The International Symposium on Ocular Pharmacology and Therapeutics

December 9-12, 2010, Macau, China

ISOPT

Program & Abstracts

Contents

Welcome

It is our pleasure to welcome you to the first Asian chapter of the International Symposium on Ocular Pharmacology and Therapeutics (ISOPT). This is the first ISOPT meeting in Asia, following eight previous European meetings that have become a tradition in the education and update activities in ophthalmic therapeutic modalities.

The increased activity in ophthalmic research is reflected in the long list of world-wide clinical studies in their various stages: hundreds of studies of various aspects of glaucoma, ocular surface, cornea and dry eye. Searching the web for retina clinical studies yields additional long lists of studies for macular edema and approximately 70 studies for AMD. This extensive clinical activity previews changes that will soon reshape the practice of ophthalmology.

In addition to the main theme of ocular therapeutics, ISOPT 2010 focuses on the latest novelties in medical devices including innovations in ocular drug delivery such as slow release devices implanted in the eye and new imaging technology that improve our capability to evaluate the effect of drugs and other therapeutic modalities.

ISOPT Asia will follow the footsteps of ISOPT 8th in Rome allowing participants to scan the near future with a critical look at the best current practices available to our patients today. The ISOPT program is geared to provide a continuum, from basic development of therapeutic concepts/ compounds to their utilization as drugs and technologies in clinical practice. Considerations of drug development will be discussed with the main players in the field i.e. researchers based in the academia, clinical investigators, regulatory affairs and industry professionals. Topics on drug development process of mutual interest such as the evolution of endpoints will be raised in open round table discussions.

Asia has become a center of excellence in clinical research and innovative ideas. The interplay of innovative ideas on one side and traditional medicine on the other may offer new venues of development and progress. ISOPT is therefore seeking to become a foundation of combined east and west wealth of ocular therapeutic knowledge.

In keeping with our tradition, ISOPT organization is geared to provide a comfortable atmosphere for open discussions and face to face updates. The current meeting venue, The Venetian Macau Resort Hotel, offers magnificent options for any sort of formal and informal meetings that will complement ISOPT's main hall activities.

The ISOPT organizing committee and faculty is committed to bring most acclaimed speakers to provide most recent updates of ocular therapeutics, medications and disease management.

We welcome you to join us in Macau for the initiation of the Asia chapter of ISOPT meetings.

S. Krupsky R. Neumann

Sara Krupsky, MD **Ron Neumann, MD**

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R. Neumann, Israel

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H.S. Uy, Philippines
R. Vogel, USA
M. Zierhut, Germany
X. Zhang, China

General Information

Venue

The Venetian Macau Resort Hotel
Estrada da Baía de N. Senhora da Esperança, s/n,
Taipa, Macau SAR, P.R. China
Tel: +853 2882 8888
Email: inquiries@venetian.com.mo
Web: www.venetianmacao.com/en

Language

English is the official language of the congress.

Registration and Hospitality

The registration desk will be situated in the entrance to the meetings halls and will be open as follows:

Wednesday, 8 December	16:00 – 18:30	Friday, 10 December	07:00 – 17:45
Thursday, 9 December	07:00 – 17:45	Saturday, 11 December	07:00 – 16:00

Symposium Kit and Name Badge

Upon registering you will receive your kit, containing your personal name badge. Please remember to wear your name badge to all symposium activities and to the Welcome Reception.

Please note there will be a charge of $50 to replace lost badges.

Internet Facilities

Free internet and e-mail facilities are located in the exhibition area and are available during exhibition opening hours. Please be considerate of fellow participants when using the facilities.

Certificate of Attendance

A certificate of attendance will be available at the registration desk on Saturday, Dec. 11th, noon time.

Exhibition Opening Hours

All participants are invited to view the exhibition in the hotel. Exhibition opening hours are as follows:

Thursday, 9 December	08:00 – 17:00
Friday, 10 December	09:00 – 17:00
Saturday, 11 December	09:00 – 17:00

Oral Presentations

If using a PowerPoint presentation, please note you need to bring it on a CD or on a Memory stick (using the USB port in the computer) and load it on one of the Symposium computers in the Speaker Preview Room, at least 1 hour before the start of the session.

If combining video films with PowerPoint, please make sure to check it in the session hall where your lecture is taking place during a coffee or lunch break prior to your session, at least 30 minutes before the start of the session.

Please note: You cannot use your own personal laptops for the presentation, only the computers available at the Preview room.

E-Poster Presentations

E-posters will be available for viewing through the conference in the exhibition area.

ISOPT Symposium Secretariat

Paragon Conventions
18, Avenue Louis-Casai, 1209 Geneva, Switzerland
Web: www.isopt.net, Email: isopt@isopt.net

Social Events

Welcome Reception
sponsored by
BAUSCH + LOMB

18:00 – Thursday, December 9

All registered participants are invited to the Welcome Reception at the exhibition area.

Lunches

Friday, December 4 & Saturday, December 5 – Lunch will be provided during the Allergan Sponsored Sessions

Coffee & Refreshments

Coffee will be served in the exhibition area at the times indicated in the Scientific Program.

Satellite Symposium – December 12, 2010

Harbour Grand Kowloon Hong Kong
08:00-13:00
Meeting Room – Salon III, 1/F

The satellite meeting will include the E-posters present during the meeting, and will provide ample time and a comfortable environment to review them.

Sponsors and Exhibitors

Senju Pharmaceutical CO., LTD.

Contact Name: Ms. Reiko Mori (Licensing)
Address: 2-5-8, Hiranomachi, Chuo-Ku, Osaka, 541-0046, Japan
Telephone +81 662019698
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Contact Name: Krishna Sai
Address: 460 Alexandra Road; #05-01A,
PSA Building, Singapore 119963
Telephone: +65 6747 7077
fax: +65 6276 8153
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Our robust research and development investment upholds our unwavering commitment to advancing eye care treatments. Visual impairment due to the diseases affecting the eye affects millions of patients each year. Over the next decade, major progress will be made in the management of these diseases affecting the eye, and Allergan expects to be in the forefront of these advances.

In Asia Pacific, Allergan established its first office in Australia in 1968, expanding its presence to having more than 900 employees cover 11 markets directly today. It is the company's fastest-growing region and provides a broad portfolio of eyecare, neuroscience, medical aesthetics and obesity products.

Bausch & Lomb

Contact Name: Wicks Chung
Address: Room 1502-07, 15/F., One Kowloon,
1 Wang Yuen Street, Kowloon Bay, Hong Kong
Telephone +85 222133172
fax: +85 222133672
E-mail: wicks.chung@bausch.com
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Contact Name: Karin Cebulla
Address: Göschwitzer Strasse 51-52, 07745 Jena, 07745, Germany
Telephone +49 3641220334
fax: +49 3641220112
E-mail: k.cebulla.@meditec.zeiss.com
website: www.meditec.zeiss.com

Medical systems from Carl Zeiss allow doctors to further improve the efficiency, safety and reliability of diagnosis and treatment: with innovative solutions for ophthalmology and ophthalmic surgery and visualization systems.

TRB Chemedica International SA

Contact Name: Xavier DAL MOLIN
Address: Rue Michel-Servet 12, P.o. box 352,
CH-1211 Geneva 12, Switzerland
Telephone: +41(0) 227034937
fax: +41(0) 227034901
E-mail: xavier.dalmolin@trbchemedica.com
Website: http://www.trbchemedica.com/

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- VISIOL®: a viscoelastic to aid surgery of the anterior & posterior eye segment

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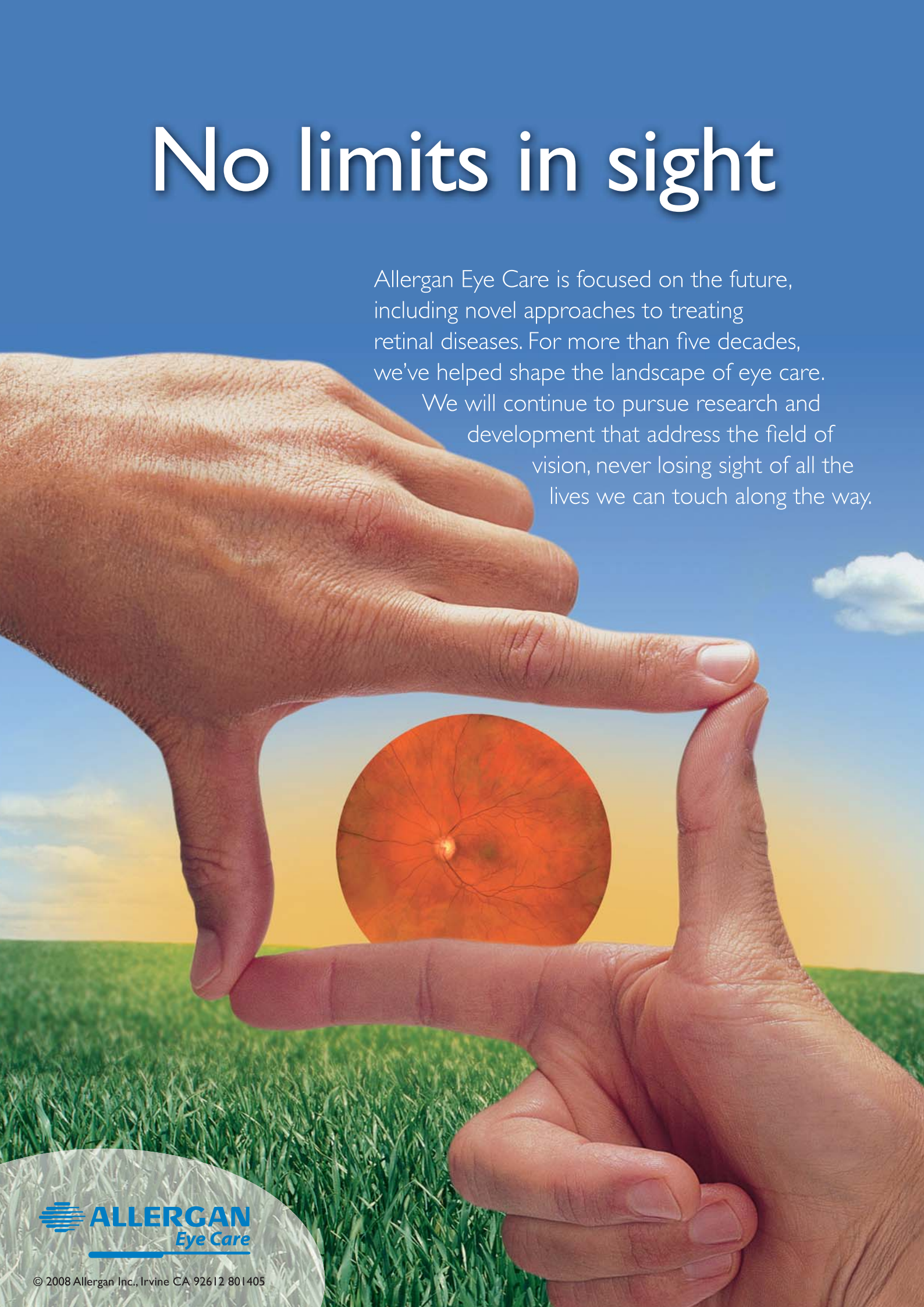
ISOPT

Scientific Program

No limits in sight

Allergan Eye Care is focused on the future, including novel approaches to treating retinal diseases. For more than five decades, we've helped shape the landscape of eye care. We will continue to pursue research and development that address the field of vision, never losing sight of all the lives we can touch along the way.



