-1. In Aire KO mice, topical application of N-94, N-94/C-6 and lacritin improved tear secretion, with significant sex differences noted between treatments.
Conclusions: The lacritin C-terminus is sufficient for promotion of ocular cell health, increased corneal nerve activity and tearing. G.W. Laurie: F; TearSolutions Inc. P; UVa Patent Foundation

SIMPLE LIMBAL EPITHELIAL TRANSPLANTATION- A WAY FORWARD.

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Purpose: This study describes the long-term clinical outcomes of autologous simple limbal epithelial transplantation (SLET Design: This was a single-center prospective interventional cases series. Participants: The study included 125 patients, 65 adults and 60 children, who developed unilateral limbal stem cell deficiency after suffering ocular surface burns and underwent SLET between 2010 and 2014.
Methods: A 1-clock hour limbal biopsy was obtained from the unaffected eye. At the same sitting, the recipient eye was surgically prepared and the donor tissue was divided into small pieces and transplanted using an amniotic membrane scaffold with fibrin glue. Main Outcome Measures: The diagnosis and outcome in every case was validated by five independent masked assessors. The primary outcome measure was restoration of a completely epithelized, stable, and avascular corneal surface. The secondary outcome measure was improvement in visual acuity. Complications, risk factors for failure, and immunohistochemistry analysis of corneas that underwent SLET also were described.
Results: At a median postoperative follow-up of 1.5 years (range, 1 - 4 years), 95 of 125 eyes (76%, 95% confidence interval, 68.5% - 83.5%) maintained a successful outcome. Kaplan-Meier analysis revealed a comparable survival probability at 1 year of 80% in adults and 72% in children ($P = 0.304$). Two-line improvement in visual acuity was seen in 75.2%, and 67% of successful cases attained 20/60 or better vision ($P < 0.0001$). Progressive conjunctivalization occurred in 18.4% of eyes. The clinical factors associated with failure were identified as acid injury, severe symblepharon, SLET combined with keratoplasty, and postoperative loss of transplants ($P \leq 0.0075$). Success rates were comparable among faculty and trainees ($P = 0.71$).
Immunohistochemistry revealed successful regeneration of normal corneal epithelium ($CK3^+/12^+$) without admixture of conjunctival cells ($Muc5AC^-/CK19^-$) and replenishment of the limbal stem cell ($\Delta Np63a^+/ABCG2^+$) reserve.
Conclusions: Autologous SLET is an effective, reliable and replicable technique for long-lasting corneal regeneration and vision restoration in unilateral chronic ocular surface burns. Works equally well in children as well as in adults and it eliminates the need for cGMP laboratory.

UPPER AND LOWER CONJUNCTIVAL FORNIX DEPTH IN HEALTHY WHITE CAUCASIAN EYES: A METHOD OF OBJECTIVE ASSESSMENT.

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Purpose: Evaluating anti-scarring therapies requires objective assessment of scarring, and knowledge of normal fornix anatomy. Measurement of conjunctival scarring has focused on inferior fornix shortening, whilst reduction in superior fornix depth (FD) is often overlooked. There is data on normal FD in South Asians, but no studies investigating normal conjunctival FD in White Caucasians. We designed a custom- made fornix depth measurer (FDM) for objective measurement of upper and lower conjunctival FD. The purpose of this study was to evaluate intra- and inter-observer variability, and to establish a reference for normal conjunctival FD measurements in an ethnically White Caucasian population.
Methods: Prospective epidemiologic cross-sectional study evaluating conjunctival FD in 252 clinically normal White Caucasian participants aged 20 to 80 was undertaken. Paired observers evaluated inter-and intra-observer variability. Data was analysed using Bland-Altman plots and analysis of variance.
Results: For White Caucasian subjects, mean upper and lower conjunctival fornix depths were 15.6mm (95% CI, 12.5 – 18.8) and 10.9mm (95% CI, 8.0 – 13.7) respectively. Females have smaller FDs than males (mean upper FD 15.3mm ± 1.6 females, 16.2mm ± 1.4 males $p < 0.001$; mean lower FD 10.6mm ± 1.3 females, 11.3mm ± 1.4 males, $p<0.001$). There was a progressive decline in FD with age (upper fornix depth 16.3mm ± 1.2 at age 20-29, and 15.0mm ± 1.8 at age 80+ ($p = 0.04$). There was 94 -100% intra-observer and inter-observer agreement for upper and lower fornix measurements.
Conclusions: Using an alternative custom-designed FDM, central conjunctival fornix depth in White Caucasian eyes appears to be similar to data previously reported in South Asian eyes. Fornix depth measurements were repeatable and reproducible. [This research was supported by the NIHR Biomedical Research Centre at Moorfields and UCL Institute of Ophthalmology. No financial disclosures.]

HARNESSING NON-TRADITIONAL, 10-YEAR, REAL WORLD DATA TO GENERATE PATIENT INSIGHTS INTO DRY EYE DISEASE.

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Purpose: To obtain insights into patient experiences with dry eye disease (DED) from unsolicited, self-reported real world data, using technology driven data collection approaches.
Methods: Patient experiences, including dry eye symptoms, comorbid conditions, and treatment outcomes, were collected from available real-world sources, including social media. A combination of natural language processing, machine learning and manual curation techniques were used to structure, categorize and qualify patient postings into the sample for analysis. Postings were categorized based on reporting of symptom and treatment experiences relating to both DED and associated comorbid diseases/treatments. Patients were also categorized into age/gender subgroups. Only reports in the English language were included in this study.

Results: A total of 256 data sources were accessed to identify 479,303 DED reports from 137,230 patient profiles within the study period (2005–2015). 75.5% of the patients were from the US, and 24.5% from outside the US (mostly UK/Ireland). Ages ranged from 18 to >90y with a trend toward increasing social media reporting among older age groups over time. 67.2% of DED reporters were women, compared with 62.3% across all chronic diseases combined. The most frequent symptom complaints were dryness and irritation, followed by pain, redness and visual disturbances. Several comorbid conditions and medications were common among DED reporters, including anxiety and depression, which were more common among those aged <48y.
Conclusions: This novel approach to capturing patient-reported data allows us to characterize a broad range of real world patient experiences in large numbers of subjects with DED. Demographic, disease, and treatment characteristics of this real world DED population reflect known epidemiological features of DED. This study was funded by Shire Development LLC. The authors thank Ira Probodh of Excel Scientific Solutions, who provided medical writing assistance, funded by SARcode Bioscience, a fully owned company of Shire PLC.

TREATMENT FAILURES WITH PROSTHETIC REPLACEMENT OF THE OCULAR SURFACE ECOSYSTEM [PROSE] DEVICE USE.

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Purpose: The PROSE device is used as a treatment option for difficult to manage ocular surface disease and ectasia. Many prior studies have demonstrated positive treatment outcomes. The purpose of this study is to document cases of treatment failure in order to better tailor treatment and address limitations.
Methods: Respective chart review of all PROSE fits performed at our institution between 2012 - 2016. Cases of treatment failure with PROSE lens were noted and treatment courses were thoroughly reviewed.
Results: The total number of eyes treated were 125. 55 eyes had a prior diagnosis of ectasia, 67 eyes had ocular surface disease and 3 eyes had evidence of both ectasia and surface disease. The total number of eyes that failed treatment were 8. Reasons for using the lens in those who failed treatment included 5 eyes status post penetrating keratoplasty for keratoconus with decreased endothelial cell count in the grafts, 1 of which had coexistent dry eye syndrome. 2 eyes had keratoconus and Fuch's dystrophy. 1 eye had graft versus host disease. Average BCVA pre insertion was 20/40, with an average BCVA post insertion of 20/25. The average duration of lens use before discontinuation was 3.5 months. 7/8 eyes discontinued use secondary to increasing corneal edema with the device. 1/8 eyes discontinued use secondary to intractable debris accumulation on the device causing blurred vision.
Conclusions: Although PROSE is a highly successful treatment option for ectasia and ocular surface disease, corneal edema secondary to endothelial dysfunction is a potential complication that may lead to treatment failure. We also report 1 case of ocular graft versus host disease with dry eye syndrome that discontinued wear secondary to intractable debris on the surface of the lens.
There are no commercial relationships for any author.

PLASMA GELSOLIN IS PART OF THE HUMAN TEAR FILM AND PROMOTES RE-EPITHELIALIZATION OF CORNEAL WOUNDS.

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Purpose: Disorders of wound-healing characterized by impaired or delayed re-epithelialization are a serious medical problem. These conditions affect many tissues, are painful, and difficult to treat. In this study using cornea as a model, we demonstrate the importance of human plasma gelsolin (hupGSN) in re-epithelialization of wounds in order to establish a novel therapy of delayed/complicated wound-healing after epithelial injury, eye surgery or dry eye disease (DED).
Methods: Tissues of the ocular surface, related cell lines and tear fluid were analyzed by means of WB, ELISA, RT-PCR and IHC. The effect of recombinant (r)hupGSN on cell proliferation and wound-healing was analyzed *in vitro* using FACS analysis, electric cell impedance sensing and a cell migration assay. In a model of corneal wound-healing, alkali-induced corneal wounding, we analyzed the wound-healing process ex vivo in a mouse model. In addition, the effect of rhupGSN on the expression of smooth muscle actin (SMA) was analyzed by gene knock down. Results: We found that GSN is expressed in all tissues of the ocular surface studied and in tears. Exogenous application of rhupGSN to the corneal wounds accelerates significantly in ex vivo model wound-healing. The concentration of hupGSN is significantly increased in tears of patients suffering from DED. The expression of smooth muscle actin mRNA is significantly decreased after GSN gene knock down.
Conclusion: The findings reveal a pivotal role for gelsolin in corneal wound-healing mechanism. The synthesis of SMA, as an important part in the wound-healing process is regulated by GSN and seems to be a key protein of cell conversion and modulates the wound-healing effects. Therefore, it has broad implications for developing novel therapeutic strategies for treating nonhealing wounds and DED.

COMPARISON OF THREE GEL BASED TOPICAL LUBRICANTS ON TEAR FILM THICKNESS IN MODERATE AND SEVERE DRY EYE.

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Purpose: The objective of the study was to compare the effect of three gel based topical lubricants on tear film thickness (TFT) in patients with dry eye disease (DED).
Methods: Sixty patients with DED were included in this randomized, double-masked, parallel group study. They were randomized to receive either unpreserved trehalose 3% + hyaluronic acid 0.15% + carbomer (TH, Thealoz Duo Gel®, Laboratoires Thea, France), hyaluronic acid 0.2% (HA, HyloGel®, Ursapharm, Germany), or polyethylene glycol 0.4% + propylene glycol 0.3% (PP, Systane Gel Drops®, Alcon Pharma, USA) eye drops. TFT was measured using a custom-built ultrahigh-resolution optical coherence tomography (OCT) system.
Results: There was a significant difference in the time course of TFT between the three groups ($p=0.001$). Ten and 30 minutes after instillation, TFT increased significantly in all three groups. Sixty and 120 minutes after administration, a significant increase in TFT was only seen for the TH group, but not for the other products (60 min: $p<0.021$ between groups; 120 min: $p<0.037$ between groups).
Conclusions: We found significant differences in TFT after administration of the three different topical lubricants. A pronounced increase in TFT was observed in all groups 10 minutes after instillation. The combination of trehalose 3% + hyaluronic acid 0.15% offered a longer increase in TFT indicating for a longer residence time on the ocular surface compared to the other products. This research was sponsored by Laboratoires Thea, France.

DIFFERENCE IN THE FREQUENCY OF USE OF LACHRYMAL SUBSTITUTES IN PATIENTS WITH MODERATE TO SEVERE DRY EYE DISEASE.

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Purpose: To test whether topical treatment with a lachrymal substitute gel alone results in lower instillation frequency compared to the use of artificial tears during the day combined with a gel before going to bed.

Methods: 40 patients with moderate to severe dry eye disease (DED) were included in the present randomized, observer-masked, cross over study. After a washout period, patients received either Thealoz Duo® eye drops for use during the day combined with Thealoz Duo® gel before going to bed or Thealoz Duo® gel only to use PRN for one week. Then, another washout period was scheduled and patients crossed over to the other treatment group. Patients were handed out a diary to record instillation frequencies. In addition, clinical standard tests for DED, such as measurement of break up time (BUT), corneal fluorescein and conjunctival lissamine green staining, Schirmer I test and completion of the Ocular Surface Disease Index (OSDI) questionnaire were performed at the beginning and end of each study period.

Results: Mean instillation frequency was 3.1±2.6 drops/day when using eye drops and 1.9±2.2 drops/day when using the gel ($p=0.02$). A significant increase in BUT was observed with both treatment regimens (time effect: $p<0.001$). Corneal fluorescein and conjunctival lissamine green staining score significantly decreased in both groups (time effect: $p<0.001$ each). No significant changes in Schirmer I test score or OSDI were observed.

Conclusions: With both treatment regimens, a comparable improvement in BUT, corneal fluorescein and conjunctival lissamine green staining score was observed. Instillation frequency was significantly lower when using the gel compared to artificial tears. This might indicate for a longer corneal residence time of Thealoz Duo® gel caused by the increased viscosity due to the additional carbomer component of the product. This research was sponsored by Laboratoires Thea, France.

FRICTION, LUBRICATION AND WEAR: THE IMPACT OF INTERACTING OCULAR SURFACES IN RELATIVE MOTION

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Altered lubrication of interacting ocular surfaces in relative motion can result in both mechanical and biological stresses. Lubricin, or Proteoglycan 4 (PRG4), is a mucin-like glycoprotein originally discovered in synovial fluid that exists on the ocular surface, where it plays a protective role and functions as a boundary lubricant of ocular tissues and biomaterials. Lubricin has also recently demonstrated biological, in addition to its classical mechanical, activity. Specifically, lubricin has demonstrated anti-inflammatory properties through binding of CD44 and toll-like receptors. Furthermore, lubricin expression is subject to both mechanical and biological regulation. As such, altered or diminished composition of lubricin in ocular tissues could lead to, and/or result from, both mechanical and biological stresses at the ocular surface.

The mechanical and biological properties of lubricin, evaluated through the use of complementary and sophisticated biomechanical, biochemical, and biophysical methods in collaboration with biologists, engineers, and clinicians will be presented. The properties and potential therapeutic applications of a newly available, clinical grade, full-length recombinant human lubricin (rhPRG4) will also be discussed. Mechanobiological coupling is common in human physiology, and both mechanical and biological homeostasis is necessary for ocular surface health. Future studies in the area of friction, lubrication and wear of the ocular surface should continue to recognize both the mechanical and biological aspects of ocular surface health, as well as in potential dry eye disease initiation, progression, and/or treatment.

[TA Schmidt has received consulting fees from Lubris BioPharma and Johnson & Johnson Vision Care, owns stock in Lubris Biopharma, and holds patents related to the use of recombinant human proteoglycan 4 (rhPRG4). This work was supported by grants from the Natural Sciences & Engineering Research Council of Canada and the Canada Research Chairs Program, and funding from Johnson & Johnson Vision Care.]

CONTACT LENS LIPID UPTAKE AND CORRELATION TO COMFORT.

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Purpose: The objective of this assessment was to evaluate the relationship between lipid uptake and subjective comfort using four different lens materials after 1 month of daily wear.

Methods: Four monthly replacement CL materials (samfilcon A, comfilcon A, lotrafilcon B and senofilcon C) were evaluated for total lipid uptake after 1 month of daily wear. Worn contact lenses were collected and analyzed for cholesterol and cholesteryl esters via liquid chromatography-mass spectrometry analytical methodology. A randomized, 4-arm parallel group one month dispensing clinical study (~130/ lens) was conducted in which subjective comfort data (overall comfort, lens awareness and dryness) was collected from each patient using a 5 point Likert scale questionnaire. The percentage of subjects rating of comfort attributes as excellent/very good was plotted against lipid uptake values and the correlation coefficient obtained.

Results: The average lipid uptake and 95% CI from ex-vivo analysis of worn lenses after 30 days of wear was 20.4 (± 2.31), 9.8(± 1.48), 9.0 (± 0.85) and 0.5(± 0.05) ug/lens for senofilcon C, samfilconA, comfilcon A and lotrafilcon B respectively and the % of subjects who rated overall comfort excellent/very good was 69%, 50%, 55%, 46% . Clinical measures of subjective performance were analyzed separately using Linear regression model with the ex vivo lipid uptake as the main effect. Subjective Comfort measures were statistically correlated (adjusted $r^2 = 0.85$ or higher) with the average lipid uptake.

Conclusion: While this data suggests a strong correlation between lipid uptake of the four lens materials and subjective comfort, additional analysis evaluating the correlation at the subject level using individual values of lipid uptake and the corresponding subjective comfort measures will need to be investigated in order to give better insight in determining if lipid uptake can be used as a potential predictor for contact lens performance. [The Authors are employees of JJVCI]

MEIBOMIAN GLAND AND TEAR FILM CHARACTERIZATION IN A HEALTHY UNIVERSITY POPULATION.