ALLERGAN
Eye Care

Thursday, December 09, 2010

09:00 - 09:45 **IP and the Path to Commercialization & Free Papers** **Hall A**
Chair: Roger Beuerman, Singapore

09:00 **Success in Public Private Partnerships in Collaborative Research**
M. Tabiin
Singapore

09:12 **Contractual and Commercial Aspects of Collaborative Research**
M. Entzeroth
Singapore

09:24 **Investigation of the Effects of Ultrasound on Protein Transport through the Sclera**
Y. Chau; A.C.Y. Cheung; Y. Yu
Hong Kong

09:34 **Ophthalmic Medication Adherence Behaviors among Asian Patients in America**
S. Kwok[1]; A. Tam[2]
[1]University of California, Berkeley, San Francisco, CA, USA; [2]Univeristy of California, Berkeley, San Francisco, CA, USA

09:00 - 09:45 **Dry AMD** **Hall B**
Chair: Baruch D. Kuppermann (USA)

09:00 **Overview of Pathways and Treatments for Dry AMD**
David Boyer
USA

09:11 **Complement Inhibition for AMD - Overview**
Francine Behar-Cohen
France

09:22 **A Phase 2 Study of Encapsulated CNTF Secreting Cell Implant (NT-501) in Patients with Geographic Atrophy Associated with Dry AMD**
Baruch Kuppermann
USA

09:33 **Macular Pigment Imaging in AREDS II Participants: Baseline Studies from an Ancillary Study at the Moran Eye Center**
P.S. Bernstein; F. Ahmed; A. Liu; M. Sharifzadeh; I. Ermakov; W. Gellermann
USA

09:45 - 10:30 **Endpoints in Clinical Trials** **Hall A**
Chair: Paul Kaufman (USA)

09:45 **NEI and FDA Hold Second Glaucoma Endpoints Meeting**
Paul Kaufman
USA

10:00 **Endpoints in Ophthalmology Trials – A Regulatory Perspective from Europe**
K. Wickstrom
Sweden

09:45 - 10:30 **Infectious Uveitis** **Hall B**
Chair: Ron Neumann (Israel)

09:45 **Corticosteroid Drug Delivery Systems for Inflammatory Eye Diseases**
Harvey Uy
Philippines

10:00 **Ocular Tuberculosis: Diagnosis and Treatment**
P. Choopong
Thailand

10:15 **PCR-Guided Management of Anterior Uveitis**
G. Cheung
Singapore

10:30 - 11:00 **Coffee Break** **Exhibition Hall**

11:00 - 11:45 **Latest Thinking on Mechanisms in Glaucoma** **Hall A**
Chair: Jost Jonas (Germany) & Xiulan Zhang (China)

11:00 **TRPC6: A Potential Target for Human Glaucoma**
X. Zhang
China

11:09 **The Activation and Modulation of Astrocyte in Glaucoma**
J. Wu
China

11:18 **Trabecular Meshwork Outflow / Gene Therapy / Cochlin Update**
P. Kaufman
USA

11:27 **Amyloid Beta, A Potential Target of Neuroprotection in Glaucoma?**
J. Ge
China

11:36 **Ocular Perfusion Pressure and Hemodynamics in Glaucoma**
Alon Harris
USA

11:00 - 11:45 **Inhibition of Diabetic Retinopathy** **Hall B**
Chair: Arup Das

11:00 **Diabetic Retinopathy and Inihibitors of RAF Kinase**
R. Kowluru; G. Mohammad
USA

11:11 **Does IGFPB3 have a Role in the Inhibition of Diabetic Retinopathy?**
T. Chan-Ling[1]; P. Hu[1]; E. McFarland[1]; J. Kielczewski[2]; L. Shaw[2]; Y. Jarajupu[2]; S. Caballero[2]; S. Li Calzi[2]; T. Gardiner[3]; S. Firth[1]; R. Baxter[1]; M. Boulton[2]; M. Grant[2]
[1]Australia; [2]USA; [3]Northern Ireland

11:22 **Targeting the GAPDH Nuclear Translocation Pathway as a Potential New Strategy to Prevent Hyperglycemia-Induced Retinal Damage**
S. Mohr
USA

11:33 **Role of Arginase in Diabetes-Induced Retinal Vascular Dysfunction**
R.W. Caldwell; H.F. Toque; W Zhang; S. Elms; R.B. Caldwell
USA

11:45 - 12:30 **New Drug Classes on the Horizon for Glaucoma Therapy** **Hall A**
Chair: Jost Jonas (Germany) & Xiulan Zhang (China)

11:45 **Options for Localized Drug Delivery in Glaucoma**
T. Wong
Singapore

12:00 **Wound Modulation in Glaucoma Surgery**
K. Nagpal
India

12:15 **Statins and Glaucoma**
D. Leung
Hong Kong

11:45 - 12:30 **Anti-VEGF Drugs** **Hall B**
Chair: Xiaoxin Li (China)

11:45 **A Novel Thermo-Sensitive Biodegradable Hydrogel for Extended Release of Bevacizumab**
Y-S. Hwang; Y-S. Chiang; C-C. Lai
Taiwan

11:56 **Molecular Design and Research Development of KH902, A Novel Multi-target Drug against Neovascular Age-related Macular Degeneration**
D. Luo; M. Zhang; X. Hao; Z. Ke; X. Li
China

12:07 **Preoperative Use of Intravitreal Bevacizumab for Severe Retinopathy of Prematurity**
P-Q. Zhao; Y. Xu
China

12:18 **The Treatment of ROP Type1: Laser or Anti-VEGF**
X. Li
China

12:30 - 14:00	**Lunch Break**	
14:00 - 15:30	**Dry Eye Disease/Biomarkers for Ocular Surface Disease** Chair: Penny Asbell (USA)	**Hall A**
14:00	**Proteomics for the Diagnosis of Ocular Surface Disease** Roger Beuerman Singapore	
14:11	**Protein Profiling of Meibum Using Mass Spectrometry and Quantitative Protein Arrays** Kelly Nichols USA	
14:22	**Protein Biomarkers and Tear Film and Dry Eye Disease** Franz Grus Germany	
14:33	**Impression Cytology and Dry Eye Disease** P. Asbell USA	
14:00 - 15:30	**Diabetic Macular Edema** Chair: Baruch D. Kuppermann (USA)	**Hall B**
14:00	**Anti-Vascular Endothelial Growth Factor Plus Laser in Diabetic Macular Edema** Raja Narayanan India	
14:09	**Overview of Steroids for Diabetic Macular Edema** M. Gillies Australia	
14:18	**Ozurdex for DME** Baruch Kuppermann USA	
14:27	**Iluvien FAME for DME** David Boyer USA	
14:36	**How do Steroids Work on Macular Edema?** Francine Behar-Cohen France	
14:45	**The Potency of Glucocoticoids: What do We Measure?** Francine Behar-Cohen France	
14:54	**Lucentis for DME Clinical Trials** Michaella Goldstein Israel	
15:03	**DME and VEGF Trap-Eye Phase 2: DA VINCI Study** Raja Narayanan India	
15:12	**Role of The Lallikrein-Kinin System in Diabetic Retinopathy** Pierre Belichard France	
15:30 - 16:00	**Coffee Break**	**Exhibition Hall**

16:00 - 17:30 **Reading Centers** **Hall B**
Chair: Ronald Danis (USA)

16:00 **Regulatory Considerations on Efficacy and Safety Endpoints Based on Imaging Techniques**
Kerstin Wickstrom
Sweden

16:15 **Non-Standardization of Technology in Ophthalmology**
Yijun Huang
USA

16:30 **Data Quality Issues in Clinical Trials**
Michael Ip
USA

16:45 **Validation of New Surrogate Endpoints in Clinical Research**
Carol Yim-lui Cheung; Tien Yin Wong
Singapore

17:00 **Imaging Technology in Clinical Trials in China**
Xiaoxin Li
China

17:15 **Who Needs A Reading Center?**
R. Danis
USA

Friday, December 10, 2010

08:00 - 09:00 **Glaucoma Cases** **Hall A**
Chair: Jost Jonas (Germany) & Xiulan Zhang (China)

08:00 - 09:00 **Poserior Uveitis Panel** **Hall B**
Chair: Moderators: David Chu (USA)

09:00 - 09:45 **EVER Symposium** **Hall A**
Chair: Leopold Schmetterer (Austria)

09:00 **Pathogenic Hints for Glaucoma from the Optic Nerve Head**
Jost Jonas
Germany

09:11 **Autoimmunity and Glaucoma**
Franz Grus
Germany

09:22 **Impact of Long Term Use of Preservatives on the Ocular Surface**
Christophe Baudouin
France

09:33 **What Can We Expect from Functional OCT for Glaucoma**
Leopold Schmetterer
Austria

09:00 - 09:45 **Treatments for Retinal Vein Occlusion** **Hall B**
Chair: Baruch D. Kuppermann (USA)

09:00 **Lucentis (Ranibizumab) for Central Retinal Vein Occlusion with Macular Edema: The CRUISE Study**
N. Fischer; M. Goldstein; U. Soiberman; S. Shulman; A. Loewenstein
Israel

09:09 **Lucentis (Ranibizumab) for Branch Retinal Vein Occlusion: BRAVO**
N. Fischer; M. Goldstein; U. Soiberman; S. Shulman; A. Loewenstein
Israel

09:18 **Ozurdex for Retinal Vein Occlusion**
M. Gillies
Australia

09:27 **SCORE Study - 3 Year Neovascularization Rates**
Michael Ip
USA

09:36 **SCORE STUDY - Incidence of Collateral Vessel Formation and Effect on Visual Acuity**
Michael Ip
USA

09:45 - 10:30 **Vascular Targets** **Hall A**
Chair: Chris Paterson

09:45 **Role of Endothelins in Ocular Disease**
G. Garhoefer
Austria

09:56 **Retinal Circulation in Diabetes**
T. Nagaoka
Japan

10:07 **Dynamic Blood Flow Autoregulation in Experimental Glaucoma**
L. Wang; G. Cull; C.F. Burgoyne; Y. Liang; K. Rittenhouse
USA

10:18 **Interaction Between Intraocular Pressure and Blood Flow: Relevance for Glaucoma**
L. Schmetterer
Austria

09:45 - 10:30 **Retina Miscellaneous (1) & Free Papers** **Hall B**
Chair: Baruch D. Kuppermann (USA)

09:45 **Neuroprotection Update**
M. Gillies
Australia

09:56 **rh-RdCV**
Pierre Belichard
France

10:07 **Intraocular VEGF Concentration and Refractive Error**
J. Jonas[1]; Y. Tao[2]; M. Neumaier[1]; P. Findeisen[1]
[1]Germany; [2]China

10:18 **Fundus Autofluorescence Imaging of Chorioretinal Inflammatory Diseases**
M. Kramer; S. Brastishevsky; E. Priel
Israel

10:30 - 11:00 **Coffee Break** **Exhibition Hall**

11:00 - 12:30 **Ocular Infection** **Hall A**
Chair: Irina Barequet (Israel)

11:00 **The Evaluation of Antibiotics in the Prophylaxis or Treatment of Endophthalmitis Using Animal Model**
T. Suzuki
Japan

11:10 **Comparison of Antibiotic Effect and Corneal Epithelial Toxicity on Fluoroquinolone Antibiotics**
C-K. Joo
South Korea

11:20 **Bacteriologic Profile of the Conjunctiva and Susceptibility to Fluoroquinolones**
N. Maeda
Japan

11:30 **Keratitis in Vietnam: A Study of Clinical and Microbiological Characteristics and Treatment during 10 years (1998-2007)**
T.M.C. Hoang; A.T. Le; T.K.V. Pham
Vietnam

11:40 **Antibacterial Prophylaxis for Ophthalmic Surgery – an Ongoing Challenge**
I. Barequet
Israel

11:50 **Multicenter Surveillance of Microbial Keratitis in Korea**
J. Y. Hyon
South Korea

12:00 **Latency and Suppression of Reactivation of HSV**
S. Higaki
Japan

12:10 **TRUST: Tracking Resistance of Ocular Infections**
P. Asbell
USA

11:00 - 12:10 **Macular Edema (Allergan)** **Hall B**

11:00 **Pathogenesis of Macula Edema in Retinal Diseases - What do we Know?**
B. Kuppermann
USA

11:10 **Dexamethasone Intravitreal Implant in the Management of Macular Edema**
M. Gillies
Australia

11:25 **Combination Therapy - the Future of Retinal Vascular Disease Management**
F. Bandello
Italy

11:35 **Steroids in the Management of Uveitis**
H. Uy
Philippines

11:45	**Dexamethasone Intra-vitreal Implant & Patient Experience** Michaella Goldstein Israel	
12:00	**Panel Q&A** All Speakers	
12:10 - 12:30	**Toxicology**	**Hall B**
12:10	**The Potential Toxicity of LEDs** F. Behar-Cohen France	
12:20	**New Monitoring Guidelines for Hydroxychloroquine** W.F. Mieler USA	
12:30 - 14:00	**Lunch Break**	**Exhibition Hall**
14:00 - 15:30	**Meibomian Gland Dysfunction: Tear Film and Ocular Surface Society** Chair: David Sullivan, Kelly Nichols & Penny Asbell (USA)	**Hall A**
14:00	**Introduction** K. Nichols USA	
14:11	**Definition and Classification of Meibomian Gland Dysfunction (MGD)** K. Nichols USA	
14:22	**Anatomy, Physiology and Pathophysiology of the Meibomian Gland** D. Sullivan USA	
14:33	**Tear Film Lipids, and Lipid-Protein Interactions, in Health and Disease** D. Sullivan USA	
14:45	**Epidemiology of, and Associated Risk Factors for, MGD** K. Nichols USA	
14:56	**Evaluation, Diagnosis and Grading of Severity of MGD** M. Rolando Italy	
15:07	**Management and Therapy of MGD** C. Baudouin France	
15:18	**Design and Conduct of Clinical Trials** P. Asbell USA	

14:00 - 15:30 **Wet AMD** **Hall B**
Chair: Baruch D. Kuppermann (USA)

14:00 **Lucentis (Ranibizumab) versus Avastin (Bevacizumab) for CNV/AMD**
N. Fischer; U. Soiberman; R. Jung; G. Heilweil; D. Varssano; M. Goldstein; A. Barak; S. Shulman; A. Loewenstein
Tel Aviv Medical Center, Tel Aviv, Israel

14:09 **Lucentis for non-AMD CNV**
M. Goldstein
Israel

14:17 **Ozurdex as Adjunctive Therapy to Lucentis in Patients With Choroidal Neovascularization Secondary to Age-Related Macular Degeneration**
B. Kuppermann[1]; M. Singer[1]; D. Weinberger[2]; M. Goldstein[2]; A. Loewenstein[2]; C.C. Liu[3]; L. Jean[1]; X.Y. Li[1]; S. Whitcup[1]
[1]USA; [2]Israel; [3]Taiwan;

14:25 **Topical Therapy for CNV/AMD**
B. Kuppermann
USA

14:33 **PDGF plus Lucentis for CNV**
D. Boyer
USA

14:41 **VIEW 2 - VEGF Trap-Eye Investigation of Efficacy and Safety in Wet AMD (VIEW 2)**
M. Goldstein
Israel

14:49 **Inhibition of 51 Integrin in Neovascular AMD - a Phase 1 Study**
B. Kuppermann
USA

14:57 **Radiation for CNV/AMD**
D. Boyer
USA

15:05 **POT RACE Study**
D. Boyer
USA

15:13 **DENALI/Mt BLANC/EVEREST**
D. Boyer
USA

15:21 **Soluble Receptors for TNF Alpha: Anti-Inflammatory and Anti-Angiogenic Properties**
F. Behar-Cohen
France

15:30 - 16:00 **Coffee Break** **Exhibition Hall**

16:00 - 17:30 **Traditional Chinese Medicine - Basic Research** **Exhibition Hall**
Chair: Junguo Duan (China)

16:00 **Neuroprotection in Glaucoma Using Gouqizi (Wolfberry)**

16:15 **Establishment and Evaluation of the High Throughput Screening System for Antagonistic Agents of Dry Eye Based on TGF-¦1 and Bcl-2**
Q. Peng; X. Yao; H. Tan
China

16:30 **The Protection of Compound Chinese Medicine MingMuWuZi on Rat Model of Light-Induced Retinal Injury**
H. Ye
China

16:45 **Research of QiDengMingMu Capsule Therapy Effect on STZ Induced Diabetic Rat fs Blood-Retinal Barrier and Visual Function Damage**
F. Zhang; J. Duan; X. Lu; H. Ye
China

17:00 **Effects of Chinese Medicine QiDengMingMu Capsule on Protein Kinase C in Retinas and VEGF in Vitreous of Spontaneous Diabetic Rats**
Q. Li; J. Duan; N. Gao; F. Zhang
China

17:15 **Experimental Research on Compound Danshen Dripping Pills Treating Early Diabetic Retinopathy**
J. Ma; X. Shen; J. Hu; F. Yang; Y. Zhu
China

16:00 - 17:30 **Drug Delivery** **Hall B**
Chair: Diane Tang Liu (USA) & Robert Gurny (Switzerland)

16:00 **Phase 2 Studies of Encapsulated CNTF Secreting Cell Implant (NT-501) in Patients with Geographic Atrophy or Retinitis Pigmentosa**
W. Tao
Neurotech, Lincoln, RI, USA

16:15 **Intravitreal Brimonidine Drug Delivery System Enhances Sweep Visual Evoked Potential**
J. Burke; K.M. Zhang; T. Lin; P. Hughes; B. Kuppermann; L. Wheeler
USA

16:30 **Pharmacokinetic and Pharmacodynamic Considerations in Posterior Segment Drug Delivery**
J-E. Chang-Lin
USA

16:45 **Optimization of Ocular Drug Delivery Profile of Tasocitinib (CP-690,550) to Support Clinical Success**
M. Shiue; W. Collette III; W. Huang
USA

17:00 **Biocompatibility of Thermo-Response Hydrogel as Ocular Drug Delivery System**
J. Kang-Mieler; W. Mieler
USA

17:15 **Protein Delivery to the Posterior Segment of the Eye: Novel Technologies**
F. Behar-Cohen
France

08:00 - 09:00 **Post Lasik Cases** **Hall A**
Chair: Penny Asbell (USA)

08:00 - 09:00 **Wet AMD Panel** **Hall B**
Chair: Baruch D. Kuppermann (USA)

09:00 - 09:45 **New Devices in Glaucoma Therapies** **Hall A**
Chair: Jost Jonas (Germany) & Xiulan Zhang (China)

09:00 **OCT in Glaucoma**
M. He
China

09:09 **Applications of Ocular Response Analyzer in Normal Tension Glaucoma**
D. Leung
Hong Kong

09:18 **The Use of the Express Implant in Asian Eyes**
C.L. Ho
Singapore

09:27 **One Year Follow-Up of Selective Laser Trabeculoplasty in Primary Open-Angle Glaucoma**
T. Wang; W. Ningli
China

09:36 **Glaucoma Screening with a Self-Operated, Inexpensive, Comprehensive Instrument: Can it be done?**
A. Walsh
USA

09:00 - 10:30 **Retina Miscellaneous (2) & Free Papers** **Hall B**
Chair: Baruch D. Kuppermann (USA)

09:00 **Control Sustained Release from Biodegradable Thermo-Responsive Hydrogel**
J. Kang-Mieler; W. Mieler
USA