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Purpose: The health of the Meibomian glands (MG) is critical for the integrity of the tear film and to prevent symptoms related to dry eye and ocular discomfort. However, published literature documents discrepancies between signs and symptoms in dry eye. The aim of this study was to assess the health of the MG in a university population to gain a better understanding of the complex relationship between MG, tear film parameters and ocular discomfort.

Methods: Forty-eight healthy subjects (23 males) aged between 20 and 31 years participated in the study, conducted at the School of Optics and Optometry of Terrassa. All participants completed an Ocular Surface Disease Index (OSDI) questionnaire. In addition, participants

reported any discomfort localized at the palpebral margin. A placido-disc based corneal topographer was used to measure non-invasive break-up time (NIBUT). Tear film meniscus height and regularity was assessed with a slit-lamp (TOPCON SL-D701, 16X). The same slit-lamp with a camera attachment was used to assess the palpebral margin and to capture images of everted upper and lower eyelids, which were later analyzed with the ImageJ software to determine the area of the eyelids containing MG, recorded as MG ratio value.
Results: MG ratio was larger in the lower (median of 48.9%) than the upper (median of 38.1%) eyelid ($Z=-4.236$; $p<0.001$), without differences between males and females. Participants with palpebral margin discomfort had higher OSDI scores than asymptomatic participants (median of 27 vs 14.2; $Z=-3.386$; $p=0.001$). Palpebral margin abnormalities were associated with higher OSDI scores (median of 26.5 vs 16.4; $Z=-1.961$; $p=0.048$) and with an inferior MG ratio at the lower eyelid (median of 38.1 vs 48.5; $Z=-2.089$; $p=0.035$). No association was found between NIBUT scores, meniscus height and regularity and MG ratio.
Conclusion: The joint exploration of the MG, signs and symptoms may yield useful information on the health of the ocular surface in health and disease.

ENHANCED WOUND HEALING IN HUMAN CORNEAL EPITHELIUM IN RESPONSE TO HISTATIN-1 APPLICATION.

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Purpose: Histatin peptides are the primary wound healing agent found in human saliva. They are histidine-rich peptides that are amphipathic, anti-microbial and bind LPS. In addition, histatin-1 is expressed by human lacrimal epithelium. Previous experiments have shown that Histatin-1 can promote epithelialization in multiple tissue types. We investigated the effects of applying histatin-1 to a human corneal epithelial wound model *in vitro*.
Methods: Human corneal epithelial (HCE) cells were utilized to perform a standard scratch based wound healing assay. A confluent monolayer of HCE cells were wounded manually by scraping with a 200ul pipette tip. Cells were then exposed to different concentrations of Histatin-1 in a medium essential media containing 2% serum. Cell migration was followed for 24 hours after scraping and imaged using time-lapse microscopy. Images were analyzed using Neuro Image-J. Cell pathfinding was also assessed. Effects of Histatin-1 on cell proliferation and cell death were assessed.
Results: Our findings demonstrate that cell migration rates were increased with increasing Histatin-1 concentration. We also noted no significant change in LDH levels or MTT levels at tested levels, suggesting a non-proliferative, non-toxic mechanism for wound healing enhancement.
Conclusions: Histatin-1 peptides promote human corneal epithelial migration and wound healing *in vitro*. Future studies to investigate these findings *in vivo* will be necessary to develop therapeutic applications for Histatin peptides. This research was supported by grants from the National Eye Institute, Eversight, Fight-For-Sight, and the American Society of Cataract and Refractive Surgeons Foundation.

OCULAR SURFACE MICROBIOME IN THE POST-GENOMICS ERA.

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The composition of homeostatic ocular surface (OS) microbiota has been extensively studied over several decades using both classical microbiology and culture-independent techniques. The introduction of next generation DNA sequencing (NGS) has contributed to the discovery of much higher diversity of human microbiome, including the one at the ocular surface. Despite some controversy, most studies utilizing 16S rRNA sequencing strategy revealed that average bacterial diversity on human conjunctiva is about two hundred bacterial genera. The overall microbial density, however, is much lower than in other human niches, likely due to potent barrier function at the ocular surface. The NGS has demonstrated a polymicrobial nature of ocular infections and has uncovered dramatic changes that ocular microbial community undergoes at the onset of infectious or autoimmune disease, like bacterial keratitis and dry eye disease (DED). Such changes in diversity and prevalence of commensal species are commonly referred to as dysbiosis, a known contributing factor to multiple human pathologies. Another important discovery, the role of the gut microbiota in shaping up immune response in the ocular tissues, was made using gnobiotic mice. These studies have demonstrated the role of gut microbiota and potential contribution to autoimmune ocular diseases in mouse models. Along with unprecedented sensitivity of different NGS approaches, their utility for characterization of ocular microbial community has certain limitations and challenges. The biggest challenges stem from very low microbial density and lack of negative controls for human ocular samples. Additional errors in calculation of relative abundances are introduced by variability in 16S rRNA gene copy number and false positives, resulting from sequencing errors. The development of standard operating procedures, obligatory controls and robust bioinformatics pipelines is required prior to introduction of NGS into research arsenal and clinical practice.

EVALUATING THE EFFECT OF DRY EYE DISEASE ON CORNEAL SUB-BASAL NERVE DENSITY AND MORPHOLOGY

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Purpose: Published studies on diabetes and corneal nerves did not evaluate the tear function's effect on corneal nerves. We investigated the effect of dry eye disease on corneal sub-basal nerve density and morphology.
Methodology: Six participants with dry eye (corneal fluorescein staining grade 2 or above) and six controls were recruited. Patients were from a tertiary referral clinic in Singapore. Symptoms (SPEED), Schirmer's I test (ST), fluorescein staining, conjunctival hyperemia (CH) grading and non-invasive tear breakup times were assessed. In-vivo confocal microscopy of the corneas was undertaken by one investigator using the HRT III. Three best central images and another 3 images over the inferior whorl region were analysed using CCModule software. In the central regions, the nerve fiber density, nerve fiber length, nerve branch density, nerve tortuosity (NT) were evaluated, and the nerve fiber length (IWL) was evaluated in the inferior whorl region.
Results: The dry eye group had significantly ($p<0.05$) higher age (mean 66.2+/-8.2 years) than the controls (27.2+/-2.0). All dry eye participants but only 1/6 controls were female. As expected there was significantly higher SPEED, ST and CH scores in the dry eye group. Comparison of corneal sub-basal density and morphology between the two groups showed no differences, except NT in the dry eye group was high ($p=0.03$) and IWL shorter in the control group ($p=0.05$). If the outlying participant was excluded in the IWL analysis, the difference was significant ($p=0.01$). Corneal sensation was similar between groups.
Conclusions: The results suggest that NT and IWL are altered in patients with dry eye. Previous studies did not find an association of either age or gender with NT and IWL. In future studies comparing two groups of patients (e.g. diabetics with non-diabetics) it is crucial to objectively assess the ocular surface as a potential confounder.

OCULAR SURFACE MICROBIOME IN PATIENTS WITH DRY EYE CAUSED BY CHRONIC GRAFT-VERSUS-HOST DISEASE (CGVHD).

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Purpose: Commensal microbiota co-evolves with their hosts and can exert pathologic effects. However, pathogenic roles of mucosal microbiome in cGVHD are still unclear. This study aims to elucidate the state of microbiome on the ocular surface in patients with cGVHD.

Methods: A prospective study was performed in dry eye clinic at Keio University. Firstly, we utilized a conventional cultured method with cotton swab. 21 eyes from GVHD patients, 14 form nonGVHD patients and 7 from normal subjects. Furthermore, impression cytology (IC) was performed to conduct closer investigation into mucosal microbiome in 5 samples from each group. Variable regions 3–4 (v3-4) of the 16S rRNA gene in each sample were amplified and analyzed conjunctival microbiome.

Results: As demonstrated by the conventional cultured method, the GVHD-affected ocular surface had a total of 10 species including Staphylococcus epidermidis, Corynebacterium species and Propionibacterium acnes, whereas only few gram-positive cocci were detected in the other groups. The 16S rRNA gene in each IC sample was successfully amplified by PCR. Staphylococcus and Corynebacterium were dominant species in the GVHD-impaired ocular surface, but this was not the case with the nonGVHD or normal samples. Severe cGVHD patients detected rare population of species, which were not found in others. Principal coordinate analysis based on the UniFrac metric revealed (1) that the cGVHD-affected ocular surface had different genera of microbiota from the other samples and that (2) the diversity of ocular surface microbiota has a propensity to increase in the case where the subjects are female and/or 50 years of age or younger.

Conclusion: Different patterns and pathogenic changes of microbiome on the ocular surface might be involved in the development of ocular cGVHD. [Authors thank to Japanese Ministry of Education, Science, Sports and Culture for the grant support #26462668.]

LONG-TERM HOMEOSTASIS IN AN *IN VITRO* EPITHELIAL STEM CELL NICHE MODEL.

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Purpose: We have previously reported a protocol to maintain primary limbal epithelial sheets for over 6 months. We further sought to determine if epithelial cells cultured as a stratified layer with proper cell polarity can maintain homeostasis *in vitro* for over one year.

Methods: Human limbal epithelial sheets were maintained in DMEM/F12 based medium containing fetal bovine serum (4%), human FGF7, Y27632, insulin, hydrocortisone, tri-iodo-thyronine and isoproterenol. Immunohistochemistry was done for various epithelial markers, and cell proliferation following wound-healing assays were observed by Fluorescent ubiquitination-based cell cycle indicator (Fucci) and EdU pulse labeling.

Results: Human limbal epithelial cells continued to shed cells daily for 1 year. Cell turnover rate and the expression pattern of the stem cell marker, KRT15 reached a steady state within 3 months, at which point densely packed clusters of KRT15 positive cells associated with dendritic melanocytes became apparent. Fluorescent ubiquitination-based cell cycle indicator (Fucci) and EdU pulse labeling showed that cells initially migrated into the wound, followed by robust proliferation.

Conclusion: Steady state cultures showed integrated wound healing. This novel epithelial layer culture technique is a powerful tool in the study of human epithelial stem cell homeostasis and wound healing.

CASE-CONTROL STUDY OF CORNEAL FINDINGS IN DIABETIC AND NONDIABETIC PATIENTS.

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Purpose: Diabetic keratopathy, a major ocular complication of diabetes mellitus, impairs tear secretion and corneal sensation. However, reports of diabetic keratopathy in the literature are relatively few. The aim of this study is to compare corneal findings in diabetic and nondiabetic patients in a case control study.

Methods: We examined Schirmer test, corneal sensation by Cochet-Bonnet esthesiometer and corneal endothelial cell density of age-matched and sex-matched diabetic and nondiabetic eyes (n=104 each) that underwent vitrectomy between February 2014 and February 2016 at our hospital. We excluded eyes using glaucoma eye drops, or contact lenses. Eyes diagnosed with dry eye, with an abnormal ocular surface, or a history of ocular surgery within 6 months were also excluded.

Results: The average tear secretion volume was low in diabetic eyes (10.1 ± 6.3mm vs 12.5 ± 9.4mm, p=0.04), and corneal sensation was significantly lower in diabetic eyes (44.9± 17.0mm vs 53.7 ± 8.0mm, p<0.01). Corneal endothelial cell density was not different between diabetic and nondiabetic eyes (2696 ± 373/mm^2 vs 2623 ± 327/mm^2, p=0.12). The average diabetes disease duration of diabetic patients in this study was 12.2 ± 8.2 years, and the average HbA1c value before vitrectomy was 7.0 ± 1.1%.

Conclusion: Diabetic eyes showed significantly decreased tear secretion and corneal sensation. Despite normal findings in slit lamp microscopy, the diabetic ocular surface may have subclinical abnormalities. [Commercial relationship: none]

OVERVIEW OF CLINICAL EFFICACY AND SAFETY OF LIFITEGRAST OPHTHALMIC SOLUTION 5.0% FOR TREATMENT OF DRY EYE DISEASE.

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Purpose: To evaluate the combined evidence from five randomized controlled trials of the efficacy/safety of lifitegrast ophthalmic solution 5.0% (LIF) vs placebo (PBO) in subjects with dry eye disease (DED).

Methods: Adults with DED were randomized to LIF or PBO (1:1) in four 12-week efficacy/safety studies (phase 2 n=116; OPUS-1=588; OPUS-2=718; OPUS-3=711) and a 1-year safety study (SONATA n=331). We evaluated change from baseline to day 84 in DED signs: inferior corneal staining score (ICSS), and symptoms: eye dryness score (EDS, visual analog scale [VAS], 0–100) and visual-related function subscale of a symptom scale, across the 12-week studies. Pooled safety data from all five trials were analyzed.

Results: LIF improved ICSS vs PBO in the phase 2 study (secondary endpoint; treatment effect 0.35, nominal P=0.0209) and OPUS-1 (co-primary; 0.24, P=0.0007). The OPUS-1 co-primary symptom endpoint of visual-related function subscale did not achieve statistical significance. LIF reduced EDS (VAS) vs placebo in OPUS-2 (co-primary; 12.61, P<0.0001) and OPUS-3 (primary; 7.16, P=0.0007). The OPUS-2 co-primary sign endpoint of ICSS did not achieve statistical significance. In pooled safety analysis (LIF n=1287, PBO=1177; total exposure in person-years, LIF=415.65, PBO=332.15), adverse events were mostly mild/moderate in severity;

there were no serious ocular TEAEs and withdrawals due to TEAEs were infrequent.
Conclusions: LIF improved signs and symptoms of DED in adults with DED across the four 12-week clinical studies. LIF appeared to be well tolerated in all studies with no serious ocular TEAEs. Based on overall findings from all the trials, LIF shows promise as a new treatment option for signs and symptoms of DED. The studies in this abstract were sponsored by SARcode Bioscience (now a wholly owned subsidiary of Shire, PLC) and Shire Development LLC. The authors thank Ira Probodh of Excel Scientific Solutions, who provided medical writing assistance, funded by SARcode Bioscience, a fully owned company of Shire, PLC.

DO CHANGES IN MEIBOMIAN AND TEAR LIPIDS CORRELATE WITH COMFORT IN CONTACT LENS WEARERS.

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Purpose: To evaluate the correlation and predictive ability of meibomian gland morphological changes and tear evaporation in contact lens discomfort.
Methods: A cross sectional study was performed on thirty contact lens (CL) wearers. Subjects were asked to complete contact lens dry eye questionnaire (CLDEQ-8), clinical changes in meibomian glands (MG) secretions and tear evaporation rates were evaluated. Correlation coefficients and area under the curve (AUC) statistics, sensitivity and specificity values from receiver operating characteristic (ROC) curves were analysed to evaluate the predictability of the signs in discriminating symptoms of contact lens discomfort (CLD).
Results: Subjects were classified as symptomatic (n=13) or asymptomatic (n=17) CL wearers. Median ± IQR (correlation coefficient) for meibomian foam, secretion's expressibility, quality and volume were 2 ± 1 (r=0.592, 0.574, 0.561, 0.543, respectively; $p < 0.05$) for symptomatics and 0 ± 0 for asymptomatics who had no significant correlations with discomfort. Median ± IQR for tear evaporation rate with and without contact lens were 121 ± 25 and 107 ± 48 $gm^{-2}h$ in symptomatics, and 99 ± 16 and 71 ± 24 $gm^{-2}h$ in asymptomatics respectively. Tear evaporation without contact lens wear alone showed was significantly correlated with comfort scores in symptomatic (r=0.517, p=0.033) but not asymptomatic lens wearers. AUC scores for MG expressed secretions quality (sensitivity=1.000, specificity=0.929; p values=0.00), foam (1.000, 0.929; 0.00), volume (0.938, 0.929; 0.00) and expressibility (0.938, 0.929; 0.00) were 0.969, 0.944, 0.935, 0.933 respectively and for tear evaporation rate without (0.875, 0.643; 0.007) and with (0.813, 0.714; 0.009) contact lenses were 0.788, 0.779 respectively.
Conclusions: This study has shown that clinical signs of MG secretions and tear evaporation significantly correlate with CLD symptoms. Meibomian and tear film signs that are influenced by meibomian and tear lipids are able to discriminate symptoms of CLD. Partly supported by Cornea and Contact Lens Society of Australia.

PHYSIOCHEMICAL PROPERTIES OF HYALURONIC ACID-BASED EYE DROPS.

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Purpose: Hyaluronic acid (HA) solutions are commonly prescribed for dry eye. HA polymer size may have a large range, with higher molecular weights considered more desirable for their ability to build viscosity at low concentration, and decreased likelihood of inflammatory reactions. This project assessed the molecular weight (MW) of the HA in commercial HA formulations, along with rheological performance as a predictor of clinical efficacy.
Methods: MW and polydispersion index (PDI) of 16 commercial eye drops were measured using a light-scattering method on a Agilent Technologies 1200 series HPLC with a Dawn Heleos-II MALS detector and an Optilab rex RI detector (both from Wyatt Technology). Rheological performance was measured on an DHR-3 rheometer (TA Instruments), with shear rate varied from 1 to 10,000 reciprocal seconds. To further characterize formulations containing polymers in addition to HA, molecular weight analysis was repeated after hyaluronidase digestion.
Results: MW ranged from 204 to 2026 kDa, with PDI from 1.05 to 4.94. Following hyaluronidase treatment, some products decreased and others increased overall MW, indicating that HA was the larger or smaller (respectively) polymer in a mixed-polymer formulation. 5 of the 16 formulations contained relatively low (<500 kDa) MW HA, and 3 had very high (>1000 kDa) MW HA. All formulations exhibited shear-thinning, with viscosity being a function of both MW and concentration. 3 formulations had low-shear viscosity above 40 cPs, and 7 had low-shear viscosity below 10 cPs.
Conclusions: MW of HA in eye drop formulations varies substantially, and is likely to impact clinical performance. Lower PDI is indicative of polymer purity. Low-shear viscosity of 10-40 cPs is associated with longer ocular retention time and minimal blur. This optimum range may be obtained using a relatively low concentration of high-MW HA, enhanced by the inclusion of an additional synergistic polymer. PA Simmons, H Wang, and T Wang are employees of Allergan plc, USA. P Aragona has served as a consultant for Allergan plc, USA.

HUMAN INDUCED PLURIPOTENT STEM CELLS.

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Tissue engineering and stem cells are a potential approach for the replacement of degenerated cells of the eye and to study ophthalmic diseases. Tissue specific stem cells and human pluripotent stem cells (hPSC), including human induced pluripotent stem cells (hiPSC) both have their own benefits and drawbacks. For ocular surface defects, shortage of donated human corneas for transplantation has driven the search of novel cell sources including hiPSC. In healthy cornea, epithelium is renewed by limbal stem cells (LSCs) and LSCs transplantation has been used to treat limbal stem cell deficiency (LSCD). However, this is only possible if enough healthy limbal tissue is available. Human iPSC provide unique opportunities for differentiation of limbal and corneal cells. We and others have previously demonstrated that hPSCs provide new opportunities for corneal epithelium regeneration. In addition, field is moving towards regeneration of corneal stromal and endothelial layers as well.
This presentation will give a critical overview of current state of the hiPSC research in ophthalmology and special demands regarding cells used in these applications highlighting experience we have gained from hPSC based research in ocular surface regeneration.

THE NORWEGIAN OSMOLARITY PROJECT.

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Purpose: To determine the overall prevalence of tear film hyperosmolarity with or without symptoms of dry eye disease in a national study of optometry patients.
Methods: 391 subjects (256 females, age 18 years and above) coming for a scheduled regular eye examination were recruited consecutively at 22 optometry clinics across Norway (subjects coming for a dry eye examination were excluded from this study). Bilateral tear film osmolarity, with a measurement in either eye ≥ 308 mOsm/L defined as hyperosmolar and symptoms using the OSDI questionnaire, were evaluated. Use of contact lenses at the time of the visit was recorded.
Results: 47.3% of all subjects had hyperosmolar tear film, indicating a

loss of homeostatic control of the lacrimal system. Of these hyperosmolar subjects 51.9% reported symptoms. Conversely 45.3% of all subjects reported symptoms, of these 54.2% had hyperosmolar tear film. 24.6% of all subjects had hyperosmolar tear film AND symptoms, and finally 32.0% of all subjects had normal tear film AND no symptoms. Of interest, of the 177 subjects aged below 50 years, 42.4% had hyperosmolar tear film, and of these 46.7% reported symptoms. 19.8% of the subjects aged below 50 years had hyperosmolar tear film AND symptoms, whereas 31.1% had normal tear film AND no symptoms. Of 214 subjects aged 50 years and above, 51.4% had hyperosmolar tear film and of these 55.5% reported symptoms. 22.0% of all subjects wore contact lenses at the evaluation.
Conclusion: In this study of 391 subjects at centers across Norway, 47.3% had hyperosmolar tear film but only 51.9% of these had symptoms, reflecting the lack of correlation between signs and symptoms in dry eye disease. The limited difference in findings between the group of younger (age below 50 years) and the group of older subjects (50 years and above) indicates that age plays a minor role as overall risk factor for tear film hyperosmolarity and for symptoms.
(This study was supported by a research grant from AMWO ApS)

BLOOD, SWEAT AND TEARS: HUMAN SOCIAL CHEMOSIGNALING IN HEALTH AND DISEASE.

Noam Sobel, Weizmann Institute of Science, Rehovot, Israel.
Most animals communicate using social chemosignals, namely chemicals emitted by one member of the species, which then produce chemical and behavioral changes in other members of the species. Such communication is prevalent in insects and terrestrial mammals, and mounting evidence implies that it is also common in human behavior, albeit primarily at a subliminal level. Human social chemosignals are responsible for a host of effects ranging from driving menstrual synchrony in women to conveying fear across individuals. Here I will describe our findings on mechanisms of human chemosignaling in both health and disease. I will concentrate on the possibility of a social chemosignal in human emotional tears. Based on these findings I will argue that in contrast to common notions, humans are highly olfactory animals.

VERNAL KERATOCONJUNCTIVITIS – THERAPEUTIC ADVANCES OF AN ENIGMATIC DISEASE.

Avi Solomon, MD, Department of Ophthalmology, Hadassah Medical Center, Jerusalem, Israel
Vernal keratoconjunctivitis (VKC) is a severe bilateral chronic allergic inflammatory disease of the ocular surface, with a yet unknown etiology. The disease affects children, mainly boys, and may last for many years, usually resolving at puberty. In its moderate form it may be limited to the tarsal conjunctiva and the limbus. Constant ocular irritation, manifested by itching, tearing, redness and photophobia, can impair the quality of life of these children. Corneal involvement in the more severe cases may lead to potentially sight threatening complications such as shield ulcers and plaques, infectious keratitis, keratoconus, scarring and limbal stem cell deficiency, resulting in permanent decrease or loss of vision.
Initial stimulation by air-borne allergens, coupled with as yet undefined genetic predisposition, lead to a vicious cycle of inflammatory responses, augmented by a set of reciprocal interactions between cells and mediators of the entire ocular surface. These include mainly the Th2 lymphocytes, mast cells, eosinophils, ocular surface epithelia and fibroblasts. Inflammatory mediators participating in these responses include histamine, the Th2 cytokines, leukotrienes, chemokines, adhesion molecules, matrix metalloproteinases, growth factors, neural mediators and eosinophil derived cationic proteins, which cause the final damage to the surface epithelia. Circulating sex hormone levels in different phases of the disease were also implicated in the pathogenesis and activity of VKC. Advanced proteomic analysis of VKC tear samples have recently found additional players such as albumin, transferrin, hemopexin, alpha-1 antitrypsin, and the TGF-beta / Smad pathway.
Until recently the management of VKC had been frustrating. Topical anti-histamines and mast cell stabilizers were largely ineffective, whereas topical corticosteroids gave partial and temporary control of inflammation, limited by their potential side effects. The most dramatic advance in the management of VKC was the recent introduction of the topical calcineurin inhibitors (TCIs): Cyclosporine A (CSA) and Tacrolimus. While topical CSA therapy is limited by poor bio-availability and solubility, and problems with its carrier solvent causing ocular irritation and poor compliance, the recent introduction of topical Tacrolimus was a major breakthrough in the management of VKC. Tacrolimus, a 50-fold more potent inhibitor of IL-2 synthesis compared to CSA, was found to dramatically alter the course of the disease, with complete resolution of signs and symptoms, and even complete resolution of the tarsal papillae.

RELATIONSHIP BETWEEN CHEMOTHERAPY-INDUCED LACRIMAL DRAINAGE OBSTRUCTION AND OBSTRUCTIVE MEIBOMIAN GLAND DYSFUNCTION.

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Purpose: To investigate the relationship between chemotherapy-induced lacrimal drainage obstruction (LDO) and obstructive meibomian gland dysfunction (MGD).
Methods: Eleven patients, who complained of epiphora and were diagnosed of chemotherapy-induced LDO, were enrolled as the LDO group. Other ten patients, who had chemotherapy, but did not have epiphora, were used as the control group. Upper and lower meibomian gland losses were evaluated using a meibography and tear film lipid layer thickness was measured using an interferometer. The mean values of right and left eyes in each patient were used to compare parameters between the two groups.
Results: The LDO group showed higher mean values of meibomian gland loss in the both upper (43.6 $\pm$ 15.5%) and lower meibomian glands (78.7 $\pm$ 16.1%) when compared with the control group (17.1 $\pm$ 7.4% and 22.6 $\pm$ 12.7%, respectively) ($P < 0.001$ and $P < 0.001$, respectively). In the LDO group, the meibomian gland loss in lower eyelids was significantly greater than that of upper eyelids ($P < 0.001$). However, there was no significant difference in the meibomian gland loss between the upper and lower eyelids in the control group ($P = 0.235$). The lipid layer thickness was significantly thinner in the LDO group (31.3 $\pm$ 13.4 nm) than in the control group (72.9 $\pm$ 22.5 nm) ($P < 0.001$).
Conclusions: All patients who had chemotherapy-induced LDO showed significant meibomian gland loss and decreased lipid layer thickness compared to patients without LDO. Chemotherapeutic agents which induce LDO could cause the obstruction of meibomian gland orifice resulting in obstructive MGD via the same pathogenesis.

EFFECT OF 3% DIQUAFOSOL SODIUM OPHTHALMIC SOLUTION ON SOFT CONTACT LENS WEARERS.

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Purpose: In our previous study, we showed that diquafosol sodium (DQS) ophthalmic solution significantly increases aqueous tear fluid in normal human eyes for more than 30 minutes (Yokoi et al. Am J

Ophthalmol, 2011). The purpose of this present study was to investigate the effect of DQS solution on eyes wearing soft contact lenses (SCLs).

Methods: This study involved 20 daily SCL wearers [13 females and 7 males (mean age: 35.6 years)]. Each subject was randomly dispensed an artificial tear (AT) solution for one eye and 3% DQS solution for the other eye. At 15-minutes post SCL wear, 1 drop of each solution was instilled in each eye and the tear meniscus radius (TMR, mm) and non-invasive tear-film break-up time (NIBUT, seconds) were evaluated via video interferometer (DR-1®, Kowa Co., Ltd., Japan) just prior to instillation (baseline), and at 5, 10, 15, 30, and 60 minutes post instillation.

Results: Changes in TMR from the baseline (AT group vs. DQS group; mean±SD) were significantly greater ($p<0.05$) in the DQS group from at 10-minutes to 60-minutes post instillation (at 10 minutes: 0.008±0.011 vs. 0.054±0.010; at 15 minutes: 0.008±0.008 vs. 0.057±0.016; at 30 minutes: 0.001±0.009 vs. 0.039±0.013; at 60 minutes: -0.009±0.007 vs. 0.037±0.013). Changes in NIBUT from the baseline (AT group vs. DQS group; mean±SD) were also significantly greater ($p<0.05$) in the DQS group (at 10 minutes: -0.04±0.46 vs. 1.60±0.48; at 15 minutes: -0.55±0.49 vs. 2.09±0.56; at 30 minutes: -0.96±0.42 vs. 0.88±0.55; at 60 minutes: -1.59±0.45 vs. 0.49±0.57).

Conclusions: The findings of this study show that 3% DQS solution can facilitate tear volume increase and improve tear-film stability for up to 60 minutes after instillation in healthy eyes wearing SCLs.

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OPTIMIZATION OF TEAR BIOMARKERS QUANTITATION BY CUSTOMIZED MULTIPLEXED MICROARRAYS.

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Purpose: Ocular surface disorders (OSD) are multifactorial diseases in which multiple factors may be working together, in concert, involving several biological processes. Therefore, screening for individual targets will give an incomplete picture of the pathological state. Antibody microarray improves the possibility of simultaneous detection and quantification of biomarkers, , revealing disease key factors and mechanisms related to complex diseases. In the present study, optimization of immunoassay parameters for a multiplexed quantification of three OSD biomarkers using customized microarray technology has been performed.

Methods: Three previously validated biomarkers for OSD (S100A6, CST4 and MMP9) were selected for the integration into customized microarray slides. The integration process included several steps: i) identification of specific capture and detection antibodies for biomarkers; ii) evaluation of cross-reactivity between antibodies; iii) determination of detection limits and dynamic range; iv) correlation of quantification with individual ELISA assays.

Results: Critical parameters for tear protein quantification on customized microarray slides were established. Detection dynamic ranges of the selected antibody pairs fulfilled the requirements for quantification in tears within a clinical relevance range. Minimal background and no crossreactivity were detected on the system. Correlation of values obtained from microarray slides and ELISA assays confirmed the use of microarray technology for determination of selected tear film proteins concentration.

Conclusions: A customized multiplexed microarray system was successfully developed and fulfilled technical requirements for the simultaneous quantification of three OSD biomarkers in tears. Microarray technology is a highly customizable open system, for multiplex expression profiling of the most important OSD-related proteins. Antibody microarrays constitute a good strategy for validation of candidate tear biomarkers, and characterization of tear film patients in clinical trials for diagnosis and monitoring of treatments.

LAST OPTION!!ROLE OF KERATOPROSTHESIS IN CHEMICAL INJURY.

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Purpose: Report the anatomical, functional outcomes of various keratoprosthesis in patients with corneal blindness due to stem cell failure secondary to chemical injury.

Methods: Retrospective chart review of all patients with bilateral chemical injury who underwent keratoprosthesis, a total of 75 eyes{MOOKP (36 eyes), Boston type 1 (16eyes) and its variant type 1 Lucia keratoprosthesis(7eyes),Lucia type 2 keratoprosthesis (12 eyes) ,Osteo Keratoprosthesis(3 eyes), Boston type 2 (1 eye)}between April 2005 to December 2015 was done.

Results: Anatomical success defined as retention of primary keratoprosthesis, functional success defined as vision better than 20/200 achieved and maintained, complications and surgical intervention post keratoprosthesis were analyzed. The mean age was 34.77 years and the mean follow-up was 30.19 months (range). Preoperative best vision in the operated eye was perception of light with or without accurate projection of rays.In 21 (28%)patients the eye that underwent keratoprosthesis was the only eye with the other eye having no perception of light. Functional success was achieved in 62/75(82.66%) eyes and maintained in 51/75(68%) eyes over the last follow-up. Anatomical success was attained in 55/75(73.33%)eyes. In 15/75 (20%) eyes, the keratoprosthesis was replaced by another device and in 7/75(9.3%) the keratoprosthesis was removed. Endophthalmitis occurred in 11/75 (14.66%) eyes. Optic carrier melts occurred in 14/75 (18.66%.) eyes.

Conclusion: Keratoprosthesis has reasonable success in visually rehabilitating bilateral corneal blind secondary to chemical injury. Optic carrier melts and glaucoma are complications that affect anatomical retention ,functional success and need to be managed early to avoid loss of vision.

ROLE OF ALLOSLET IN ACUTE CHEMICAL INJURY.

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Purpose: To analyze the outcome of allo- simple limbal epithelial transplantation (alloSLET) in eyes following acute chemical injury to achieve rapid epithelialization.

Patients and methods: Retrospective chart review of 17 eyes of 16 patients who underwent alloSLET for acute chemical injury between April 2013 and Jan 2016 was done. Patients with Grade 4 or worse Dua's classification for chemical injury, who presented within a month of the injury or with a non-healing epithelial defect since the injury despite earlier medical or surgical interventions, were included in the study. The time to epithelialization was the primary outcome measure and the best corrected visual acuity, the clinically assessed epithelial phenotype and symblepharon formation were the secondary outcome measures.

Results: The mean time to epithelialization was noted to be 22.5+ 9.14 days. A best corrected visual acuity of better than 20/120 was achieved in 13 eyes in a mean duration of 33.06 + 10.73 days following alloSLET. Corneal phenotype with complete epithelialization of the ocular surface was achieved in the immediate postoperative period in 16 of the 17 eyes (94.11%).7 eyes had a gradual failure of the allograft and 5 eyes underwent subsequent limbal autograft. Symblepharon formation involving 1-2 quadrants was noted in 3 eyes (17.64%).except 1 eye whihc required a lamellar keratoplasty for retained intrastromal like plaque none of the eyes developed corneal melting .

Conclusion: AlloSLET is a useful technique to achieve rapid epithelialization in severe chemical injuries thereby preventing the adverse effects of delayed epithelial healing. Visual rehabilitative

procedures in the chronic phase of chemical injury, in most instances following an alloSLET in the acute stage, did not require keratoplasty, lamellar or penetrating. No financial interest.

EFFECT OF MONOCULAR LENS WEAR ON OCULAR COMFORT.

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Purpose: Inter-eye correlations are widely accepted for processes like accommodation and the pupillary response. This study investigated the influence of contact lens (CL) wear on inter-eye ocular comfort over 8hrs.

Methods: Fifteen symptomatic, 15 asymptomatic CL-wearers, classified on Young's criteria (Young 2011) and comfortable wear-time, participated in this randomized, cross-over study. Participants were assessed on 3 mornings and randomized to 8hrs of a) no-CL, b) monocular or c) bilateral wear of comfilconA CLs. Study days were preceded by no-CL wear for at least 24hrs. Using partial-disclosure, participants were advised tearfilm parameters were assessed. Ocular comfort and dryness were rated (0-100).