09:12 **Update Regarding Use and Benefit of NSAIDs in Ophthalmology**
W.F. Mieler
USA

09:24 **Treatment and Prevention of Endophthalmitis 2011**
W.F. Mieler
USA

09:36 **Microplasmin Treatment of Vitreoretinal Disease: Update on the Phase III MIVI-TRUST Program**
A. Gandorfer
Germany

09:48 **Lucentis for non-AMD CNV**
M. Goldstein
Israel

10:00 **Intravitreal Cell-Based Production of Glucagon-Like Peptide-1**
J. Jonas[1]; R. Zhang[1]; L. Xu[1]; K. Ma[1]; C. Wallrapp[2]
[1]China; [2]Germany

10:10 **Monocyte Chemoattractant Protein-1 (MCP-1), and Adhesion Molecules ICAM-1 VCAM-1 in Exudative Age-Related Macular Degeneration**
J. Jonas[1]; Y. Tao[2]; M. Neumaier[1]; P. Findeisen[1]
[1]Germany; [2]China

10:20 **Levels of Cytokines in the Aqueous Humor of Patients with Age-related Macular Degeneration.**
M. Kramer; M. Hasanreisoglu; A. Feldman; R. Axer-Siegel; P. Sonis; I. Maharshak; Y. Monselise; M. Gurevich; D. Weinberger
Israel

09:45 - 10:30 **Glaucoma Miscellaneous & Free Papers** **Hall A**
Chair: Jost Jonas (Germany) & Xiulan Zhang (China)

09:45 **The Prevalence and Burden of Primary Glaucoma in China**
J. Zhao
China

09:56 **Preservative-Free Tafluprost 0.0015% in the Treatment of Patients with Ocular Hypertension and Glaucoma - Results of an Observational Study**
L.E. Pillunat; F. Kimmich
Germany

10:07 **Switching to Bimatoprost/Timolol Fixed Combination From Bimatoprost, Latanoprost or Travoprost Significantly Reduces Intraocular Pressure**
S Pfennigsdorf[1]; G Brief[1]; T Lammich[1]; E Nagel[1]; C Spraul[1]; S Ho[2]
[1]Germany; [2]UK

10:18 **Switching to Bimatoprost 0.01% Reduces Intraocular Pressure in Patients with Glaucoma: Preliminary Findings From an Observational Study**
S. Pfennigsdorf; M. Froboese; B. Maeder; P. Eschstruth
Germany

10:30 - 11:00 **Coffee Break** **Exhibition Hall**

11:00 - 11:45 **Ocular Surface (Senju)** **Hall A**

11:00 **The Ocular Surface in Health and Diseases**
Shigeru Kinoshita
Japan

11:15 **Stromal Hooking and Visco-Detaching Technique Enabled Deep Lamellar Keratoplasty in Treating Various Corneal Diseases**
Yu-Feng Yao
Japan

11:00 - 11:45 **Therapies of Retinal Neovascularization** **Hall B**
Chair: Moderators: Arup Das (USA) & Ruth Caldwell (USA)

11:00 **Targeted Nanocarriers for Therapy of Ocular Neovascularization**
J. Penn; A. Jayagopal
USA

11:15 **A3/A1-crystallin is Essential for the Remodeling of the Retinal Vasculature**
D. Sinha
USA

11:30 **Induction of Interleukin 6 is Required for TNF- and Endotoxin-Induced Vascular Inflammation**
W. Zhang; M. Rojas; C. Patel; Z. Xu; R. Caldwell; M. Bartoli; R. Caldwell
USA

11:45 - 12:30 **Anterior Segment Imaging/Devices** **Hall A**
Chair: Penny Asbell (USA)

11:45 **Quantitative and Qualitative Use of Anterior Segment OCT in Corneal Surgery**
J. Mehta
Singapore

11:54 **Imaging Techniques for Assessing Inflammation on the Ocular Surface**
C. Baudouin; A. Labbe; H. Liang
France

12:03 **Confocal Femtosecond Imaging Applied to the Structure of the Human Cornea and Porcine Lamina Cribrosa**
S. Rehman; C. Sheppard; D. Tan; R.W. Beuerman; Q.Y. Soh
Singapore

12:12 **DSAEK - Cornea Insertion Devices**
P. Asbell
USA

12:21 **Panel Q&A**
All Speakers

11:45 - 12:30 **Managing Uveitis in Children Panel** **Hall B**
Chair: Harvey Uy (Philippines)

12:30 - 14:00 **Lunch Break**

14:00 - 15:30 **Neuroprotection & Free Paper** **Hall A**
Chair: Samin Hong (South Korea)

14:00 **Neuroprotective Effects of CNP on Glaucomatous Neuropathy**
Xuyang Liu
China

14:15 **Neuroprotective Effects of Agmatine on Various Oxidative Stressed Neurons**
S. Hong
South Korea

14:30 **Protective Effect of GSTT on Retinal Ganglion Cells and Optic Nerve in Rabbits with Chronic Intraocular Hypertension**
L-N. Huang
China

14:45 **Immune-Mediated Injury and the Retinal Ganglion Cell Survival**
C. Zhang[1]; P. Huang[1]; S. Zhang[2]
[1]China; [2]USA

15:00 **TBA**
Rutledge Ellis Behnke
Hong Kong

14:00 - 14:45 **Diabetic Retinopathy & Free Paper** **Hall B**
Chair: Baruch D. Kuppermann (USA)

14:00 **Role of Vitreous in DR Progression**
Arnd Gandorfer
Germany

14:11 **Vascular Toxicity or Steroids**
Francine Behar-Cohen
France

14:22 **TA/Steroids for Inhibition of Progression of DR**
M. Ip
USA

14:35 **Utilization Profile, Safety, and Efficacy of Intravitreal Injections of anti-VEGF in a Single Institution**
H. Uy; P.S. Chan-Uy; A.A.S. Veloso; J. Francisco III; F.M. Cruz
Philippines

14:45 - 15:30 **Antioxidants** **Hall B**
Chair: Paul Bernstein (USA)

14:45 **Long-Chain and Very Long-Chain Polyunsaturated Fatty Acids in Ocular Aging and Age-Related Macular Degeneration**
P.S. Bernstein; A. Liu
USA

15:00 **Macular Pigment Changes in Pseudophakic Eyes Quantified with Resonance Raman Spectroscopy**
A. Obana[1]; M. Tanito[1]; Y. Gohto[1]; W. Gellermann[2]; S. Okazaki[1]; A. Ohira[1]
[1]Japan; [2]USA

15:15 **Changes of Macular Pigment Optical Density Before and After Photodynamic Therapy in Age Related Macular Degeneration**
Akihiro Ohira; Yasurou Koyama; Masaki Tanito; Akira Obana
Japan

15:30 - 16:00 **Coffee Break** **Exhibition Hall**

16:00 - 17:30 **Traditional Chinese Medicine - Clinical Trials** **Hall A**
Chair: Junguo Duan (China)

16:00 **Safety and Effectiveness Evaluation of Chinese medicine Qiming Granule on Diabetic Retinopathy: A Multicenter Randomized Clinical Trial**
J. Duan; P. Liao; H. Ye; F. Zhang; X. Lu
China

16:13 **Clinical and Mechanism Research about the Treatment of Xeroma used Runmuling**
Y. Wang; K. Li
China

16:25 **Protective Effects of Gingko Biloba Extract on Glaucoma with IOP Controlled: A Multicenter Randomized Double-Blind Controlled Clinical Trial**
X. Lu; J. Duan; H. Zhou; J. Zeng; L. Cheng
China

16:38 **Study on Yang Deficiency Mechanism of Diabetic Retinopathy Based on Metabonomics**
X. Luo; J. Duan
China

16:51 **Astragalus Membranaceus and its Prescriptions in Treating Diabetic Retinopathy: A Systematic Review**
J. Duan; L. Cheng
China

17:04 **Clinical Observation on the Treatment of Early Diabetic Retinopathy with Compound Danshen Dripping Pills**
J. Ming; Y. Wei; D. Hui
China

17:17 **The Effect Study on the Treatment of Combination of XiaoMengLing Tables With Laser to Treat Diabetic Macular Edema**
Q. Bo
China

16:00 - 17:30 **Inflammation - Free Papers** **Hall B**

16:00 **Dry Eye Disease Management in the Community**
D.A. Schaumberg; J. Li
USA

16:15 **Transeptal Triamcinolone Acetonide Injection in the Management of Non-Infectious Uveitis**
H. Uy; F.M. Cruz; J. Francisco III; P.S. Chan
Philippines

16:30 **Thymosin 4 Acts as an Antagonistic Factor of NFkB Subunit RelA/p65 in Suppressing IL-8 Gene Activation by Pro-inflammatory Factor TNF-**
P. Qiu; Y. Qiu; M. Kurpakus-Wheater; G. Sosne
USA

The International Symposium on Ocular Pharmacology and Therapeutics

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Abstracts

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Impression Cytology and Dry Eye Disease

P. Asbell
Mount Sinai School of Medicine of New York University, USA

Dry eye disease is typically diagnosed and categorized by signs and symptoms, as outlined in the DEWS report of 2007 (ref). As with other diseases, it would be helpful to have a minimally invasive metric to evaluate to use for DED analysis: diagnosis, determining severity of disease and response to treatment. We have used impression cytology (IC) to obtain conjunctival samples of surface cells and then analyzed by flow cytometry to determine the percent cells that are HLA- DR positive, as a measure of the inflammatory response of the ocular surface. Our results of repeatability, and correlation with signs and symptoms of DED will be presented.

Antibacterial Prophylaxis for Ophthalmic Surgery – an Ongoing Challenge

I. Barequet
Sheba Medical Center, Israel

Purpose: Postoperative endophthalmitis is a potentially devastating complication of cataract surgery. Efficient perioperative prophylaxis is widely studied, especially due to the continuous emergence of resistant strains. Cefuroxime is lately used for intracameral injection at the conclusion of the surgery. Topical antibiotics are frequently instilled perioperatively in order to penetrate into the anterior chamber and provide additional antibacterial coverage. The combination of two antibiotic drugs broadens the antibacterial coverage, however nteractions between different antibiotic agents may affect their potency.