Results: For symptomatic CL-wearers, after 8hrs monocular CL-wear, comfort and dryness ratings were significantly better in the non-CL wearing eye compared to the CL wearing eye: comfort 85±14 vs 71±17, dryness 85±13 vs 71±16 ($p \leq 0.02$). Comfort and dryness ratings for the non-CL wearing eye were better than ratings for the same eye at the end of the binocular CL-wear day (85±14 vs 73±14, 85±13 vs 65±26, $p \leq 0.01$) but worse than on the no-CL wear day (85±14 vs 93±8, 85±13 vs 89±10, $p \leq 0.01$). For asymptomatic CL-wearers, after 8hrs of monocular CL-wear, there were no differences between the non-CL wearing eye and the CL wearing eye for comfort (96±4 vs 94±7) or dryness (96±5 vs 95±5) ($p > 0.05$). Comfort ratings for the non-CL wearing eye were not different to ratings for the same eye at the end of the binocular (96±4 vs 94±11) or no-CL wear day (96±4 vs 97±4) ($p > 0.05$). Dryness ratings for the non-CL wearing eye were not different to ratings for the same eye at the end of the no-CL day (96±5 vs 97±3, $p > 0.05$) but better than those on the bilateral CL-wear day (96±5 vs 90±13, $p = 0.046$).

Conclusion: In symptomatic CL-wearers, ocular comfort and dryness were compromised by CL-wear in the contralateral eye, suggesting a possible inter-eye effect which should be considered for contralateral studies. Funding: CooperVision,Inc

PRACTICAL APPROACH TO MEIBOMIAN GLAND PROBBING.

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Purpose: To evaluate the short-term effectiveness of intraductal meibomian gland probbing in patients with obstructive meibomian gland dysfunction, using In Vivo Confocal Microscopy and Meibomiography. To test the validity of ocular surface assessment tools offered by a corneal topographer (Oculus Keratograph 5M) and In Vivo Confocal Microscopy in patients with meibomian gland obstructive disease.

Methods: In our study we evaluate fifteen patients presenting clinical signs of meibomian gland obstructive disease, in which we confirm the diagnosis. We have studied this patients pre-probbing and post-probbing procedure, using the HRTII-ROSTOCK Cornea Module (Heidelberg) and the KERATOGRAPH 5M (Oculus).

Results: 6 patients associated pathological acinar signs ,including dissapearence of acini, severe reduction in number and/or severe distortion of acinar structure. In this group of patients meibomian probbing showed no improvement of ocular signs while the other 9 patients improved significantly after the procedure. In this 9 patients, we could see the possitive effects of the ocular surface with meibomian gland probbing, using this image equipment. We could notice better stability in the NIKBUT station as welll as in the meiboscan display. In Vivo Confocal Microscopy showed less signs of obstruction ducts.

Conclusions: Meibomian probbing was effective and reliable in the short therm for patients with meibomian gland dysfunction. In vivo Confocal microscopy and Keratograph 5M are excellent tools to evaluate the indications and the best results of that procedures. The Keratograph 5M and In Vivo Confocal Microscopy appears to provide effective methods for assessing ocular surface situation pre and post operative. Disclosure commercial: None

AN IN-VITRO LIPID UPTAKE MODEL TO PREDICT EX-VIVO LIPID DEPOSITION ON WORN SILICONE HYDROGEL CONTACT LENSES.

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Purpose: Lipid and protein deposition on contact lenses (CLs) has been hypothesized to be associated with clinical performance. The objective of this assessment was to evaluate the predictability of an in-vitro daily wear (DW) simulated model of lipid uptake on worn CLs.

Methods: Four monthly replacement CLs (samfilcon A (L1), comfilcon A (L2), lotrafilcon B (L3) and senofilcon C (L4)) were evaluated for total lipid (TL) uptake after 1 month of DW. Worn CLs were analyzed for cholesterol and cholesteryl esters via a LC-MS method. Additionally, another set of CLs were soaked in an artificial tear solution (ATS) containing four radiolabeled lipids (phosphatidyl choline, phosphatidylethanolamine, cholesteryl oleate and cholesterol) to determine TL uptake. DW was simulated by incubating the CLs in alternating cycles of ATS (16 h) followed by a 8h cleaning in OptiFree Puremoist. After incubation, radioactive counts were determined to quantify TL uptake. The aggregated TL uptake measured on worn lenses was plotted against corresponding lipid uptake values measured in-vitro and the correlation coefficient obtained.

Results: The average TL uptake from ex-vivo analysis of worn lenses after 30 days of wear was 20.4±2.3, 9.8±1.5, 9.0±0.9 and 0.5±0.1 μg/lens for L4, L1, L2 and L3, respectively. The average TL uptake from the in-vitro 30 days DW simulated model was 20.3±0.1, 17.8±0.2, 16.6±0.1 and 7.4±0.5 μg/lens for L4, L1, L2 and L3, respectively. Linear regression analysis on in-vitro and the ex-vivo lipid uptake showed that there was a strong correlation (adjusted $r^2 = 0.94$) between in-vitro and ex-vivo lipid uptake.

Conclusions: This in-vitro 30 day DW simulated model shows high predictability of in-vivo TL uptake on worn lenses, as demonstrated by the strong correlation between TL uptake measured on ex-vivo lenses versus an in-vitro lipid uptake model.

Funding: Johnson and Johnson Vision Care, Inc.

NEW ADVANCES IN THE UNDERSTANDING OF THE ROLE OF CONTACT LENS MATERIALS AND CARE SYSTEMS IN CONTACT LENS DISCOMFORT.

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The recent TFOS report on contact lens discomfort (CLD) examined the role of contact lens material properties, design and care systems on CLD. [1] This highly cited article showed that there are surprisingly few proven links between CLD and the aforementioned factors. The only material-related factor that was shown to correlate with CLD was coefficient of friction. A number of other factors showed only weak links with CLD, including oxygen transmissibility, wettability, surface modification, modulus and lens dehydration. Improved comfort was shown to be linked with increased lens replacement frequency. Lenses with thin, tapered edge designs and lenses with lower mobility were

shown to result in improved comfort. Although deposition of tear film components did not correlate with subjective symptoms, it was found that the degree of denaturation of protein had a significant correlation with subjective comfort. The report also indicated that the presence of certain wetting agents in a lens care system could result in reduced CLD. To understand and manage CLD better, it is essential to study the role of the contact lens material, design, and the care system. Since the publication of the report, newer lens materials and care systems have been launched and this talk will focus on new advances in the understanding of the role of lens materials and solutions in CLD. In addition, areas for future research that would help in enhancing our understanding of CLD and the key factors associated with materials, design, and care systems will be discussed. With generous funding and intellectual input from both industry and academia, it is vital to conduct several fundamental studies to better understand the role of materials, design and care regime in CLD.

Reference: 1. Jones L, et al. The TFOS International Workshop on Contact Lens Discomfort: report of the contact lens materials, design, and care subcommittee. Invest Ophthalmol Vis Sci 2013;54:TFOS37-70.

HYPEROSMOLARITY-INDUCED GLYCODEFICIENT CORNEAL EPITHELIOPATHY.

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Purpose: Increasing evidence suggests that the electrical, mechanical and structural features of the epithelial glycocalyx play a critical role in the maintenance of a stable tear film. This interfacial layer is functionally distinct from secreted mucins and plays a direct role in maintaining a low friction, hydrophilic, wettable surface. Upon exposure to a hyperosmolar tear film, one of the stress responses of the corneal epithelium is to downregulate vesicle production and alter the morphology of the glycocalyx. With increasing severity of hyperosmolarity, glycocalyx function will become compromised at a molecular level, and the squamous epithelium will eventually slough off to expose the immature, hydrophobic cells beneath. Similar cellular responses are observed following induced androgren deficiency, suggesting a direct link between androgen deficiency, tear film hyperosmolarity and corneal epitheliopathy.

Methods: We review pertinent literature and discuss the results of recent clinical trials that explore replenishment of the ocular surface glycocalyx in patients with varying levels of dry eye disease severity.

Results: As compared to anti-inflammatory therapy and hydrodynamic lubrication, preliminary data on glycocalyx replenishment shows a rapid, significant reduction in a broad cross section of signs and symptoms of dry eye.

Conclusion: These data suggest that the ocular surface glycocalyx plays a dominant role in tear film homeostasis, and replenishment of this layer may help normalize the ocular epithelial phenotype to great clinical effect.

MÉNAGE À TROIS: SEX, SEX STEROIDS AND DRY EYE DISEASE.

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One of the most compelling epidemiologic features of dry eye disease (DED) is that it occurs predominantly in females. In fact, the female sex is a significant risk factor for the development of DED. That such a sex-related difference exists in the prevalence of an eye disease is not a surprise. The influence of sex on the eye has been known since the time of Hippocrates. Indeed, in the late 1800s there was widespread belief among physicians that ocular health was dramatically influenced by sex, and that males were by no means as prone to diseases of the eye from sexual causes as females. Since that time, many sex-related differences in the eye have been attributed to the effects of sex steroids (e.g. androgens and estrogens). Sex steroids act on the meibomian gland, lacrimal gland, conjunctiva and cornea. These hormone actions occur most likely after local, intracrine synthesis and appear to be mediated primarily through nuclear, and possibly membrane, receptors. Sex steroids impact multiple structural and functional aspects of the ocular surface and adnexa. These include tissue architecture, gene expression, protein synthesis, immune activity, epithelial cell dynamics, aqueous secretion, meibum production, mucous output and tear film stability. Sex steroids have also been linked to the development or treatment of meibomian gland dysfunction (e.g. aging), lacrimal gland inflammation (e.g. Sjögren's syndrome), corneal glycocalyx deficiency (e.g. androgen insufficiency), and the pathogenesis of aqueous-deficient and evaporative DED. A foremost consideration is that a number of these hormonal effects may be sex-specific (i.e. unique to males or females). We believe that recognition of these sex-related differences and the determination of their underlying basis (e.g. sex steroid action) are extremely important. We also believe that such understanding may be translated into new insights into the physiological control of ocular tissues, as well as the generation of novel therapeutic strategies to treat DED. This presentation will highlight these interrelationships between sex, sex steroids and DED.

THE ANALYSIS OF POST-BLINK TEAR FILM SURFACE QUALITY TOWARDS UNDERSTANDING THE EATIOLOGIES OF OCULAR SURFACE DISEASE.

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Purpose: To investigate the post-blink tear film build-up (BLD) phase dynamics in healthy subjects and those diagnosed with dry eye syndrome (DES).

Methods: Nineteen healthy individuals (9F, 10M), aged (mean ± SD) 29±9 years and 10 female subjects with DES, aged 52±14 years took place in the study. None of the subjects were using ocular or systemic medications on the day of measurement. The Lateral Shearing Interferometer (LSI) has been used to measure the tear film surface regularity in natural blinking conditions. Two 30-seconds sequences of images with sampling frequency of 25Hz were recorded for each subject. The interferometric image analysis that leads to a time-varying estimate of tear film surface quality (TFSQ) has been reported earlier. Each time series was fitted with an exponential function of the form $f(t)=a*\exp(-b*t)+c$. Normality of data was rejected (Jarque-Bera) and the Mann-Whitney test (with $a=0.05$) was used to assess differences between the groups.

Results: The exponential decay constant (parameter b) significantly increased for the DES group ($p=0.027$) and the level of TFSQ stability (parameter c) was statistically significantly lower for healthy subjects ($p=0.006$). No statistically significant difference was found for parameter a ($p=0.371$).

Conclusions: The LSI is a high sensitive tool for evaluation the subtle changes in tear film surface regularity. It has ability to distinguish different post-blink tear film dynamics in a group of subjects with DES. The results of this study indicate that dry eye subjects have substantially different BLD phase. This study adds to the previous knowledge of TFSQ dynamics showing that BLD phase in subjects with DES is quicker than in that observed in normal subjects.

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UNRAVELING LACRIMAL GLAND STEM CELL DYNAMICS BY LINEAGE TRACING

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Makarenkova[1] [1]The Scripps research institute, Department of Cell and Molecular Biology, La Jolla, CA, USA; [2]University of California, Gavin Herbert Eye Institute, Irvine, CA, USA, [3]Center for Regenerative Medicine and Skeletal Development, School of Dental Medicine Department of Reconstructive Sciences University of Connecticut Health Center, Farmington, USA [4] Schepens Eye Research Institute/Massachusetts Eye and Ear, Department of Ophthalmology, Harvard Medical School, Boston, MA, USA.
Purpose: Adult tissue specific stem cells are slow cycling, undifferentiated cells that have a critical role in self-renewal of many tissues. The lacrimal gland (LG) is an exocrine tubuloacinar gland that secretes the aqueous layer of the tear film. A lack of LG regeneration during inflammation leads to tear-deficiency dry eye. However, little is known regarding the identification of stem or progenitor cells and the fate of these populations following LG homeostasis, damage and regeneration.
Methods: It is well known that LG is composed of epithelial (EPC: ductal and acinar), and myoepithelial (MECs) cells, but it is not clear whether they contain lineage specific or common stem cells. In this study we followed the EPC and MEC cell lineages in normal (uninjured) and regenerating (injured) lacrimal glands *in vivo* using the Runx1- and -smooth muscle actin promoter-directed tamoxifen inducible Cre mice combined with the floxed ROSA26-tdTomato and R26R-Confetti reporter strains. We also used an *in vivo* histone2B green fluorescent protein (H2B-GFP) pulse-chase strategy to identify slow-cycling, label-retaining cells (LRCs) of the LG. Results. Labeling of the EPC cell lineage identified cells with clonal behavior, suggesting a presence of slow-cycling stem/progenitor cells within this lineage. Analysis of the MEC lineage showed that MEC progenitor cells originate from the external layer of the distal end of the epithelial bud. During postnatal development, MECs proliferate and concentrate around the lacrimal gland secretory acini. Long-term labeling strategy of MECs in adult uninjured LG suggests that MECs represent a distinct myoepithelial cell lineage and do not differentiate into other lineages. At the same time, analysis of LG regeneration induced by injection of IL1 showed that both EPC and MEC cell lineages contributed to LG regeneration. We evaluated LRCs at different chase time points and identified long-term LRCs (stem) and short-term LRCs (slow-cycling progenitor) cells. In the LG long-term chased LRCs were localized mainly in the basal layer of large and small ducts. They expressed Runx1, sox9 and Krt5. The short term chased LRCs expressed -smooth muscle actin. This suggests that MEC lineage contains relatively slow proliferating progenitor cells. Conclusions. Taken together, we conclude that adult stem cells that reside in the LG can self-renew by dividing and can differentiate into all specialized LG epithelial lineages. We also showed that in normal uninjured LG, MEC lineage contains relatively slow-cycling progenitor cells that, upon injury, contribute to repair of other epithelial components of the LG.
This work was supported by NIH NEI EY021292 to HPM and DAD and by The Scripps Research Institute Summer Undergraduate Research Fellows (SURF) Program to NT

MMC INJECTION-ASSISTED PTERYGIUM EXCISION- A NOVEL TECHNIQUE.

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Purpose. To determine the results of a new technique using standard dose of mitomycin-C (0.005μg/0.1 ml) intraoperative injection combined with conjunctival flap in primary pterygium surgery.
Methods: 13 patients (13 eyes) with primary pterygium underwent pterygium excision. Mitomycin-C (0.005μg/0.1 ml) was injected under the body of the pterygium at the beginning of the surgery, followed by wide pterygium excision. A conjunctival flap was used to restore the deficit in a standard manner. The flap was secured in place with 9-0 nylon (9 patients) or 8-0 vicryl sutures (4 patients), while matrix sutures were used to anchor the conjunctiva to the limbus. At the end of the surgery a therapeutic contact lens was used for a period of two weeks. Standard post-operative treatment included nepafenac 0.1% three times a day and chloramphenicol 0.1% with dexamethasone 0.5% four times a day. Additional 5-FU injections were applied as needed during the follow-up visits, ranging from 0 to 5 (mean 2.2).The follow-up period ranged from 6 to 16 months (mean 9 months).
Results: At the end of the follow up period there was no apparent recurrence in any patient. No major complications occurred. Mild conjunctival hyperemia appeared in 8 patients, primary tissue dehiscence in 2 patients and reaction to the sutures appeared in 1 patient, but was controlled by using our standard post operative treatment. The cosmetic results at the last visit were considered excellent in 90% of cases and very good by the rest. All patients reported that they were completely satisfied with the procedure and the results.
Conclusions: MMC injection-assisted pterygium excision combined with conjunctival flap appears to be a safe, effective and promising technique in pterygium surgery. More patients and a longer follow up period are needed in order to verify our preliminary results.

ANALYSIS OF TEAR CYTOKINE LEVEL ALTERATIONS AND CLINICAL CORNEAL FINDINGS FOLLOWING PENETRATING KERATOPLASTY.

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Purpose: To investigate the correlation of the cytokine alterations with corneal clinical findings following penetrating keratoplasty (PK).
Methods: Fifteen consecutive Japanese patients who underwent PK at Tokyo Dental College and 25 healthy subjects were included in this prospective consecutive case series. A total of 85 tear samples in 15 eyes of 15 patients who underwent PK and healthy controls were analyzed. The tear cytokine levels of Interleukin (IL)-1α, -1β, IL-2, IL-4, IL-6, IL-8, IL10, IL17a, interferon (IFN)-γ, monocyte chemotaxis protein (MCP)-1 and tumor necrosis factor (TNF)-α were measured using multiplex beads assay. Best corrected visual acuity, percentage of remaining endothelial cell density (%ECD) and corneal neovascularization (NV) were analyzed before and at 1week, 1 and 3 months after PK, and the correlation of with tear cytokine levels were assessed
Results: In this study, no one had any rejection, infection and traumatic episodes during the follow-up period. The visual acuity (logMAR) improved from 1.25 $\pm$ 0.62 to 0.86 $\pm$ 0.64 at 3 months (p=0.02).IL-1α, IL-2, IL-10 and IL-17a levels at post-operative 1M were significantly higher than controls (P<0.05). IL-1α, IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, IL-17a and TNFα levels at post-operative 1M tended to be higher than the other points and controls. Significantly correlation were observed between pre-operative NV and IL-10 and %ECD (p=0.038 r=0.65, p=0.037 r=-0.53), IL-1α and %ECD at post-operative 3M (p=0.012, r=-0.727) and pre-operative SPK and iL-1β and IL-8 (p=0.003, r=0.884, p=0.041 r=0.707).
Conclusions: Assessment and reduction of preoperative inflammation of the ocular surface is one of the potential ways to decrease the endothelial cell loss after PK. The authors have no commercial or proprietary interest in any of the products mentioned in this presentation.

PHYSIOLOGICALLY-RELEVANT MEASUREMENT OF CONTACT LENS FRICTIONAL ENERGY AFTER A SIMULATED 1-DAY WEAR CYCLE.

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Purpose: Few in-vitro tools exist to simulate the effects of wear on contact lens (CL) material lubricity (CLml) despite the suggested

predictive potential of lubricity on end-of-day (EOD) comfort. Additionally, an obstacle in the evaluation of CLml is the difficulty in assigning a coefficient of friction to soft-soft and soft-hard contacts since the ratio of lateral-to-normal forces (FT/FN) may not be constant. The purpose of this study was to evaluate whether the CLml of two commercially available CL were altered after exposure to in-vitro ageing, and in addition to derive a novel strategy to represent CLml devoid of presumptions regarding linearity of FT/FN.

Method: To simulate CL wear, senofilcon A (ACUVUE Oasys 1-day) (AO) and delefilcon A (DAILIES Total One) (DT1) CLs were cycled for 0/2/6/14/18h resp. between a tear-like-fluid (TLF) and air at 20sec intervals to mimic a blink-cycle. Tribological properties were characterized according to work of Sterner et al. (Tribology Letter, 2016) involving Mucin-coated glass counter-surfaces, a 0.25-4.0mN normal force range, 1mm stroke lenght, 0.1mm/s speed, TLF as lubricant and a optical microscope to determine the effective contact area between counter-surface and CL.CLml was quantified in terms of the average of a non-linear equation fitted to the lateral vs normal force data, multiplied with a sliding distance of 2mm and reported in units of energy i.e. frictional energy.

Results: The frictional energy (mean ± 95% CI) expended during sliding the counter-surface across the AO lens increased marginally from 66±7nJ to 86±11nJ after 18h of simulated wear, while the frictional energy for DT1 increased from 71±8nJ to 610±75nJ during the same time interval

Conclusion: The lubricity of two CL materials has been found to be susceptible to in-vitro ageing, albeit to a significantly different extend. A decrease in CLml with ageing may have clinical implications in terms of reduced EOD comfort. Frictional Energy is proposed as a single figure-of-merit of CLml.

EXPRESSION OF K+ CHANNELS BY HUMAN CORNEAL LIMBAL EPITHELIAL CELLS.

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Purpose: In the context of studies of activation of K^+ channels in human corneal limbal epithelial (HCLE) cells by UVB, we have previously reported that UVB-induced K^+ currents are partially blocked (50-60%) by the specific $K_V3.4$ blocker, BDS-1, and completely blocked by Ba^{2+} (Singleton et al. Exp Eye Res. 89:140, 2009; Glupker et al. Ocular Surf. doi: 10.1016/j.jtos.2016.05.001). This suggests that HCLE cells express K^+ channels in addition to $K_V3.4$. The goal of this study was to identify K^+ channels in HCLE cells and determine whether these channels are activated by UVB.

Methods: HCLE cells were screened for K^+ channel expression using a Human Neuronal Ion Channels RT^2 Profiler PCR Array (Qiagen). Expression of channels for which the C_T was ≤ 33 on the PCR arrays was confirmed by immunofluorescence microscopy using appropriate antibodies. Activation of K^+ currents was measured by whole-cell perforated patch-clamp recording after exposure of cells to 80 mJ/cm^2 UVB. Specific blockers (if available) for channels detected by PCR and immunofluorescence were used to determine whether these channels were activated by UVB.

Results: PCR gave evidence for expression of the genes for $K_V1.2$, $K_V2.1$, $K_V2.2$, $K_V4.2$, $K_V11.1$, $K_V12.2$, MaxiK and $K_{2p}1.1$ channels. Immunofluorescence confirmed the presence of $K_V2.1$, $K_V2.2$, $K_V3.4$, $K_V4.2$, Kv11.1, MaxiK and $K_{2p}1.1$ channels, while relatively weak signals were detected for $K_V1.2$ and $K_V12.2$. Heteropodatoxin-2, a $K_V4.2$ channel blocker, and iberiotoxin, which blocks MaxiK channels, had no effect on UVB-induced K^+ currents.

Conclusions: The data show that HCLE cells express a large number of K^+ channels which may be involved in cell volume regulation, responses to environmental stimuli and regulation of intracellular signaling pathways. The lack of effect of blockers of the strongly expressed $K_V4.2$ and MaxiK channels on UVB-induced currents suggests that $K_V3.4$ channels dominate the response of the cells to UVB, although involvement of channels for which blockers are not available cannot be ruled out. [Supported by NIH grant EY023836 and the Arnold and Mabel Beckman Foundation]

EFFECT OF REBAMIPIDE ON TRANSMEMBRANE MUCIN BIOSYNTHESIS IN STRATIFIED OCULAR SURFACE EPITHELIAL CELLS.

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Purpose: Mucins are a group of highly glycosylated glycoproteins responsible for the protection of wet-surfaced epithelia. Recent data indicate that transmembrane mucins differ in their contribution to the protective function of the ocular surface, with MUC16 being the most effective barrier on the apical surface glycocalyx. We investigated the role of the mucoprotective drug rebamipide in the regulation of transmembrane mucin biosynthesis using stratified cultures of human corneal and conjunctival epithelial cells.

Methods: Telomerase-immortalized human corneal and conjunctival epithelial cells were plated at a seeding density of 5x10^4 cells/cm^2. After reaching confluence, cells were switched to DMEM/F12 medium supplemented with 10 ng/mL epidermal growth factor and 10% calf serum for 7 days to promote cell stratification and differentiation. Stratified cells were incubated with increasing concentrations of rebamipide (0.01−100 μM) in DMEM/F12 for 24 hours. Proteins were separated by gel electrophoresis, transferred to nitrocellulose membranes, and probed with antibodies to MUC1, MUC4, MUC16, MUC20, Notch1, Notch2, and Notch3.

Results: We find that the addition of rebamipide to corneal, but not conjunctival, epithelial cells increased MUC16 protein biosynthesis in a dose-dependent manner. Rebamipide did not affect the levels of MUC1, 4 and 20 compared to control. Rebamipide had no effect on the expression levels of Notch intracellular domains, suggesting that the rebamipide-induced increase in MUC16 biosynthesis in differentiated corneal cultures is not regulated by Notch signaling.

Conclusions: These findings indicate that rebamipide induces the differential upregulation of MUC16 in stratified cultures of human corneal epithelial cells, which may have implications to the proper restoration of barrier function in ocular surface disease.

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TEAR CYTOKINES OF STEVENS-JOHNSON SYNDROME IN THE CHRONIC STAGE.

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Introduction: Stevens-Johnson syndrome (SJS) is an acute inflammatory vesiculobullous reaction of the skin and mucosa, such as the ocular surface, oral cavity, and genitals. In patients with extensive skin detachment and a poor prognosis, the condition is called toxic epidermal necrolysis (TEN). Severe ocular complications appear in not all, but some of SJS/TEN patients who diagnosed by dermatologists. To investigate the pathophysiology of ocular surface inflammation of Stevens-Johnson syndrome in the chronic stage, we examined the various cytokines in the tear of Stevens-Johnson syndrome patients in the chronic stage and healthy controls.

Methods: To measure various cytokine levels in the tears, we used BD™ CBA Flex sets. Tear samples from SJS/TEN eyes in the chronic stage (n>6) and healthy eyes (n>7) were collected on Schirmer's measurement strips, which with collected tears were immersed in 100 ul Tris-buffered

saline with Tween 20 for 10 min at room temperature and 50 ml of TBST containing the tears were used for measuring the various cytokines.
Finding: IP-10 and IFN-g were significantly higher in SJS/TEN eyes in the chronic stage than healthy eyes. IL-6 and FasL were also significantly higher in SJS/TEN eyes in the chronic stage than healthy eyes, although they were detected in not all SJS/TEN eyes in the chronic stage. IL-8, Rantes and IFN-α tend to be higher in SJS/TEN eyes in the chronic stage than healthy eyes, but not significantly. On the other hand, there were not significant different in total IgE, Eotaxin, MIP-1b and MCP-1. IL-10 of the cytokine was not detected in both SJS/TEN eyes in the chronic stage and healthy eyes except only two SJS/TEN eyes in the chronic stage.
Conclusions: These findings suggest that IP-10, IFN-g, IL-6 and FasL in the tear could be markers for SJS/TEN eyes in the chronic stage.

REDUCING THE OCULAR AND SYSTEMIC SIDE EFFECTS OF TROPICAMIDE 0,5% EYEDROPS BY REDUCING THE DROP VOLUME.

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Purpose: Eyedrops disrupt the balanced condition of the tear film which can induce ocular and systemic side effects. For the development of a micro drop device we performed a study to compare 2.4 µL microdrops of tropicamide 0,5% with regular 38 µL drops.
Methods: We performed a randomized single-blind cross-over trial in 30 healthy volunteers. On day 1, one intervention group received a micro drop (2,4 microliter) in both eyes, the other group a regular eye drop (38 microliter). Pupil size measurements were performed 10 times during a 2 hour timeframe. Side effects were assessed using a questionnaire. The test was repeated with the other eye drop after 7 days.
Results: Stinging eyes were reported by 26 subjects in the normal drop group compared to 7 subjects in the micro drop group. Dry mouth was reported by 10 subjects in the normal group versus 2 subjects in the micro drop group. Headache was reported by 12 subjects in the normal drop group versus 7 subjects in the micro drop group. All 30 subjects reported to prefer the micro drop. Less discomfort is experienced with the micro drop. Clinically equivalent mydriasis was achieved with both drops.
Conclusions: Microdrops of tropicamide 0.5% reduce the occurrence of ocular and systemic side effects. A drop that is 15 times smaller still produces clinically noninferior mydriasis. Development of ocular micro drops offers new possibilities in improving the tolerability of eye drops.
Commercial relationships. Hans van der Heiden is patent-owner and co-owner at mu-Drop BV. Grant support: none

INFLUENCES OF INDOOR ENVIRONMENT QUALITY AND DRY EYE IN A MODERN DESIGN OFFICE.

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Purpose: Work productivity (WP), daily activity and illness perception can be adversely influenced by dry eye. As recommended by the DEWS Report, modification of the environment can be a management option. The use of an Indoor Environmental Quality (IEQ) questionnaire could identify specific features of the working environment that influence ocular comfort and WP. The aim of this study was to utilise the IEQ in employees working in a modern, glazed, open-plan office reporting varying levels of ocular comfort.
Methods: In this clinical study, employees of a modern glazed open-plan office were invited to participate by general email and completed Dutch cultural translations of the Ocular Surface Disease Index (OSDI) and IEQ containing 20 Likert questions.
Results: 63 participants completed the study (21m, 42f: mean age 48.09 sd 2.08, 47.8 sd 1.38). Females had higher OSDI mean scores 2.89 sd 0.17 than males (mean scores 1.87 sd 0.16) (p=0.001) and were more dissatisfied with air quality and workspace temperature and constancy over the winter period than males (p=0.018, p=0.023, 0.015 respectively). Participants with mild-severe OSDI scores were more dissatisfied with the amount of artificial light at their workspace and with visual comfort of the lighting in the summer (p=0.003, p=0.016). Whilst work productivity was not adversely affected by overall air quality or sound those with mild-severe OSDI scores were more affected by overall temperature and lighting.
Conclusion: This in-office investigation demonstrates the influence of the indoor environment, particularly on female employees and those reporting symptoms of dry eye with temperature having the greatest impact on WP. Individual advice on optimising the environment should be considered for patients reporting dry eye, especially those working in modern, open-plan offices.

METABOLOMIC FINGERPRINTS EXIST IN DRY EYE DISEASE.

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This presentation will discuss the utility of metabolomic studies in dry eye disease, the results of our recently completed serum metabolomic study on dry eye disease, and the most important directions for future research in this area. The metabolome refers to the complete set of small molecule metabolites -the intermediates and products of metabolism- that are found within a biological sample. The study of metabolomics is an emerging approach for biological research and its power in the analysis of complex traits has been demonstrated in many studies. Metabolites may act as biomarkers and help identify functional pathways in complex diseases. Because of the known association of dry eye disease with many systemic and metabolic traits, our group performed a metabolomics study exploring the relationship between serum metabolites and dry eye disease. 280 metabolites were measured in almost 3000 subjects and 5 androgens were found to be highly associated with dry eye disease. This hypothesis-free study adds important evidence to the growing body of research linking androgens to ocular surface parameters and dry eye disease.

DIAGNOSTIC PERFORMANCE OF TEAR PROTEINS FOR PRIMARY SJÖGREN'S SYNDROME.

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Purpose: to estimate the diagnostic performance of tear protein analysis for Sjögren's syndrome (SS).
Methods: This is a retrospective analysis of prospective collected data from 110 patients referred to our units for a suspect of SS diagnosis. The following parameters had been analyzed prior to diagnosis, and data were retrieved from charts: subjective discomfort symptoms (Ocular Surface Disease Index, OSDI), Break Up time (BUT), Schirmer test, Tear Clearance (TC, fluo diluition 0 to 5), surface vital staining, tear protein analysis related to total protein content (TP-t), Lysozyme-C (LYS-C), Lactoferrin (LACTO), Tear lipocalin 1 (LIPOC-1) as biomarkers for lachrymal gland function, ((%) vs TP-t). Standardized scintigrafic score (SCINTI) for salivary gland impairment, ANA, ENA, rheumatoid factor (RF), and μ-globulins, albumin (ALB-b), total protein (TP-b) levels in blood were also retrieved. The diagnostic accuracy (ranging 0 to 100) and odds ratio (OR) were calculated for each parameter and tear protein.
Results: 35 of 110 patients (31,8%) had been later diagnosed as affected by SS, (Vitali et al 2002). Ocular parameters showed the lowest diagnostic accuracy: OSDI> 44 score (accuracy=49%), Schirmer≤7mm/5min (63.6%), BUT ≤ 8 sec (71.3%), TC > 2 (77.4%), Cornea staining (64.4%), Conjunctiva staining (61.1%). Blood analytes showed slightly lower

accuracy (ANA=79.8%; ENA=90.7%; RF=75.9%; TP_b=64.5%; ALB_b=72%; μ-globulins=68.5%; SCINTI=75.9%) as compared to tear proteins: TP-t $\leq$ 5.8 mg/ml (86.8%), LYS-C $\leq$ 19% (85.7%), LACTO $\leq$ 17.3% (90.9%), LIPOC-1$\leq$9% (82.9%). The areas under the ROC curves ranged from 0.573 for OSDI score to 0.945 for tear LACTO%. TP-t, LYS-C %, LACTO %, LIPOC-1% showed an higher positive association in predicting SS versus non-SS patients (OR, respectively 43.5; 42.1; 60.0; 20.1) as compared to Schirmer test, BUT, OSDI score, Cornea staining (OR, respectively 2.5; 5.8; 1.1; 4.1). Conclusions: In this study tear proteins showed significantly higher accuracy as compared to eye clinical parameters and to blood analytes for SS diagnosis. Given the non-invasive collection of tears, and the relative fast and inexpensive analytical procedure, the prospect of the test development for a first line screening may be worth exploring.

TEAR PROTEINS IN YOUNG HEALTHY ADULTS. DIFFERENCES BETWEEN MALES AND FEMALES IN TWO MENSTRUAL CYCLE PHASE.

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Purpose: To evaluate tear proteins in healthy young males and females, these collected in different phases of the menstrual cycle.