Methods: Clinical isolates of Streptococcus pneumonia (x2 strains), Coagulase-negative Staphylococcus (x2 strains), Methicillin-sensitive Staphylococcus aureus, Methicillin-resistant Staphylococcus aureus, and Pseudomonas aeruginosa were used. Minimum inhibitory concentrations (MICs) were determined for each of the clinical isolates. Testing for synergy was determined by the checkerboard technique. Combinations of moxifloxacin and cefuroxime were tested against the clinical isolates in BHI broth. The fractional inhibitory concentration (FIC) index for each antibiotic in every combination was calculated. A synergistic effect was determined when FIC index was >2.

Results: The FIC index was 2 and 2.5 for each of the two S. pneumonia strains respectively, 1.5 for each of the staphylococci strains, and 2.5 for P. aeruginosa. These results suggest a synergistic effect of this antibiotic combination for S. pneumonia and P. aeruginosa and an additive effect of staphylococci. No antagonism was detected.

Conclusions: The Checkerboard method showed evidence of either synergy or additive effect between moxifloxacin and cefuroxime with no evidence of antagonism. This data provides additional support for advantage of combining the two antibiotics for enhanced prophylaxis in cataract surgery.

Impact of Long Term Use of Preservatives on the Ocular Surface

C. Baudouin [1]; H. Liang [1]; A. Labbe [1]; F. Brignole-Baudouin [2]
[1]Quinze-Vingts Hospital, France; [2]Vision Institute, France

There is a large body of evidence from experimental and clinical studies showing that the long-term use of topical drugs may induce ocular surface changes, causing ocular discomfort, tear film instability, conjunctival inflammation, subconjunctival fibrosis, epithelial apoptosis, corneal surface impairment, and the potential risk of failure for further glaucoma surgery. Subclinical inflammation has also been described in patients receiving antiglaucoma treatments for long periods of time. The most frequently used preservative, benzalkonium chloride, has consistently demonstrated its toxic effects in laboratory, experimental, and clinical studies. As a quaternary ammonium, this compound has been shown to cause tear film instability, loss of goblet cells, conjunctival squamous metaplasia and apoptosis, disruption of the corneal epithelium barrier, corneal hypoesthesia, and damage to deeper ocular tissues. Preservative-induced adverse effects are therefore far from being restricted to only allergic reactions, and side effects are often very difficult to identify because they mostly occur in a delayed or poorly specific manner. On the basis of all these experimental and clinical reports, it would be advisable to use benzalkonium-free solutions whenever possible. Indeed, mild symptoms should not be underestimated, neglected, or denied, because they may very well be the apparent manifestations of more severe, potentially threatening subclinical reactions that may later cause major concerns.

Imaging Techniques for Assessing Inflammation on the Ocular Surface

C. Baudouin ; A. Labbe ; H. Liang
Quinze-Vingts Hospital, France

New investigation techniques have been developed at the ocular surface level and now provide histological-like images in a noninvasive way. We evaluated the potentials of new-generation in vivo confocal microscopy in the ocular surface of patients suffering from various ocular surface diseases and in animal models. The Rostock Cornea Module of the Heidelberg Retina Tomograph was used to examine ocular epithelia in large series of patients with ocular surface inflammatory diseases and/or neovascularization. Impression cytology specimens were also taken and processed for immunostaining in order to allow comparisons with in vivo patterns. Animal models of drug-induced ocular surface inflammation or neovascularization were also developed for confocal microscopy assessments. The potential of spectral domain OCT was also investigated in ocular surface diseases. Using confocal microscopy, we could identify in various inflammatory eye diseases cell processes at a level allowing detection of inflammatory cell rolling, diapedesis, chromatin fragmentation, or quantification of dendritic cell infiltration, all of which being well correlated with cytological patterns. The animal models we developed also confirmed the usefulness of noninvasive confocal microscopy in models of inflammation, toxicology or angiogenesis. The identification of CALT in live animals was also possible and provided useful information for toxicological purposes. OCT still suffers from poorer resolution but this non contact technique may also bring valuable information in specific cases. Therefore the new generations of imaging systems may now provide in a noninvasive way excellent histologic-like patterns of the ocular surface epithelia, in human diseases as well as in animal experimentation. Such technologies are complementary and could thus become routine methods to explore ocular surface disorders and also have many promising applications in immunology, pharmacology, and angiogenesis research.

Protein Delivery to the Posterior Segment of the Eye: Novel Technologies

F. Behar-Cohen
Universite Paris Descartes, France

Because the eye is protected by ocular barriers but is also easily accessible, direct intravitreous injections of therapeutic proteins allow for specific and targeted treatment of retinal diseases. Low doses of proteins are required in this confined environment and a long time of residency in the vitreous is expected, making the eye the ideal organ for local proteic therapies. Monthly intravitreous injection of Ranibizumab, an anti VEGF Fab has become the standard of care for patients presenting wet AMD. It has brought the proof of concept that administering proteins into the physiologically low proteic concentration vitreous can be performed safely. Other antibodies, Fab, peptides and growth factors have been shown to exert beneficial effects on animal models when administered within the therapeutic and safe window. To extend the use of such biomolecules in the ophthalmology practice, optimization of treatment regimens and efficacy is required. Basic knowledge remains to be increased on how different proteins/peptides penetrate into the eye and the ocular tissues, distribute in the vitreous, penetrate into the retinal layers and/or cells, are eliminated from the eye or metabolized. This should serve as a basis for designing novel drug delivery systems. The later should be non or minimally invasive and should allow for a controlled, scalable and sustained release of the therapeutic proteins in the ocular media.

We propose to use non-viral gene therapy techniques to produce therapeutic proteins in a sustained and minimally invasive manner, for the treatment of various retinal diseases.

Macular Pigment Imaging in AREDS II Participants: Baseline Studies from an Ancillary Study at the Moran Eye Center

P.S. Bernstein ; F. Ahmed ; A. Liu ; M. Sharifzadeh ; I. Ermakov ; W. Gellermann
University of Utah, USA

Purpose: The Age-Related Eye Disease Study II (AREDS II) is evaluating the potential protective role of the macular pigments lutein and zeaxanthin against age-related macular degeneration (AMD) in a randomized, placebo-controlled manner in over 4000 patients nationwide at nearly 100 sites. Only our site, however, is measuring tissue levels and distributions of the macular pigments at each visit. Here we provide baseline characteristics of our enrolled subjects prior to randomization.

Methods: Baseline levels and distributions of macular pigment carotenoids were determined via HPLC for serum, autofluorescence imaging (AFI) for retina, and resonance Raman spectroscopy (RRS) for skin.

Results: 53 subjects (29 female and 24 male) out of a total of 55 Moran Eye Center AREDS II patients enrolled in this ancillary study. Total serum carotenoids and, to a lesser extent, zeaxanthin + lutein correlate with skin Raman values (r=0.4131, p=0.0039), but peak macular pigment optical density (MPOD) did not. Many of the participants have peak MPOD well above our age-adjusted normal range for unsupplemented individuals, consistent with the fact that >70% of our patients reported regular consumption of lutein and/or zeaxanthin supplements prior to enrollment.

Conclusions: Noninvasive skin measurements of total carotenoids are a good surrogate marker for blood values at the baseline visit, but not for peak MPOD in the retina. The high levels of peak MPOD at enrollment suggest that our site's subjects were already very aware of the potential benefits of lutein and zeaxanthin supplementation. Over the next five years, our ancillary AREDS II study will continue to provide unique information on the relationship of macular carotenoids and prospective risk of advanced AMD at a tissue level in a well defined cohort of high risk AMD patients with and without carotenoid supplementation.

Long-Chain and Very Long-Chain Polyunsaturated Fatty Acids in Ocular Aging and Age-Related Macular Degeneration

P.S. Bernstein ; A. Liu
University of Utah, USA

Purpose: Retinal long-chain polyunsaturated fatty acids (LC-PUFAs, C12-C22), play important roles in normal human retinal function and visual development, and some epidemiological studies of LC-PUFAs intake suggest a protective role against the incidence of advanced age-related macular degeneration (AMD). On the other hand, retinal very long-chain PUFAs (VLC-PUFAs, Cn>22) have received much less attention since their identification decades ago due to their minor abundance and more difficult assays, but recent discoveries that defects in VLC-PUFA synthetic enzymes are associated with rare forms of inherited macular degenerations have refocused attention on their potential roles in retinal health and disease.

Methods: We developed improved gas chromatography coupled with mass spectrometry (GC-MS) methods to detect LC-PUFAs and VLC-PUFAs, and we then applied them to the study of their changes in ocular aging and AMD.

Results: With ocular aging, some VLC-PUFAs in retina and retinal pigment epithelium (RPE)/choroid peaked in middle age. Compared to age-matched normal donors, docosahexaenoic acid, adrenic acid and some VLC-PUFAs in AMD retina and RPE/choroid were significantly decreased, while the ratio of n-6/n-3 PUFAs was significantly increased.

Conclusions: All these findings suggest that deficiency of LC-PUFAs and VLC-PUFAs, and/or an imbalance of n-6/n-3 PUFAs may be involved in AMD pathology.

Confocal Femtosecond Imaging Applied to the Structure of the Human Cornea and Porcine Lamina Cribrosa

S. Rehman [1]; C. Sheppard [2]; D. Tan [3]; R.W. Beuerman [1]; Q.Y. Soh [1]
[1]Singapore Eye Research Institute, Singapore; [2]National University of Singapore, Singapore; [3]Singapore National Eye Center, Singapore

Purpose: To develop the applications of a new femtosecond imaging platform for the cornea and to determine the application to understanding the structure of the porcine lamina cribrosa (LC).

Methods: A fiber laser, with 100 femto-second pulses at a wavelength of 800 nm and average power of 110 mW, was used to excite the stromal collagen in the human cornea to image the back-scattered second harmonic generated signal. A sensitive dection path was used to collect weakly back-scattered second harmonic siganl. Longer wavelength facilitates deep tissue imaging and nonlinear contrast comes from the asymmetry of collagen matrix in the stroma. Freshly enucleated pig eyes were used. In the first batch of nine eyes, dissection was carried out to reveal the retinal surface of the LC, followed by the imaging of seven-hundred-and-thirty-four LC pores using a second-harmonic-generation microscope.

Results: Differently than a conventional confocal microscope, the contrast obtained with second harmonic signal from the femtosecond laser comes from the stromal collagen. Second harmonic signal gives a strong imaging contrast from collagen fibers lying deep in the stroma. The longer wavelength helps in deep tissue imaging and back scattered nonlinear signal can be potentially used for in vivo imaging of cornea. Collagen structure is visualized at greater depths of corneal stroma. The fibrilar orientation of collagen can be selectively excited by linear polarization of the illumination. The femtosecond image of the lamina cribrosa was sufficient to create 3-dimensonal reconstructions of the entire LC.