Methods: 10 μl unstimulated tears were collected in both eyes from healthy 30 males and 30 females, aged 20-24 years. Only females who reported regular cycle (26-34 days) were included and sampling occurred at day 12±2 (high estrogen H-E, i.e., follicular phase) and day 28±2 (low estrogen L-E, i.e., premenstrual phase). Protein analysis was performed in individual samples with the 2100 Bioanalyzer (Agilent Technology, CA, USA), 1-D SDS-PAGE electrophoresis and characterized by western blotting and . Total protein content (TP) and the following proteins were recognized and quantified: Lysozyme-C (LYS-C), Lactotransferrin (LACTO), exudated serum albumin (ALB), Serotransferrin (TRANSF),Tear lipocalin 1 (LIPOC-1), Zinc-alpha-2-glycoprotein (ZAG-2), Lacritin (LACRT) and Protein-rich-protein 4 (PRR4). Data were statistically compared (significance $p<0.05$).

Results: Results were consistent in all samples, with a reduced variability among subjects in both males and females, except for LACRT where an higher inter individual variability was found in females. Data from both eyes in each subject were highly correlated. Statistically significant lower expression for all the protein analyzed was found in males as compared to females in both HE and LE. In particular, we found that expression of ZAG and PRR4 in males were decreased of 50% and 60%, respectively. No statistically significant differences were detected in protein levels between the two phases of the cycle in females.

Conclusions: Tear protein profile significantly differs with respect to the sex also in the youngest and without any systemic or ocular function impairment. The hormonal fluctuation over the menstrual cycle does not appear to influence tear protein expression in the normal and young females.

MAKING CONTACT LENSES MORE COMPATIBLE WITH THE OCULAR SURFACE THROUGH COATING TECHNOLOGY.

María Vidal Rohr, Leon N Davies, James S. Wolffsohn. Ophthalmic Research Group, Aston University, Birmingham, UK.

Purpose: To determine whether coating technology can make contact lenses more comfortable to the patient and to have less impact on the ocular surface physiology. Previous studies have suggested that lens surface 'lubricity' is the principal contributor to comfort, but have been confounded by the use of other differences in design and materials between the lenses investigated.

Method: Twenty-two subjects were recruited for randomised contact lens wear of monthly disposable soft contact lenses of the same design (8.6mm base curve, 14.2mm diameter, 50% water silicone hydrogel, Dk/t 140) and modulus (0.5 MPa), but with or without modifying the surface properties with a coating (6-10nm thick, reducing surface coefficient of friction from 0.071±0.005 to 0.004±0.003). Subjective and objective evaluations were conducted one week and one month after wearing each contact lens type, bilaterally in randomised order, each for one month. The principal measures were subjective assessment of comfort (Contact Lens Dry Eye Questionnaire (CLDEQ-8) and Visual Analog Scales (VAS)) and objective evaluation (Oculus Keratograph 5M) of non-invasive break-up time (NIKBUT) and ocular redness.

Results: Nineteen subjects (21.6±1.7 years, 17 female) successfully completed the study. Subjective comfort and NIKBUT were better for coated contact lenses compared to uncoated contact lenses (CLDEQ-8: 12.3±7.9 vs 16.8±7.8, F=14.408, p=0.001; VAS: 73.6±18.0% vs 55.7±19.4%, F=22.781, $p<0.001$; NIKBUT: 7.1±0.6s vs 5.8±0.5s, F=5.626, p=0.029), with no difference after a weeks' or a months' wear ($p>0.05$). Ocular redness was not statistically different between coated and uncoated contact lenses (bulbar: F=0.340, p=0.567; limbal: F=0.110, p=0.744) at either time point ($p>0.05$).

Conclusion: Surface properties of a soft contact lens alone, altered by coating technology can significantly enhance comfortable contact lens wear, providing a more stable tear film over the contact lens surface.

THE PEDIATRIC OCULAR SURFACE IS A PECULIAR SYSTEM, WITH PECULIAR DISEASES AND PECULIAR MANAGEMENT CHALLENGES.

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Purpose: To provide researchers and clinicians with new and useful information on this intriguing issue.

Methods: Basic knowledge, critical revision of recent evidences and clinical pearls.

Results: The pediatric ocular surface is not simply a "small" ocular surface. Infectious, allergic and inflammatory ocular surface diseases may all have peculiar epidemiologic, pathogenic and clinical features in children. Moreover, both diagnosis and treatment pose particular challenges in infants.

Conclusions: The physiopathology of pediatric ocular surface has not yet been fully understood. The awareness of the ophthalmologists, together with specific skills and dedicated strategies, are essential to get the best clinical management of ocular surface diseases in our young patients.

[Support and conflict of interest: None]

SCLERAL LENS SURFACE COATING IMPROVES VISION AND OCULAR COMFORT.

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Purpose: This study evaluated the effects of a polyethylene glycol-based contact lens coating on the comfort and vision of scleral lens wearers.

Methods: Eleven established scleral lens wearers suffering from contact lens discomfort were recruited. Over a period of 2-3 months, subjects wore both uncoated and coated study lenses for a period of one week each, coming to the clinic approximately 4 hours after lens insertion for each study visit. At each visit, visual acuity was measured (logMAR), comfort evaluated (1-10, visual analogue scale), lens fit characteristics assessed (biomicroscopy), the tear film integrity measured (video topography), and the tear film reservoir evaluated for midday fogging (ocular coherence tomography). Statistical comparisons were made using the Student t-tests.

Results: All outcome measures show improvement in vision and comfort with the coated lenses, although none reached statistical significance with this sample size. Coated lenses showed a higher end of day comfort (7.85±1.52 out of 10) compared to the uncoated lenses (7.27±1.20) (p=.12) and the reduction in comfort over the day was less in the coated lenses (0.55±0.82 points) compared to the uncoated lenses (1.45±1.57 points) (p=.11).Visual acuity (logMAR) was -0.18±0.20 coated,

+0.18±0.20 uncoated, (p=.56). There were minimal differences in the midday fogging scores: 2.13±1.32 coated, and 2.00±1.23 uncoated (p=.73), and the tear film quality scores: 0.14±0.12 coated, 0.16±12 uncoated (p=.75). 64% of the subjects preferred the coated lenses to uncoated lenses (9% preferred habitual; 27% showed no preference).
Conclusion: Most patients preferred the coated lens, presumably due to improved comfort and vision, despite these values not generating statistical significance. Ongoing evaluation of a larger population will further elicit the potentials of this new technology, which shows promise to alleviate contact lens discomfort, the leading cause of contact lens dropout.

IL-1R CONTRIBUTES TO THE ABSENCE OF A MICROBIOME AT THE MOUSE CORNEAL SURFACE.

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Purpose: Whether a stable microbiome exists on the cornea is a hotly debated topic. While 16S rRNA sequencing has suggested a diverse set of microbes on the ocular surface, it detects bacterial DNA not live microbes. Here, we used an alkyne functionalized D-alanine (alkDala) probe that incorporates into the cell wall of metabolically active bacteria to search for live bacteria at the corneal surface.
Methods: Corneas of C57BL/6 wildtype or IL-1R KO mice were neither injured nor inoculated with bacteria before adding alkDala (10mM) for 2h with buffer only or with antibiotics (gentamicin, ofloxacin and vancomycin). Incorporated alkDala was detected using an azide fluorophore (copper-catalyzed click chemistry). Corneas were imaged by confocal microscopy. Images represent ~0.04mm^2. To validate the method works on the eye, control WT mice eyes were inoculated with RFP-expressing *P. aeruginosa* for 5 hours, a time point when they are not yet cleared, to verify colocalization of the two fluorophores.
Results: While alkDala did label bacteria remaining on deliberately inoculated eyes (11.00 ± 3.30 bacteria/image), bacteria were rarely detected on uninoculated eyes (1.88 ± 1.35 bacteria/image). In contrast, numerous bacteria were detected on corneas of IL-1R KO mice (76.00 ± 39.30 bacteria/image, P<0.05 compared to wildtype), and they were present throughout the corneal epithelium not only at the surface. Antibiotic treatment reduced bacterial detection to wildtype eye levels (0.78 ± 0.46 bacteria/image, P<0.05 compared to untreated IL-1R KO).
Conclusions: C57BL/6 mice corneas lack a stable microbiome, regulated by IL-1R. Signaling via the IL-1R is already known to be critical to innate and acquired immunity. The results of this study suggest IL-1R also plays a constitutive role in maintaining health, and that corneal health does not depend upon the presence of a microbiome at it surface.
The authors have no commercial disclosures. Supported by grants R01-EY011221 and T32-EY007043.

BARRIERS TO GLAUCOMA MEDICATION COMPLIANCE AMONG VETERANS: DRY EYE SYMPTOMS AND ANXIETY DISORDERS.

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Purpose: To identify barriers to compliance of medical treatment for glaucoma among veterans.
Methods: Glaucoma patients from the Miami Veterans Affairs Eye Clinic filled out a 63-question survey regarding dry eye symptoms, concurrent systemic disease, and medications. The association between glaucoma medication compliance was defined as self-reported adherence to drop regimens >75% of the time.
Results: Eighty percent of veterans (n=59) reported compliance with glaucoma therapy. Dry eye symptoms (as defined by Dry Eye Questionnaire 5 [DEQ5] score >=6) were reported by 39% (n=29) and their presence was associated with decreased compliance (63% vs 89%, p=0.007). Anxiety and posttraumatic stress syndrome (PTSD) were also associated with significant noncompliance (64% vs 83%, p=0.05 and 58% vs 84%, p=0.02, respectively). Other studied factors including demographics, depression (p=0.11), and glaucoma regimens did not play a significant role in glaucoma medication compliance.
Conclusions: Dry eye symptoms, PTSD, and anxiety were associated with decreased compliance to medical treatment of glaucoma. Identifying and treating underlying ocular surface disease and anxiety disorders may lead to increased adherence to glaucoma treatment. [This research was supported by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Clinical Sciences Research EPID-006-15S (Dr. Galor), NIH Center Core Grant P30EY014801 and Research to Prevent Blindness Unrestricted Grant]

A NOVEL METHOD USED TO MEASURE THE CONTACT ANGLE OF DRY EYE DROP SOLUTIONS.

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Purpose: Topical eye drops to relieve dry eye symptoms come in a range of compositions and viscosities, and intuitively many clinicians assume that greater viscosity increases efficacy. However, drops that spread most easily on the ocular surface are well tolerated and cause less blurring. This study assessed the contact angles that dry eye drops make when first applied to a simulated ocular surface.
Methods: A novel in vitro eye model was designed with high speed video capture of the application of eye drops as they fell onto a mounted contact lens, used to replicate the dimensions of the ocular surface under moist and air-dry conditions. An auto-pipette set at 50 μL was used to expel the drops onto wet and dry contact lenses whose surface characteristics were maintained throughout. Nine dry eye drops were assessed: Hyabak®, Thealoz®, Thealoz® Duo (Laboratoires Thea), Hyco-san® Extra (Scope Ophthalmics), Systane® Ultra (Alcon), Blink® Tears (Abbott), Murine® Dry & Tired (Murine), Optrex™ Refreshing (Optrex), PF Drops™ Hypromellose (Moorfields Pharmaceuticals). Consistent time frames after first contact were selected, and contact angles were analysed using imageJ software.
Results: Significant differences were observed for contact angles amongst the drops in both moist and air-dry (p<0.0001). Post hoc analysis revealed that under moist conditions, the contact angles ranged from 33.093°-41.710° with Thealoz® and Hyabak® having significantly lower contact angles on application (p<0.005 and p<0.005 respectively). Under air dry conditions, the contact angles ranged from 43.053°-61.576° with Hypromellose having significantly higher contact angles (p<0.002).
Conclusions: By looking at the dry eye products Hypromellose has the most significant difference with the highest contact angles, whereas Thealoz® and Hyabak® have the most significant difference but with the lowest contact angles suggesting a lower viscosity, similar to tears. Commercial relationships: Wilcox (none), Purslow (Employee of Lab Thea), Drijfhout (none).

EASE OF USE OF TWO PRESERVATIVE FREE BOTTLE SYSTEMS FOR DRY EYE DROPS.

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Purpose: Dry eye drop bottles come in all different shapes and sizes

and the product chosen is often down to personal preference. These bottles must be easy to hold, simple to operate and not require too much pressure when distilling a drop. This study will focus on a human participation questionnaire study comparing two well-known dry eye drop bottles.

Methods: A questionnaire was created to focus on the shape and size of the bottles along with pressure required, but not treatment efficacy. Two leading European bottle systems were compared: the ABAK bottle (Laboratoires Thea, France) and the COMOD bottle (Ursapharm, Germany). 145 participants were presented with masked bottles to obscure brand names, and independently completed a questionnaire. Responses were divided by age into two groups: Group 1 (17-29yrs) and group 2 (30-92yrs).

Results: Mean age for Group 1 (n=101) was 23.7±24.1yrs (50%F), and Group 2 (n=43) 50.6±16.5yrs (56%F). Group 1 participants tended to prefer the handling of ABAK compared to COMOD (53% vs 30% respectively), but this preference was much greater in the older group 2 participants (74% vs 14% respectively). A similar result was recorded for responses about the pressure required to expel a drop: in group 1 participants tended to prefer the pressure required of ABAK compared to COMOD (64% vs 32% respectively), again this preference was greater in the older group 2 participants (79% vs 21% respectively). When only female participants were considered, more preference was observed for the ABAK system, for all features. This was true for both groups but particularly in the older group.

Conclusions: The ABAK system appears more acceptable than the COMOD system, especially for older patients. Dry eye drop manufacturers need to be aware of patient preference for bottle design, particularly when many dry eye sufferers are older and female.

Commercial relationships: Wilcox (none), Purslow (Employee of Lab Thea), Drijfhout (none).

CENTRAL CONNECTIONS OF THE LACRIMAL FUNCTIONAL UNIT.

Catherine Willshire[1], Roger Buckley[1] and Anthony Bron[1,2]. [1]Vision and Eye Research Unit, Anglia Ruskin University, Cambridge, UK, [2]Nuffield Department of Clinical Neurosciences and Nuffield Laboratory of Ophthalmology, University of Oxford, UK.

Purpose: To study the contribution of each eye to the reflex tear response measured by the Schirmer test, after unilateral and bilateral topical anaesthesia.

Method: A closed eye, single masked, modified Schirmer test was performed bilaterally in 8 normal subjects, in a controlled environment chamber set to 23°C, 45% relative humidity and 0.08m/s airflow. In 3 experiments, eye drops were instilled into each eye 10 minutes before the Schirmer test. Experiments were: a) bilateral saline (control) b) unilateral anaesthesia (ipsilateral anaesthetic; contralateral saline) and c) bilateral anaesthesia.

Results: There was no difference in between-eye wetting lengths in the saline control eyes (p=0.394) or the bilaterally anaesthetised eyes (p=0.171). Wetting length was reduced in both eyes after bilateral anaesthesia compared to their saline controls (p=0.001; p=<0.0005). In the unilateral anaesthesia experiment, wetting length was reduced in the anaesthetised eye compared to its saline control (p=<0.0005) and its fellow unanaesthetised eye (p=0.005). The fellow eye was also reduced compared to its saline control but not significantly (p=0.06).

Conclusions: Wetting length was reduced by topical anaesthesia, in both eyes when instilled bilaterally and unilaterally after unilateral instillation. The latter response implies ipsilateral central feedback. In the unanaesthetised fellow eye the reduction compared to its saline control was not quite significant. This implies a relative lack of central, sensory, reflex cross-innervation, although the possibility cannot entirely be ruled out. These results are relevant to the possibility of reflex lacrimal compensation from a normal, fellow eye in cases of unilateral corneal anaesthesia as in neurotrophic keratitis. Results contrast with the effect of unilateral anaesthesia of the nasal mucosa (Gupta et al.1997), which results in an equal reduction in reflex tear secretion (Schirmer I) in both eyes, suggesting a central cross-innervation from nasal inputs.

ENDOCRINE REGULATION OF MUCOSAL BARRIER PROTECTION IN THE HUMAN FEMALE REPRODUCTIVE TRACT.

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Sexually transmitted infections (STI) have reached epidemic proportions worldwide with at least 20 pathogens including HIV accounting for more than 300 million new infections annually that are transmitted between men and women through sexual intercourse. Consisting of the innate and adaptive immune systems, mucosal immune protection in the human female reproductive tract (FRT) has evolved to meet the constraints of protecting against viral, bacterial and fungal pathogens while ensuring reproductive success of a semi-allogeneic conceptus (Wira et al. Nature Rev. Immunol. 2015 Apr. 15(4):217-30). The FRT is made up of several compartments including the Fallopian tubes, uterus, endocervix, ectocervix and vagina, with each site independently regulated by the ovarian production of estradiol (E_2) and progesterone (P). These hormones act both directly and indirectly through cytokines, chemokines and growth factors, to regulate immune cell phenotype and function as well as immune protection throughout the reproductive tract. Estradiol and P4 secreted during the menstrual cycle act on epithelial cells, fibroblasts and immune cells in the FRT to modify immune protection and susceptibility to STI in ways unique to the FRT. These hormones regulate immune epithelial cell barrier protection (tight junctions and antimicrobial peptides), dampen inflammatory responses as well as regulate fibroblast and immune cell phenotype and function. Cyclical changes of the E_2 and P across the menstrual cycle, to optimize conditions for fertilization and pregnancy, leads to the creation of a Window of Vulnerability during the secretory stage of the menstrual cycle, the time interval when risk of HIV other STI infection is increased. The goal of this presentation is to summarize the multiple levels of protection against HIV infection in the FRT, the contribution of different cell types including epithelial cells, macrophages, T cells and dendritic cells to this, and their regulation by E_2 and P. Understanding the unique immune environment in the FRT will allow for the development of novel therapeutic interventions such as vaccines and microbicides that may reduce or prevent STI infections at mucosal surfaces throughout the body. Supported by AI102838 and AI117739 from NIH.