Conclusions: The ability to visualize ordered structures such as collagen offers considerable advantages over confocal images where only cellular images are observed within a largely featureless surround. As the LC can be visualized in realtime in living tissue it offers advantages for understanding the response to imposed stress.

Iluvien FAME for DME

D. Boyer
Retina Vitreous Assoc Med Group, USA

The Retisert is a chronic release fluocinolone implant that has been approved for the treatment of non infectious uveitis. It is implanted in the operating room.

The Iluvien implant has just completed a 3 year study utilizing fluocinolne in a chronic release formula that is injected into the eye as an outpatient. The results of two years of the study will be described. The drug is currently being evaluated by the FDA for approval. The results of the studies using this device to treat Diabetic macular edema are very encouraging.

Overview of Pathways and Treatments for Dry AMD

D. Boyer
Retina Vitreous Assoc Med Group, USA

A number of new studies have tried to reduce progression of Dry age related macular degeneration. These include visual cycle modulators, anti-inflammatory agents, nueroprotectants and anticompliment drugs. Recent study results for some of these trials have been released and will be discussed.

DENALI/Mt BLANC/EVEREST

D. Boyer
Retina Vitreous Assoc Med Group, USA

PDT in combination with antiVEGF may reduce the frequency of injections. The results of 2 randomized trials addressing these issues will be discussed. The Everest trial will discuss the use of PDT to treat polypoidal choroidal disease.

POT RACE Study

D. Boyer
Retina Vitreous Assoc Med Group, USA

Premise Compliment has been implicated to play a role in both Dry and Wet Age Related Macular Edema. Blockage of C5 may downregulate VEGF as well as other inflammatory markers. Blockage of C3 downregulates C5 and may be an area that can be used to treat AMD.

Results of high dose POT (a C3 inhibitor) will be discussed.

PDGF plus Lucentis for CNV

D. Boyer
Retina Vitreous Assoc Med Group, USA

Theory: Anti-VEGF therapy is more effective for immature vessels. Mature vessels have more pericytes. PDGF actively recruits pericytes.

Study: Anti-VEGF therapy combined with anti-PDGF will make the vessels more likely to decrease leakage and improve visual acuity. The results of the phase one study will be discussed.

Intravitreal Brimonidine Drug Delivery System Enhances Sweep Visual Evoked Potential

J. Burke [1]; K-M. Zhang [1]; T. Lin [1]; P. Hughes [1]; B. Kuppermann [2]; L. Wheeler [1]
[1]Allergan, Inc., USA; [2]University at California, Irvine, USA

Purpose: Brimonidine tartrate, an alpha-2 adrenergic receptor agonist, has been shown to prevent retinal damage in a number of animal models. The purpose of this study was to evaluate the effects of brimonidine formulated in a biodegradable drug delivery system on sweep visual evoked potential (sVEP) in normal eyes.

Methods: Dutch-Belted (pigmented) rabbits were randomly assigned to receive brimonidine DDS into the OS at a dose of 66 ug (N=10), 200 ug (N=10), 600 ug (N=10). Placebo DDS implants were placed into the OD of each animal. Fundus photography and sVEP measurements were performed at baseline and 2, 4, 8, 12, and 16 weeks after implantation in animals. Acuity (linear regression fits to zero amplitude of the 2nd harmonic)were made with the PowerDiva system. Data are presented as mean ± standard error of the mean. A paired Student's 't' test compared brimonidine-treated with placebo eyes. Retinal histology was performed on eyes from animals receiving 600 ug of brimonidine DDS at 6 months (n=3) and at 12 months (n=2).

Results: sVEP acuities for the 66 ug group in OS were 1.95 ± 0.09 cpd ($p>0.05$), 2.48 ± 0.11 cpd ($p=0.0008$) and 2.20 ± 0.11 cpd ($p=0.045$) for baseline, 2 weeks and 4 weeks, respectively. Acuities for the 200 ug group at similar time points were 2.47 ± 0.1 cpd ($p>0.05$), 2.59 ± 0.18 cpd ($p=0.02$) and 2.02 ± 0.15 cpd ($p=0.006$), respectively; and were 1.98 ± 0.15 cpd ($p>0.05$), 2.68 ± 0.22 cpd ($p=0.0034$) and 2.16 ± 0.1 cpd ($p=0.0031$) for the 600 ug group, respectively. There were no statistically significant differences between OD and OS at later time points, nor were there any abnormalities noted on color fundus photography. Retinal histology showed no difference between brimonidine DDS and placebo DDS eyes.

Conclusions: Intravitreal brimonidine in a sustained drug delivery system enhances sVEP recordings in animal eyes in the absence of funduscopic or histologic changes.

Induction of Interleukin 6 is Required for TNF-α and Endotoxin-Induced Vascular Inflammation

W. Zhang ; M. Rojas ; C. Patel ; Z. Xu ; R. Caldwell ; M. Bartoli ; R. Caldwell
Medical College of Georgia, USA

Increases in TNF-α expression have been linked to vascular inflammation during ischemic retinopathy, but the underlying mechanisms are as yet unknown. Here we determined the specific role of IL-6 in this process. Studies were performed using TNF-α-treated endothelial cells (ECs) and in mice treated with TNF-α or endotoxin. Quantitative PCR and ELISA showed that TNF-α treatment of ECs induced a rapid increase in IL-6 mRNA and a 2.1 fold increase in IL-6 protein. The IL-6 increase was followed by a robust and sustained increase in tyrosine phosphorylation of STAT3, a transcription factor downstream of IL-6 signaling. Leukocyte adhesion to the vascular endothelium is a common feature of vascular inflammation and is an important step in leukocyte infiltration. TNF-α treatment increased the adherence of monocytes to ECs by 2.4 fold. Blockade of IL-6 by neutralizing antibodies against IL-6 or IL-6 receptor abolished TNF-α-induced STAT3 phosphorylation and significantly attenuated TNF-α-induced monocyte adhesion ($P<0.05$). Consistently, treatment with structurally different specific inhibitors for STAT3 (Stattic or Stat3-VII) prevented TNF-α-induced monocyte adhesion and blocked the upregulation of ICAM-1 and VCAM-1. In vivo, intravitreal injection of TNF-α (1 ng/eye) induced a >5-fold increase in leukocyte adhesion to the retinal vessels. This was reduced by 55% in IL-6 deficient mice and by 83% by inhibiting STAT3 (Stat3-VII, 240nmol/kg, i.v.). The role of IL-6 was further studied in acute vascular inflammation produced by lipopolysaccharide injection (LPS, 1 mg/kg). LPS dramatically increased IL-6, TNF-α and ICAM-1 expression in the retina. Deleting IL-6 did not affect TNF-α expression. However LPS-induced increases in ICAM-1 expression, leukostasis, and oxidative stress were all significantly reduced ($P<0.05$). Taken together, these data show that TNF-α or endotoxin treatment causes vascular inflammation by a mechanism involving IL-6 induced activation of STAT3.

Role of Arginase in Diabetes-Induced Retinal Vascular Dysfunction

R.W. Caldwell ; H.F. Toque ; W Zhang ; S. Elms ; R.B. Caldwell
Medical College of Georgia, USA

Purpose: Marked impairment of endothelial cell (EC)-dependent vasorelaxation has been demonstrated in retinal arteries of STZ-induced diabetic vs non-diabetic rats, suggesting a decreased availability of vasodilator nitric oxide (NO). However, many studies have shown enhanced levels of NO products (nitrate/nitrite and OONO- biomarker nitrotyrosine [NT]) in models of diabetic retinopathy (DR). This study assessed levels of retinal vascular function and bioavailable NO during DR and determined the role of arginase (ARG) enzyme, which competes with NO synthase for arginase, in vascular dysfunction and reduced bioavailable NO.

Methods: Studies were performed in streptozotocin-induced diabetic rats and mice and in retinal ECs treated with normal glucose or high glucose (25 mM, HG).

Results: Measurement of NT and nitrate/nitrite levels confirm significant increases in total NO products in diabetic retinas. However, levels of NO biomarkers nitrite and S-nitrosylated cysteine are reduced by diabetes. Imaging analysis using NO indicator DAF-2DA and superoxide ($O_2^{\cdot-}$) detector DHE showed decreased NO formation in diabetic retinas that was accompanied by increased $O_2^{\cdot-}$ formation. Diabetic retinas showed marked elevation of ARG activity and expression (isoform I). Studies in knockout mice showed that ARG gene deletion enhanced NO formation and reduced $O_2^{\cdot-}$ formation in diabetic retinas. EC-dependent relaxation of diabetic retinal arteries was reduced, but adrenergic vasoconstriction was enhanced vs control. In ECs, HG treatment increased ARG activity and reduced NO release. ARG inhibitor treatment reversed these diabetes/HG effects in retinal vessels and EC.

Conclusion: Diabetes-induced increases in oxidative stress are associated with retinal vascular dysfunction, increases arginase activity and expression (form I), decreased bioavailable NO, and increased $O_2^{\cdot-}$ formation. Our results suggest a role of arginase in DR by increasing oxidants and reducing bioavailable NO.

Pharmacokinetic and Pharmacodynamic Considerations in Posterior Segment Drug Delivery

J-E. Chang-Lin
Allergan, Inc., USA

Development of effective management strategies for the treatment of vitreoretinal diseases has been hampered by the difficulties associated with overcoming the unique structural and physiological barriers within the eye. Essentially, these barriers have made it difficult to deliver the appropriate amount of drug for a reasonable length of time to achieve desired beneficial effects while minimizing adverse effects. An effective strategy to overcome these limitation is local administration of drug containing biodegradable sustained release Drug Delivery System (DDS) as formulated in the recently approved OZURDEX® (dexamethasone intravitreal implant) for treatment of retinal vascular diseases and ocular inflammation. The development of a sustained release formulation over months for continuous treatment of vitreoretinal diseases requires pharmacokinetic and pharmacodynamic considerations. Key considerations from preclinical translation to clinical outcome will be reviewed to help with a more successful development strategy of sustained release formulation for optimal treatment of vitreoretinal diseases.

Does IGFPB3 have a Role in the Inhibition of Diabetic Retinopathy?

T. Chan-Ling [1]; P. Hu [1]; E. McFarland [1]; J. Kielczewski [2]; L. Shaw [2]; Y. Jarajupu [2]; S. Caballero [2]; S. Li Calzi [2]; T. Gardiner [3]; S. Firth [4]; R. Baxter [4]; M. Boulton [2]; M. Grant [2]
[1]Retinal and Developmental Neurobiology Laboratory, Australia; [2]University of Florida, USA; [3]Queens University Belfast, Northern Ireland; [4]Kolling Institute of Medical Research, Australia

Insulin-like growth factor 1 (IGF1) is required for normal retinal vascular development because vascular development is arrested in its absence despite the presence of VEGF. The effects of IGF1 are mediated by IGF Receptor 1 and modulated by complex interactions with IGF binding proteins (IGFBPs). Six IGFBPs function as transporter proteins and storage pools for IGF1 in a tissue- and developmental stage-specific manner. Phosphorylation, proteolysis, polymerization, and cell or matrix association regulates the functions of IGFBPs. Specific IGFBPs have been shown to either stimulate or inhibit IGF1 action. IGFBP3, the best studied and most abundant of these binding proteins, carries ≥75% of serum IGF1 and IGF2 in heterotrimeric complexes. IGFBP3 has auto- and paracrine actions affecting cell mobility, adhesion, apoptosis, survival, and the cell cycle. IGFBP3 expression is increased by hypoxic conditions and enhances angiogenesis in some systems while inhibiting it in others, thereby demonstrating potentially contradictory effects on the vasculature. Utilizing intravitreal injection of endothelial specific IGFBP-3 expressing plasmid and various expereimental models including oxygen-induced retinopathy (OIR), laser-induced choroidal neovascularization models and GFP+ chimeric mice we have shown that IGFBP3 prevents hyperoxia-induced vaso-obliteration and reduces neovascularization in neonatal mice subjected to the OIR model.Further, we have shown that IGFBP3 mediates protective effects on BRB integrity, reduced the number of apoptotic neuronal, pericytic and astrocytic cells in the retina, and increased differentiation of GFP+ hematopoietic stem cells into pericytes and astrocytes, thus enhancing vessel stability. IGFBP3 reduced the number of activated microglia by enhancing microglial apoptosis, thus asserting immunomodulatory influence. These studies suggest that IGFBP3 may be an attractive therapeutic candidate for ocular complications such as diabetic retinopathy.

Astragalus Membranaceus and its Prescriptions in Treating Diabetic Retinopathy: A Systematic Review

J. Duan [1]; L. Cheng [2]
[1]Key Research Institute of Visual Function Protection of State Administration of TCM, China, Peoples Republic; [2]Sichuan Provincial Hospital, China, Peoples Republic

Objective: To evaluate the efficacy and safety of astragalus membranaceus and its prescriptions for diabetic retinopathy.

Design: A systematic review of randomized controlled trials. Methods: Selected the RCTs about astragalus membranaceus and its prescriptions for diabetic retinopathy by electronic and manual searches. No blinding and language limitations were applied. The methodological quality of trials was assessed by the Jadad-scale plus allocation concealment and the clinical data were analyzed by RevMan 5.0 software.

Results: 18 randomized trials with 1375 patients were identified. The compared results showed that astragalus membranaceus and its prescriptions had more positive effect on PBG, TG hemorheology indexes and relieving symptoms. The combined results also showed that astragalus membranaceus and its prescriptions had no effect of statistics on sight, reducing patients¡¯FBG HbA1,etc. Obvious adverse reaction had not been found in those studies.

Conclusion: Some clinical symptoms of diabetic retinopathy patients can be relieved by astragalus membranaceus and its prescriptions. However, more randomized controlled trials of high quality will be needed to for stronger evidence. Key words: Astragalus membranaceus and its prescriptions, Diabetic Retinopathy, Systematic review, Evidence-based medicine, Randomized controlled trials

PCR-Guided Management of Anterior Uveitis

G. Cheung
Singapore National Eye Centre, Singapore

The value of polymerase chain reaction (PCR) as an adjunct in the management of suspected infectious posterior uveitis has been reported in many studies. Recently, underlying viral aetiologies have been identified in certain types of anterior uveitis previously thought to be idiopathic, including Posner-Schlossmann syndrome and Fuch's heterochromic Iridocyclitis. This talk will present our experience with PCR-guided therapy for anterior uveitis, including aspects on laboratory requirements, sample handling, selection of clinical cases and management strategies guided by PCR results.

Validation of New Surrogate Endpoints in Clinical Research

C. YL. Cheung ; Tien Yin Wong
Singapore Eye Research Institute, Singapore

There is a need for surrogate endpoints in clinical research and trials to identify clinical outcomes earlier, to allow more accurate estimation of these outcomes, and to evaluate new risk factors and pathways for novel drug targets. Ideally, such surrogate endpoints should precisely predict clinical endpoints (benefit, harm, or lack of benefit or ham) but can be measured much earlier, more conveniently (e.g., non-invasively), or more frequently than the clinical endpoint. In ophthalmology, common surrogate endpoints are optical coherence tomography (OCT) changes (as a measure of macular edema and vision loss in diabetic retinopathy or age-related macular degeneration) and intraocular pressure (as a measure of visual field loss in glaucoma). Other surrogate endpoints are retinal vascular caliber changes (as a measure of diabetic retinopathy signs).

Before a new surrogate endpoint can be used as an indicator of a clinical outcome, the endpoint must be formally validated. This presentation will discuss what is the appropriate data (e.g. data from case-control, epidemiologic and clinical trial studies) that needs to be acquired before a new surrogate endpoint and methodology is ready to be used as a clinical outcome. Validation of new surrogate endpoints in clinical research require data demonstrating the measure of the new endpoint add independent information of prognosis/risk of clinical events, and the measure is reproducible, sensitive, specific and easily measured. Examples using OCT and retinal vascular imaging will be discussed

Ocular Tuberculosis: Diagnosis and Treatment

P. Choopong
Siriraj Hospital, Mahidol University, Thailand

Tuberculosis (TB) is an airborne communicable disease caused by Mycobacterium tuberculosis or its relatives. It is still very common and being a devastating problem in developing countries especially in South East Asia and sub-Saharan Africa. Ocular TB is a rare form of extrapulmonary TB infection but could leads to severe visual loss and blindness if not recognized and not properly treated. It may affect many parts of the eye involving both extraocular and intraocular tissue. Intraocular tuberculosis is the great mimicker of non-infectious uveitis. It may presents either as anterior, intermediate, posterior, or panuveitis. Among these, choroidal involvement is the most common manifestation.

The presence of acid-fast bacilli from smear and culture or histopathological finding is still a gold standard for diagnosis of TB although it is difficult to retrieve adequate ocular specimen. Purified protein derivative (PPD) skin test is a quick and easy procedure to provide presumptive diagnosis of ocular TB. New methods such as polymerase chain reaction of M. tuberculosis from intraocular fluid and interferon-gamma TB blood test are also useful.

Isoniazid, rifampicin, pyrazinamide, ethambutol, and streptomycin are first-line medications for the treatment of ocular TB. It is recommended to continue anti-TB regimen for 6-12 months to get rid of all active and semi-dormant bacilli. Furthermore, concomitant systemic corticosteroid may be useful in controlling of inflammation.

Who Needs A Reading Center?

R. Danis
University of Wisconsin School of Medicine and Public Health, USA

The need for a reading center depends upon the specific requirements of the clinical trial. In many cases, a reading center adds logistical complexity and cost beyond the value it may add. However, the need for standardized independent, masked assessments is a critical element of many clinical trial designs. It is often possible to produce highly detailed assessments at a reading center that may not be feasible at clinical sites. A new role for reading centers is for the harmonization of data from disparate makes and models of imaging devices in an environment where standards compliance is not optimal.

Safety and Effectiveness Evaluation of Chinese medicine Qiming Granule on Diabetic Retinopathy: A Multicenter Randomized Clinical Trial

J. Duan [1]; P. Liao [2]; H. Ye [2]; F. Zhang [2]; X. Lu [1]
[1]The Teaching Hospital of Chengdu University of T.C.M., China, Peoples Republic;
[2]Chengdu University of Traditional Chinese Medicine, China, Peoples Republic

Objective: To evaluate the safety and efficacy of Chinese medicine Qiming Granule on diabetes retinopathy (DR) by contrast with Doxium.

Methods: 748 patients with DR were randomly assigned to the test group of Qiming Granule and the control group of Doxium based on GCP procedures and randomized clinical trial methods. The therapeutic efficacy were evaluated by visual acuity, fundus photography, fundus fluorescein angiography(FFA) and syndromes scales after 3 to 6 months' treatment; biochemistry test, electrocardiogram and blood, urine and stool routine examination were tested for safety index. The date management of clinical trials, fundus evaluation and statistic analysis were carried out by the third party objectively.

Results:

(1) Compared with Doxium, Qiming Granule was more effective for the treatment of DR , with total effective rate of 67.1% and 82.6% after 3 and 6 months, respectively;

(2)Qiming Granule could improve vision acuities of patients more than Doxium do.

(3) Qiming Granule could reduce micro-hemangioma and hard exudates, and help to promote the absorption of fundus hemorrhage, which is equivalent to Doxium. It could reduce soft excludes as well.

(4) Qiming Granule could improve the scores of syndrome, which was better than the control group with total effective rate of 74.2% and 89.6% after 3 and 6 months, respectively.

(5) Qiming Granule was superior to the control group in relieving the dryness and constipation of patients.

(6) Oral taken Qiming Granule was safe and reliable.

Conclusion: Compound Chinese medicine Qiming Granule was safe and effective for diabetic retinopathy.

Using the TessArae® Resequencing microarray system for detection of human adenoviruses in patients with conjunctivitis

R. Ellis-Behnke [1,2], P.C.Y. Woo [3,4,5,6], S.K.P. Lau [3,4,5,6], G.K.Y. Choi [5], H-T. Fung [7], K-C. Shek [7], J. Miao [5], B.Y.L. Chang [8], K.H.L. Ng [8], A.H.Y. Ngan [5], T-L. Que [8], C-W. Kam [7], K-Y. Yuen [3,4,5,6]
[1]Medical Faculty Mannheim of the Ruprecht-Karls-University of Heidelberg, Germany; [2]Department of Anatomy, The University of Hong Kong, Hong Kong; [3]State Key Laboratory of Emerging Infectious Diseases, Hong Kong; [4]Research Centre of Infection and Immunology, The University of Hong Kong, Hong Kong; [5]Department of Microbiology, The University of Hong Kong, Hong Kong; [6]Carol Yu Centre for Infection, The University of Hong Kong, Hong Kong; [7]Department of Accident and Emergency, Tuen Mun Hospital, Hong Kong; [8]Department of Pathology, Tuen Mun Hospital, Hong Kong

Background: Although high-density resequencing microarray is useful for detection and tracking the evolution of viruses associated with respiratory tract infections, no report on using this technology for the detection of viruses in patients with conjunctivitis is available.