ANALYSING THE PROCESS OF LYSOZYME TRANSFER INTO TEAR FILM LIPID LAYER.

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Purpose: To study (in silico) conditions and the process of passive transport of lysozyme from aqueous phase into the lipid layer of human tear film.

Methods: A large-scale molecular model of tear film was built, with 25,600 molecules of both polar and non-polar lipids as well as over 2.5 million molecules of water. Additionally, 33 molecules of lysozyme were incorporated into the bulk of water. Molecular dynamics (MD) simulations were performed employing the coarse grain MARTINI force field. Numerous MD simulations were carried out to simulate and analyze lysozyme adsorption to the lipid layer. Moreover, the configurations with lysozyme adsorbed to the film were selected to further simulations under elevated lateral pressure.

Results: Simulations demonstrate that lysozyme adsorbs at the water-polar lipids interface. Noteworthy, specificity of protein-lipids interaction upon adsorption was observed. In particular, ceramides show increased affinity toward lysozyme. The non-equilibrium simulations under elevated lateral pressure show that lysozyme, once adsorbed at the water-polar lipids interface, can undergo transfer into the lipid layer. More specifically, the protein together with its hydration layer can be encapsulated into inverse micelles of polar lipids and subsequently transported into the nonpolar lipid sublayer.
Conclusions: The observed process can be considered as a passive way of protein transport to the tear film non-polar layer that preserves its bioactivity. The non-specificity of that process suggests that any small enough hydrophilic object adsorbing at the water-lipid interface may be transferred into the TFLL during the film restructuring due to eye blinks. [This research was supported by grant from Polish National Center of Science. Computations were performed with the use of Wroclaw Center for Networking and Supercomputing resources.]

EFFECTIVENESS OF DIFFERENT THERAPIES FOR DRY EYE DISEASE MANAGEMENT.

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Purpose: To measure and compare changes in dry eye symptoms and signs following different therapies.
Methods: 98 subjects with symptoms of dry eye were enrolled across 6 UK primary care sites and randomized into one of 3 management strategies: Saline drops; Hypromellose 0.3% drops; and HOW therapy (0.2% sodium hyaluronate drops, Omega-3 tablets, warm compress). SPEED questionnaire, Tear osmolarity (TO), tear breakup time (TBUT), corneal fluorescein staining and Meibomian gland dysfunction (MGD) were measured and compared at baseline, 1 and 3-months across the 3 therapies.
Results: At 3 months, SPEED score showed significant decrease with all 3 groups ($p<0.01$). Tear osmolarity decreased at 3 months (303.5±15.9mOsm/L) vs baseline (318±26.7mOsm/L) with HOW therapy ($p<0.01$), significantly greater than with saline (311.5±11.1 vs 313.8±13.3mOsm/L, $p<0.01$) or hypromellose (309.2±19.5 vs 319.7±19.1 mOsm/L). Significant reduction in corneal staining (by -2.0±3.2 units) and MGD grade (by -1.8±2.4 units) only occurred with HOW therapy and was greater than with saline (by 0.4±2.1, 0.1±2.3) or hypromellose (by -0.1±1.4, -0.1±1.8).
Conclusions: HOW therapy was more effective at reducing both the signs and symptoms of dry eye compared to a saline control or commonly prescribed hypermellose. The significant reduction in symptoms with all 3 therapies without concurrent improvement in signs highlights the lack of specificity of symptoms in DED management. Tear osmolarity allowed an objective and sensitive clinical quantification method to track therapeutic efficacy.
Financial Disclosure: The authors does not have any financial interest in the product or therapies used in the study. The study was sponsored by TearLab Corporation and Scope Ophthalmics.

TEAR FILM CHARACTERISTICS DURING WEAR OF DAILY DISPOSABLE CONTACT LENSES.

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Purpose: To evaluate the change from baseline (BL) in tear film osmolarity (TFO) and tear fluid pH (TFpH) with daily disposable (DD) silicone hydrogel (narafilcon A) contact lens (CL) wear over time in neophyte subjects.
Methods: 30 neophytes enrolled in an 8-visit, single-masked dispensing study. At BL, TFO (TearLab Osmolarity System) and TFpH (1mm glass micro-electrode, Thermo Scientific Orion 9810BN) were measured in the morning (AM) and evening (PM), 14 hours (h) after AM visit. Subjects were then fitted with narafilcon A (1-3 days after BL). At subsequent visits (7 and 14 days after CL dispensing), measurements were repeated in the AM without CL and in the PM after 14 h DD CL wear. Comparisons between each follow-up time point and BL were carried out using 95% confidence intervals (CI) constructed of least-square means differences from a linear mixed model. Equivalency was concluded if the CI was within the clinical equivalency margin (±12 mOsm/L for TFO and ±0.5 for TFpH).
Results: N=27 completed the study. At BL, average TFO was AM 301.7(SD14.7) and PM 300.2(8.95). After 14 days of CL wear, average TFO was AM 292.5(8.27) and PM 296.8(9.90). TFO at BL and at 14-days were statistically equivalent (AM 95% CI(-10.5,0.70), PM 95% CI(-11.3,-0.1)). At BL, average TFpH was AM 6.77(0.448) and PM 6.59(0.313). After 14 days of CL wear, the pH electrode malfunctioned; therefore, only 7-day data were available for analysis. After 7 days of CL wear, average TFpH was AM 6.76(0.215) and PM 6.86(0.180). TFpH at BL and at 7-days were statistically equivalent (AM 95% CI(-0.21, 0.20), PM 95% CI(0.07, 0.47)).
Conclusions: In neophyte subjects, short term wear of narafilcon A silicone hydrogel DD CL did not result in any statistically or clinically meaningful changes in TFO or TFpH. Study results demonstrated that narafilcon A wearers maintained tear film characteristics of osmolarity and pH similar to the natural eye. Study sponsored by Johnson & Johnson Vision Care, Inc. Jacksonville, FL USA.

SHORT-TERM REPRODUCIBILITY OF TEAR FLUID COLLECTION USING A MUC5AC MUCIN ASSAY

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Purpose: The assessment of tear fluid components is a valuable approach to understand ocular surface disease and to test the efficacy of novel therapeutics. However, the interpretation of the findings can be limited by the low sensitivity and poor reproducibility of the assay due to inter- and intra-individual variability. The aim of this study was to evaluate the short-term reproducibility of consecutive tear fluid collections using a MUC5AC mucin assay.
Methods: Tear samples were collected twice within an hour interval using microcapillary tubes. The surface of the eye was then gently washed with saline and the fluid recovered. The protein concentration in each sample was determined using the micro-bicinchoninic acid assay. Tear proteins were separated by agarose gel electrophoresis, transferred to nitrocellulose, and probed with the CLH2 antibody recognizing MUC5AC. Binding was detected using chemiluminescence.
Results: No statistical difference in protein concentration was found between the two consecutive tear fluid collections, although the inter-individual variability in each group was high, with coefficients of variation exceeding 30%. As determined by western blot, positive MUC5AC staining could be detected by using as little as 0.5 μl of tear fluid. Scatterplots showed a significant correlation in both protein and MUC5AC content following collection within an hour interval, indicative of consistent intra-individual reproducibility. Loss of detection sensitivity as a consequence of a decline in tear protein content following the saline wash resulted in lack of correlation for MUC5AC. Using μg of total protein in the tear fluid, instead of volume, as a calibrator for MUC5AC content slightly reduced the intra-individual reproducibility of the assay.
Conclusions: Regardless of the high inter-individual variability, repeated collection of tear fluid within an hour interval produces reproducible intra-individual data in terms of total protein and MUC5AC mucin content. These results further suggest that the normal composition of the tear fluid can be re-established within an hour of the initial collection.

CLINICAL OBSERVATION OF LEPTIN'S ROLE IN DRY EYE DEVELOPMENT.

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Objective: To observe the role of leptin in dry eye development by measuring the concentration of leptin in tears.

Methods: Tear samples were collected from 58 dry eye patients and 39 healthy volunteers at Ophthalmology Department of Peking University Third Hospital. Body weight, height, and body mass index (BMI) were measured in all subjects. Symptoms severity assessment (OSDI score), tear meniscus height, tear break up time(tBUT), cornea fluorescein staining, schirmer I test (ST-I) and impression cytology (IC) were also performed at the same time.

Results: The OSDI scores, cornea fluorescein staining scores and Nelson's grade in dry eye patients were significantly higher than those in healthy subjects ($Z=-5.976, p<0.001$; $Z=-2.063, p=0.042$; $Z=-4.138, p<0.001$); however, the tear meniscus height, tBUT, ST-I and density of conjunctival goblet cells were significantly lower in dry eye patients ($Z=-3.628, p<0.001$; $Z=-3.885, p<0.001$; $Z=-2.862, p=0.004$; $Z=-2.941$, $p=0.003$). Age, BMI, OSDI and cornea fluorescein staining scores were significantly adversely associated with leptin concentration in tears ($r=-0.340, p=0.001$; $r=-0.332$, $p=0.001$; $r=-0.258, p=0.011$; $r=-0.424, p<0.001$), and there was a significant positive correlation between ST-I and leptin concentration ($r=0.206, p=0.045$). Multiple linear regression analysis showed that there was a strong positive correlation between dry eye disease and leptin concentration ($t=2.343, p=0.021$).

Conclusion: This is the first study measuring leptin concentration in tears, and the positive correlation between leptin concentration and dry eye disease may reveal the fact that dry eye might be a causative factor of the increased leptin levels. Besides, leptin may play a role in repairing the ocular damage and relieving the symptoms of dry eye disease.

EFFICIENCY AND SAFETY OF SUBCONJUNCTIVAL INJECTION OF ANTI-VEGF AGENT – BEVACIZUMAB – IN TREATING DRY EYE.

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Purpose: Dry eye is a chronic inflammatory ocular surface disease with high prevalence. The current therapies for dry eye remain to be unspecific and not comprehensive. This study aims to explore safety and efficacy of a novel treatment – subconjunctival injection of bevacizumab – in dry eye patients.

Methods: Sixty-four eyes of 32 dry eye patients received subconjunctival injection of 100 μL 25 mg/mL bevacizumab. Dry eye symptoms, signs (corrected visual acuity, intraocular pressure, conjunctival vascularity, corneal staining, tear break-up time, Marx line score, and blood pressure), and conjunctival impression cytology were evaluated 3 days before and 1 week, 1 month, and 3 months after injection.

Results: Significant improvements were observed in dry eye symptoms, tear break-up time, and conjunctival vascularization area at all the visits after injection compared to the baseline ($P<0.05$). The density of the goblet cell increased significantly at 1 month and 3 months after injection ($P<0.05$). There was no visual and systemic threat observed in any patient.

Conclusion: Subconjunctival injection of 100 μL 25 mg/mL bevacizumab is a safe and efficient treatment for ocular surface inflammation of dry eye disease.

THE BACTERIAL PROFILES AMONG MGD, ADDE AND HEALTHY CONTROLS.

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Purpose: This study aims to explore the differences of bacterial profiles in the meibomian gland among meibomian gland dysfunction (MGD) patients, aqueous deficiency dry eye (ADDE) patients and healthy controls.

Methods: 86 eyes (left eye was randomly selected) of 86 subjects were recruited in the study. Among the 86 subjects, 17 subjects were healthy controls, 41 subjects were MGD patients and 28 subjects were ADDE patients. Ocular surface disease index (OSDI) questionnaire, tear break up time (TBUT), conjunctival injection, corneal staining, schirmer I test, lid margin and meibomian gland assessments were recorded before the bacterial sampling. After sterilizing the ocular surface (eyelid, lid margin and conjunctival sac), meibomian gland massage was made and meibomian gland secretion was collected for bacterial culture and 16s rRNA gene identification.

Results: The bacteria positive rate was 76.5% in healthy controls, two species were cultured which were *Staphylococcus epidermidis* (80%) and *Corynebacterium macginleyi* (20%). In ADDE patients, there were 11 kinds of bacteria identified which contained *Staphylococcus epidermidis* (48%), *Corynebacterium macginleyi* (8%), *micrococcaceae* (10.7%), *bacillus cereus* (8%), *Moraxella osloensis* (4%), *Staphylococcus hominis* (4%), *Micrococcus luteus* (8%), *Paenibacillus* (4%),*brevundimonas* (4%), *Corynebacterium* (4%), *Nocardiopsis dassonvillei* (4%) . The total positive rate was 89.3%. In MGD patients, 17 kinds of bacteria were identified which included *Staphylococcus epidermidis* (21.2%), *Corynebacterium macginleyi* (9%), *Staphylococcus aureus* (15.2%), *Staphylococcus capitis* (3%), *micrococcaceae* (18.2%), *Microbacterium* (6.1%), *bacillus cereus* (3%), *Bacillus circulans* (3%), *Moraxella osloensis* (9%), *Lysinibacillus* (3%), *Staphylococcus hominis* (9%), *Micrococcus luteus* (6.1%), *Corynebacterium pseudodiphtheriticum* (3%), *Bacillus thermoamylovorans* (3%), *Xanthomonadaceae* (3%), *Staphylococcus warneri* (3%), *Paenibacillus* (3%). The total positive rate was 80.5%. Among three groups, there was no significant difference on the total positive rates ($P>0.5$), while the difference of *Staphylococcus epidermidis* positive rate was significant ($P<0.5$). The bacterial combined growth (more than one bacterium in one eye) was more common in MGD patients with no significant difference ($P>0.5$).

Conclusion: The total bacterial positive rates were similar among healthy controls, ADDE patients and MGD patients, while the bacterial constitution varied a lot.

THE EFFECTS OF 3% DIQUAFOSOL SODIUM EYE DROPS ON TEAR FUNCTIONS AND OCULAR SURFACE IN SOD-1 KNOCK OUT MICE TREATED WITH ANTI-GLAUCOMA EYE MEDICATIONS

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Purpose: To investigate the effect of 3% diquafosol sodium eye drops on the tear functions and ocular surface epithelium in SOD-1 KO mice treated with anti-glaucoma eye drops.

Methods: 40 week old SOD-1 KO mice were divided into 4 groups as: Group I: Control group with no eye drop application Group II: antiglaucoma eye drops (latanaprost eye drops once a day+0.5% timolol eye drops b.i.d+dorzolamide eye drops t.i.d), Group III: 2 weeks of antiglaucoma eye drops followed by addition of 3% diquafosol sodium eye drops (6 times/day) for 2 weeks, Group IV: Simultaneous application of antiglaucoma and 3% diquafosol sodium eye drops for 4 weeks. All mice underwent tear film break up time measurements,fluorescein and Lissamine green corneal stainings and phenol red test before and after eye drops. Eye globe specimens underwent HE and Periodic Acid Schiff (PAS) stainings and immunohistochemistry (IHC) stainings for muc5AC.

Results: Mice in Group IV had significantly better tear stability and lesser corneal staining scores compared to mice in Group II ($p<0.05$). The

conjunctival epithelium showed stratification and abundance of goblet cells in Group IV whereas the conjunctival epithelium showed thinning with desquamation and only a few goblet cells in Group II. IHC staining for muc5 AC supported the observations from PAS stainings.
Conclusion: Our findings suggest that simultaneous administration of 3% diquafosol sodium eye drops with topical anti-glaucoma drops have favourable effects on the corneal epithelium against ocular surface toxicity inflicted by the glaucoma eye drops
(This research was supported by grant from Santen Pharmaceuticals.)

ASSESSMENT OF THE IMPACT OF SACCADE ON MUCOAQUEOUS SUBPHASE.

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Purpose: It has been reported that the pre-corneal tear film, comprising the lipid layer and mucoaqueous subphase (MAS), behaves like one body (i.e., the 'Fluid Shell'), moving with the cornea during horizontal saccades. Moreover, it has been found that meniscus-induced tear-film thinning occurs in the MAS, and presents as a dark arc or band during horizontal or downward saccades. In this study, the impact of saccades on the MAS was quantitatively assessed.
Methods: In this study, the left eyes of 17 subjects [8 males and 9 females, mean age: 31.4±8.4 (SD) years] were enrolled. In each subject, a digital slit-lamp was used to assess the impact of temporal (T), upward (U), and downward (D) saccade on the MAS based on the frequency of the emergence of the dark band (or dark arc) after each return saccade. A pause for 1 or 3 seconds was imposed at the end of each primary saccade. Evaluation was done by counting the total score via dividing the cornea into 5 areas (upper, lower, temporal, nasal, and central) and allotting 0 or 1 point, respectively, when the dark band (or dark arc) was absent or present.
Results: The total score in D for 1-second was significantly greater than that in D for 3-second ($p<.05$). However, no significant differences were found in T or U. For the 1sec pause, the total score for D was significantly greater than that for T or U ($p<.05$). A similar trend was observed in the 3-second pause.
Conclusions: This study demonstrated the greater impact of the D saccade on MAS as compared to that of the T or U saccades, thus possibly indicating that the D saccade has a greater impact on the quality of vision, such as when visual display terminal work is being performed.

DIETARY FACTORS ASSOCIATED WITH MEIBOMIAN GLAND AND TEAR FUNCTIONS IN AN ADULT POPULATION.

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Purpose: To investigate associations between dietary intakes and meibomian gland (MG) functions and structure in an adult population.
Methods: 184 subjects (108 females) with an age range of 25-65 years and normal ocular and systemic history were recruited. At a single visit, following ocular surface variables were collected on both eyes: tear osmolarity, meniscus height, non-invasive tear break-up-time (NI-TBUT), meibum quality (MQ) and MG expressibility (MGE) of the lower lid, and MG drop-out of both upper and lower lids. At the end of the visit, all subjects completed the dietary questionnaire for epidemiological studies (DQES), developed by the Cancer Council Victoria, Australia. The DQES assesses usual eating habits over one year and covers a food list of 74 items and 6 types of alcoholic beverage. Data were examined for associations between each food item and clinical variables using General linear model of regression and Pearson correlation.
Results: There was no significant association between diet and age, tear osmolarity or MG drop-out. Increased MQ severity was associated with lower intake of Riboflavin and Thiamin ($r \leq -0.17$, $p \leq 0.03$), while increased MGE severity was associated with lower intake of Niacin, Iron, Zinc, proteins, cholesterol and Palmitoleic acid ($r \leq -0.17$, $p \leq 0.04$). Tear meniscus height was negatively associated with an overall consumption of fats and essential fatty acids (FAs) such as alpha-linoleic, dihomo-gammalinolenic and arachidonic acid ($r \leq -0.21$, $p \leq 0.03$); while NI-TBUT was positively associated with consumption of FAs such as Pentadecanoic and Heptadecanoic acid ($r \leq 0.18$, $p \leq 0.04$).
Conclusions: This study reinforces the suggestion that diet influences meibomian gland function and tear film behaviour. Our findings show that greater intake of omega-6 derivative fatty acids may result in tear film instability. Further research addressing dietary profiling and essential supplements for dry eye sufferers may be helpful in clinical counselling.

RELATIONSHIP BETWEEN FLUORESCEIN BREAKUP PATTERNS AND CLINICAL MANIFESTATIONS IN DRY EYE.

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Purpose: To investigate the relationship between fluorescein breakup patterns (FBUPs) and clinical manifestations in dry eye cases.
Methods: In 106 eyes of 106 subjects (19 males, 87 females; mean age: 64.2 years), FBUPs were categorized into 1 of the following 5 types [Area (A): 19; Spot (S): 22; Line (L): 24; Dimple (D): 19; Random (R): 22 eyes]. In all eyes, dry-eye-related symptoms using the visual analog scale (VAS, mm), tear meniscus radius (TMR, mm), interference grade (IG) (1-5; 1 being the best) and spread grade (SG) (1-4; 1 being the best) of the tear film lipid layer, non-invasive breakup time (NIBUT, seconds), FBU time (FBUT, seconds), corneal epithelial damage (CED) (15 points max), ocular surface epithelial damage (OSED) (9 points max), and the Schirmer 1 test (ST1, mm) were examined and compared between each FBUP.
Results: In each FBUP, dryness and eye fatigue were the severest symptom. Characteristic symptoms were sensitivity to light, heavy eyelids, pain, foreign body sensation, difficulty opening the eye, and discharge for A, heavy eyelids for S, foreign body sensation for L. Statistically significant differences were found in TMR (A-S, -D and -R; L-R), IG (A-all other FBUP; L-S and -D) and SG (A-all other FBUPs), FBUT (A-L, -D, and –R; S-D and –R; L-R; D-R) and NIBUT (A-all other FBUPs; S-D and-R, and L-R), CED (A-all other FBUPs; L-S, -D, and -R) and OSED (A-S, L, and D; L-S and D, and -R), and ST1 (A-S, D, and -L) ($p<0.05$ in each comparison).
Conclusions: The 5 different FBUPs constituted different groups, reflecting different pathophysiologies.
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ANALYSIS OF OXIDATIVE STRESS MARKERS IN TEARS OF THYROID-ASSOCIATED OPHTHALMOPATHY ACCORDING TO DISEASE ACTIVITY.

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Purpose: To evaluate the oxidative stress markers in tears of thyroid-associated ophthalmopathy (TAO) according to disease activity.
Methods: This study included 47 patients who were diagnosed with TAO and 25 control subjects. According to clinical activity score (CAS), TAO patients were divided into two groups; 35 eyes of 20 patients in active group (CAS≥3), and 48 eyes of 27 patients were inactive group (CAS<3). Tear 8-oxo-2'-deoxyguanosine (8-OHdGd), 4-hydroxynonenal (4-HNE), and malondialdehyde (MDA) levels were measured and compare between each group. In addition, correlations between CAS and oxidative stress markers were analyzed in the active and inactive TAO groups. Results. In the active and inactive TAO and control groups, the levels of 8-OHdG were 215.1±35.6, 123.4±22.6, and 56.3±16.8 ng/mL ($p<0.01$, ANOVA), 4-HNE levels were 33.4±8.3, 28.4±8.1, and 11.4±5.8 μg/mL ($p=0.01$), and MDA levels were 22.5±4.6, 13.5±3.9, and 5.3±1.3 pmol/mg ($p<0.01$), respectively. In the active TAO group, CAS was positively correlated with 8-OHdG ($r=0.68$, $p<0.01$), 4-HNE ($r=0.49$, $p<0.01$), and MDA ($r=0.51$, $p<0.01$). However, there was no significant correlation in the inactive TAO group.
Conclusions: The levels of 8-OHdG, 4-HNE, and MDA in the tear fluid increased in TAO patients, especially in the active TAO group. The levels of oxidative stress markers correlated significantly with CAS and could reflect the severity of the disease in the active stage of TAO. [Commercial relationships or grants support: none]

THE EFFECT OF ORAL ZANTHOXYLUM SCHINIFOLIUM SEED OIL IN INDIVIDUALS WITH DRY EYE DISEASE.
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Purpose: To evaluate the clinical efficacy and safety of a 10-week oral consumption of Zanthoxylum schinifolium seed oil (ZSO) in patients with mild dry eye disease.
Methods: In this double-blinded, randomized and placebo-controlled trial, 20 participants experiencing dry eye symptoms were recruited and randomly assigned to consume 4 g/day of either ZSO or soy bean oil (SBO) as a placebo for 10 weeks. Post-treatment dry eye symptoms and objective signs were then evaluated, and laboratory analyses of blood lipids and inflammatory and oxidative stress markers were performed.
Results: All participants completed the study. Successful compliance with ZSO treatment was confirmed by measuring the omega-3 fatty acid enrichment of the erythrocyte membrane. Significantly improved Ocular Surface Disease Index scores and decreased corneal fluorescein staining compared to baseline were observed in the ZSO group 10 weeks after treatment ($p=0.005$ and 0.014, respectively). However, no significant differences were observed between the ZSO and placebo groups. Tear break-up time and Schirmer scores showed no differences between two groups. Consumption of ZSO significantly decreased tear IL-1 beta concentration ($p=0.031$). Antioxidant markers, serum MDA and oxidized LDL, did not change significantly. However, significant increases in the total and LDL-cholesterol were observed in the placebo group, but not in the ZSO group.
Conclusions: The use of ZSO is effective in patients with mild dry eye disease and ZSO could be an excellent dietary source for omega-3 fatty acid supplementation. [This research was supported by Fund of Chonbuk National University Hospital Research Institute of Clinical Medicine.]

SJÖGREN SYNDROME AND COMMENSAL MICROBIOTA
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Purpose: To investigate the role of the gut microbiota in the development of dacryoadenitis in the CD25KO model of Sjögren Syndrome.
Methods: Eight-week old germ-free (GF) CD25 knock-out (KO) mice were compared to CD25KO mice raised in specific pathogen free (SPF) conditions. Corneal barrier function was assessed by dye staining. Conjunctival goblet cell density was counted in periodic acid Schiff stained sections. Total cell infiltrates were visualized in histologic sections stained for H&E. $CD4^+$T cells were isolated from cervical lymph nodes (CLN) and adoptively transferred (AT) into RAG1KO recipients. T helper (Th) phenotype in lacrimal gland (LG) and CLN of recipients was investigated by intracellular staining 5 weeks post-transfer.
Results: GF CD25KO mice have significantly lower number of goblet cells and significantly greater corneal barrier disruption and LG infiltration than CD25KO SPF mice ($P<0.05$ for all). RAG1KO recipients of adoptively transferred GF CD25KO $CD4^+$T cells had significantly greater total LG infiltration and loss of acini than recipients of SPF CD25KO $CD4^+$T cells. This was accompanied by greater percentage of $CD4^+$ $IFN\text{-}g^+$ and $CD4^+IL\text{-}17^+$ cells in the LG of GF recipients compared to SPF recipients. Reconstitution of KO mice with total bacterial communities improved corneal barrier function.
Conclusions: Lack of commensal bacteria accelerates the onset and severity of dacryoadenitis and generates autoreactive $CD4^+$T cells with greater pathogenicity. These results indicate the commensal bacteria or products secreted by them have immunoregulatory properties that protect exocrine glands in the CD25KO SS model. Support: Biology of Inflammation/BCM (CSDP and SCP), NIH T32AI053831 (FB), NEI/NIH EY-002520, RPB, the Oshman Foundation, William Stamps Farish Fund and the Hamill Foundation.

OCULAR CICATRICIAL PEMPHIGOID: INDUCED BY BIOLOGICS.
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Purpose: Biologics can induce disorders which they also can cure. IN the filed of ophthalmology that has been shown for uveitis, but never for ocular cicatricial pemphigoid (OCP).
Methods: Case report
Results: We present a 47 year old patient who has developed clinical signs of an OCP with positive linear IgG staining of the basal cell membrane of the conjunctiva under the treatment of the anti-TNF alpha blocking treatment (adalimumab), which was followed by secukinumab (anti-IL17) since 11/2015. That treatment was started due to psoriasis and had been effective. Despite stop of treatment with the biologic the inflammation continued, so that a treatment with mycophenolate acid was initiated, with slow reduction of the activity.
Conclusions: Development of OCP with 47 years is extremely uncommon.To our knowledge this is the first report of OCP, developed under treatment with biologics. But there are a few reports about dermatological chronic bullous disorders published.

MUTATIONS IN THE QUORUM SENSING GENE LASR ARE ASSOCIATED WITH WORSE CLINICAL OUTCOMES IN *PSEUDOMONAS AERUGINOSA* KERATITIS.
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In P. aeruginosa, a hierarchically arranged quorum sensing cascade regulates the coordinated production of secreted virulence factors. In the Steroids for Corneal Ulcer Trial (SCUT), 22 of 101 P. aeruginosa clinical isolates had colony morphology characteristics of strains with loss-of-function mutations in lasR, the gene that encodes a quorum sensing master regulator. We found that all 22 isolates contain nonsynonymous substitutions in LasR domains important for protein function, and we characterize these isolates as being deficient in production of quorum sensing-regulated protease and rhamnolipids. We additionally show that lasR mutants produce increased amounts of CupA fimbriae when compared with clinical isolates from the study with functional LasR. Finally, we show in a retrospective analysis that the presence of lasR mutants in infections was associated with worse vision at presentation and after three months treatment. We hypothesized that there is selection for strains with reduced LasR activity in the context of corneal infections and demonstrate that quorum sensing status can affect patient outcomes.

RNASEQ PROFILING OF REGENERATING LACRIMAL GLAND IDENTIFIES MYOEPITHELIAL CELLS AS POTENTIAL PLAYERS IN TISSUE REPAIR.

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Purpose: Murine lacrimal gland (LG) is capable of repair following experimentally induced injury. The repair starts 2-3 days following injury and is usually completed by the 5th or 7th day. The purpose of the present studies was to use RNAseq technology to identify genes involved in LG repair.

Methods: The LGs of BALB/c mice were injected (2 μl) with either saline (control) or interleukin 1 alpha (1 μg). The LGs were harvested 1, 2, 3, 4, 5, 7, or 14 days following injury and RNA extracted. Five hundred ng of RNA were used to construct sequencing libraries. The products were purified and enriched with PCR for 12 cycles to create the final cDNA libraries which were quantified using Illumina Library Quantification Kit. STAR aligner was used for genome alignment and to generate BAM files. RSEM was used for gene expression quantification and DESeq2 for downstream differential expression analysis.

Results: Of a total of 43,346 Coding DNA Sequences analyzed, the expression of only 2,188 was statistically significantly different compared to saline injected LGs. The majority of the genes differentially expressed at day 1 and 2 were associated with inflammation. Interestingly, the expression of 35 muscle-related genes was up-regulated mostly at day 2, which is when LG repair is initiated, implying the involvement of myoepithelial cells in LG regeneration. Between day 4 and 5 (tissue repair phase), there was selective upregulation of extracellular matrix (ECM) macro-components (collagens, elastin, tenascins, etc.), enzymes involved in synthesis of ECM components (lysyl oxidase) and ECM remodeling enzymes (MMPs, ADAMs, and ADAMTS).

Conclusions: Although the LG undergoes dramatic histological alterations during regeneration, the expression of only a few genes seems to be differentially altered between 3 and 7 days. The selective up-regulation of muscle related genes at day 2 suggests the involvement of myoepithelial cells in LG repair. Supported by NIH 2R01EY012383.

OCULAR SURFACE CHANGES IN PROFESSIONAL MOTORSPORT ATHLETES.

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Purpose: Ocular surface conditions and spontaneous blinking are essential for maintaining clarity of vision during driving. Unfortunately there are very few data in the literature showing possible effects of stressful conditions on the ocular surface. Therefore, we decided to build a project to study eventual ocular surface changes in elite motorsport athletes and their effect on quality of vision after a full race session.

Methods: Contrast sensitivity, spontaneous blinking rate (SBR) in standing and driving position, conjunctival hyperemia, and tear film osmolarity were evaluated in Cal Crutchlow, a British top rider of the LCR Honda team competing in world championship since 2011. The test were conducted in Jerez de la Frontera before the race (normal conditions) and 30 minutes after the end of the 29 laps competitions. Results were compared to age-matched subjects.

Results: The 30-year old rider showed a significant lower SBR rate in normal conditions compared to controls, especially in driving position. After the race the SBR values were significantly increased. Contrast sensitivity and conjunctival hyperemia did not show any changes compared to controls and after the race. In normal conditions tear osmolarity was higher than controls, while after the race demonstrated lower values.

Conclusions: The first part of our project showed that SBR rate is clearly different in a top rider and that a stressful event- like the race - can affect this behavior. Further studies are necessary to confirm these results and to better understand eventual changes of the ocular surface system.

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THE EFFECTS OF INTRANASAL NEUROSTIMULATION ON TEAR PRODUCTION AND CLEARANCE AND CONJUNCTIVAL GOBLET CELL SECRETION.

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Purpose: To investigate the effects of the Oculeve Intranasal Lacrimal Neurostimulator (ILN) on aqueous tear production, tear clearance and conjunctival goblet cell (GC) secretion.

Methods: Twenty-three subjects (5 normal and 18 dry eye) were enrolled in a three-visit study consisting of one screening and two separate randomized-masked ILN treatments (sham extranasal or intranasal). Tear meniscus height (TMH) was measured by AS-OCT before and after applications. Impression cytology (IC) was taken from the bulbar conjunctiva of the right eye for PAS and from the left eye for MUC5AC mucin immunostaining at baseline and after each treatment. The ratio of degranulated to non-degranulated GCs was measured as a marker of secretion. Tear clearance was measured fluorometrically in tear samples collected 5 and 15 minutes after instillation of 1 μl of 1% fluorescein into the inferior fornix.

Results: There was a statistically significant increase in TMH after intranasal compared to sham treatment in the normal and dry eye groups ($p= 0.04$ for both). A significantly higher ratio of degranulated to non-degranulated GCs was noted in MUC5AC-stained IC specimens from the dry eye group after intranasal stimulation (4.71 ± 4.48) compared to those taken at baseline (0.74 ± 0.62, $p< 0.001$) and after sham treatment (0.57 ± 0.54, $p< 0.001$). Tear fluorescence clearance was significantly greater 5 and 15 minutes after the instillation of fluorescein following intranasal compared to sham treatment ($p< 0.05$).

Conclusions: The Oculeve ILN not only increases aqueous tear production and clearance; it also stimulates conjunctival goblet cell mucin secretion, offering a promising new approach to treatment of dry eye. (This study was sponsored by Allergan plc, Dublin, Ireland. All authors met the ICMJE authorship criteria. Neither honoraria nor payments were made for authorship.).

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