Objectives: To test if a high-density resequencing microarray can be applied to the detection of viruses in conjunctival swabs for patients with conjunctivitis.

Study design: In this prospective proof-of-concept study, every 4 or 5 bacterial culture-negative conjunctival swab samples were pooled and subject to viral detection using the TessArae® Resequencing Pathogen Microarrays-Flu 3.1 (RPM-Flu-3.1). Results were compared with human adenovirus (HAdV) hexon gene PCR sequencing and viral culture.

Results: 32 of the 38 conjunctival swab samples were bacterial culture-negative. Four of the 7 pooled samples were positive for HAdV using RPM-Flu-3.1. Hexon gene PCR sequencing on the 38 original individual samples showed that 3 and 4 samples contained HAdVs species D and B respectively. All the 6 samples that were positive for hexon gene PCR but negative for bacterial culture were also positive by the resequencing microarray. Viral culture was positive for HAdV type 3 in 1 sample, which was also positive by PCR and resequencing microarray.

Conclusions: The TessArae® Resequencing microarray is as sensitive as PCR for detection of HAdV in conjunctival swabs. Unlike viral culture and hexon gene PCR sequencing, resequencing microarray was not able to differentiate the type and species of HAdV. Development of microarrays for conjunctivitis can be performed for rapid diagnosis of the viral cause of conjunctivitis.

The Control of Growth and Differentiation of wells With Physical Interaction

R. G. Ellis-Behnke [1,2,3], Y. X. Liang [2], S.W.H. Cheung [2], D. K. C. Tay [2]
[1]Medical Faculty Mannheim of the Ruprecht-Karls-University of Heidelberg, Germany; [2]Department of Anatomy, The University of Hong Kong Li Ka Shing Faculty of Medicine, Hong Kong, China; [3]Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, Massachusetts, USA

Background: Nanomaterials are bringing new applications and functionality to the medical field. The uses of self-assembled nanomaterials are currently changing how we deliver drugs, as well as treat central nervous system injury. Within the emerging field of stem cells there is a need for an environment that can regulate cell activity to slow down differentiation or proliferation, in vitro or in vivo, while remaining invisible to the immune system. By manipulating the cell density and self-assembling nanofiber scaffold (SAP) concentration we were able to control the nano environment surrounding PC12 cells, Schwann cells and neural precursor cells and were able to control the proliferation, elongation, differentiation and maturation in vitro.

Results: We extended the method, using SAP, to living animals with implants in the brain and spinal cord demonstrating that a combination of SAP and young cells can be transplanted into a mammal, eliminating the need for immuno-suppressants.

Conclusion: When cells are placed in a defined system it is possible to delay their proliferation, differentiation and maturation depending on the density of the cell population, density of the matrix, and the local environment.

Contractual and Commercial Aspects of Collaborative Research

M. Entzeroth
Experimental Therapeutics Centre (ETC), Singapore

Traditionally, the role understanding was that public sector scientists, with public funding, elucidate disease mechanisms and identify promising points of intervention, while Private sector scientists, with private funding, use this knowledge to identify, test and clinically develop new drugs and vaccines. This has changed within the last 10 – 20 years as universities, government funded bodies and non-profit research organizations became significantly involved in the drug discovery and development process mainly as part of a collaborative approach. As a result, liaison offices had to establish legal templates to cover the whole process from the discussion to the licensing state and develop strategies for a successful commercial process, including the proper determination of product value. The process will be exemplified with specific emphasis on critical issues and solutions.

Utilization Profile, Safety, and Efficacy of Intravitreal Injections of anti-VEGF in a Single Institution

H. Uy ; P.S. Chan-Uy ; A.A.S. Veloso ; J. Francisco III ; F.M. Cruz
Asian Eye Institute, Philippines

Purpose: To describe the indications for, outcomes following, and safety profile of intravitreal administration of anti vasculo-endothelial growth factor (anti-VEGF) drugs among 109 patients at an ambulatory surgical center (Asian Eye Institute or AEI, Philippines).

Design: Retrospective chart review

Methods: One hundred thirty-nine (139) eyes of one hundred nine (109) patients received a total of 708 anti-VEGF injections from January 1, 2008 – October 31, 2010. Their medical charts were reviewed to obtain the following data: 1) indication for treatment, 2) number of injections, 3) best corrected visual acuity (BCVA), and 4) central retinal thickness (CRT) before the first injection and a month after latest injection, and 5) adverse events. Statistical analysis was performed using paired t-Test ($p<0.05$).

Results: The most common indications for anti-VEGF injection were neovascular ARMD (40%), diabetic macular edema or DME (24%), macular edema secondary to retinal vein occlusion (16%), and proliferative diabetic retinopathy with vitreous hemorrhage (9%). The most common anti-VEGF drug administered was bevacizumab (70%), followed by ranibizumab (27%), and pegaptanib sodium (3%). Eyes with macular edema secondary to retinal vein occlusion showed a significant change in BCVA ($p<0.05$). While significant improvements in CRT ($p<0.05$) were obtained for eyes with ARMD and DME, these did not translate to a significant improvement in BCVA ($p<0.05$). There were no serious systemic or ocular adverse events recorded.

Conclusion: Use of anti-VEGF for choroidal neovascular membranes and macular edema of various etiologies is safe and effective. Visual prognosis varies and is dependent on several factors.

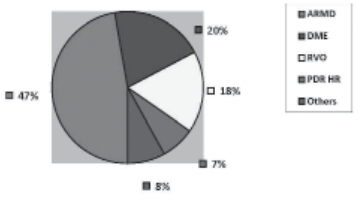


Figure 1 Distribution of anti-VEGF injections according to indication.

Effects of Chinese Medicine QiDengMingMu Capsule on Protein Kinase C in Retinas and VEGF in Vitreous of Spontaneous Diabetic Rats

Q. Li [1]; J. Duan [2]; N. Gao [2]; F. Zhang [1]
[1]Chengdu University of Traditional Chinese Medicine, China, Peoples Republic;
[2]Sichuan Povincial Hospital of T.C.M., China, Peoples Republic

Objective: To observe the effects of Chinese medicine QiDengMingMu capsule on protein kinase C (PKC) in retinas and the vascular endothelial growth factor (VEGF) in vitreous of the experimental animal model of spontaneous diabetic retinopathy rats (Goto-kakizaki rats), and to explore the pathological mechanism of Chinese Medicine on diabetic retinopathy (DR).

Methods: Evaluate the experimental animal model of spontaneous diabetic retinopathy rats (GK rats) in morphology. The GK rats with six-month course are randomly divided into 6 groups: the negative control group, treated groups with high¡¢middle¡¢low dosage of QiDengMingMu capsule, positive control group of Difral and Doxium, and normal control group, respectively. The rats were put to death after given drugs or distilled water for 3 months, and the samples were studied by means of enzyme linked immunosorbent assay£¨ELISA£© and immunohistochemistry.

Results:

(1)The spontaneous diabetic retinopathy rats can be used as the pathological model of background stage of DR in human, especially the experimental animal model of non-insulin dependent DR rat(GK rats).

(2)The Chinese medicine QiDengMingMu capsule has effects as:

(2.1) Improving the quality of life of GK rats;

(2.2) Inhibiting the activity of PKC in retinas of GK rats;

(2.3) Reducing the level of VEGF in vitreous of GK rats.

(2.4) Decreasing of blood glucose of the GK rats.

Conclusion: The Chinese medicine QiDengMingMu capsule can inhibit the activity of PKC in retinas of GK rats and can also reduce the level of VEGF in vitreous. It is considered to have the protective agents for retinal impairment, and help to repair the damage of retinas of GK rats.

Amyloid Beta, A Potential Target of Neuroprotection in Glaucoma?

J. Ge
Sun Yat-sen University, China

Abnormal accumulation of amyloid beta (abeta) plays an important role in the neurodegeneration of Alzheimer's Disease (AD). Ganglion cell degeneration, decreased thickness of the retinal nerve fiber layer, and optic nerve degeneration had been reported in AD patients. Recently, abeta is reported to be involved in experimental glaucoma, cultured ganglion cell lines, and transgenic AD models. Abnormal accumulation of abeta, amyloid plaques, was reported in the retina of several kinds of transgenic AD models. Immunotherapy targeting abeta has been proved to be neuroprotective for retinal ganglion cells both in experimental glaucoma and AD models. Interestingly, immunotherapy targetting amyloid-related peptides was found to increase microvascular deposition, astrogliosis and microglial infiltration, which might offer an new insight into the process of abeta cleaning up in retina. Further evidence is needed to identify abeta as a target of neuroprotection for glaucoma.

Role of Endothelins in Ocular Disease

G. Garhoefer
Medical University of Vienna, Austria

Endothelin is one of the most potent vasoactive substances known. Among the isoforms known, especially endothelin-1 (ET-1) exerts very potent vasoconstrictor effects also in the ocular vasculature. Based on these observations, it has become clear in the recent years that ET-1 is one of the major determinants of ocular blood flow. In addition, several lines of evidence indicate now, that altered production of endothelin may be involved in the pathophysiology of vascular related diseases, such as diabetic retinopathy or glaucoma. Beside its strong vasoactive properties, there is evidence now that ET-1 also acts as a mitogen on the vascular smooth muscle. This supports the idea of a role of the endothelin system in the pathogenesis of vascular related ocular diseases. In this talk, the physiological role of endothelin in the regulation of ocular blood flow will be covered. In addition, our current knowledge about the role of endothelin in ocular diseases will be summarized and new possible pharmacological treatment targets will be discussed.

Overview of Steroids for Diabetic Macular Edema

M. Gillies
Save Sight Institute, Australia

The use of steroids for the treatment of diabetic macular edema has been a major recent breakthrough in the management of retinal disease. First studied in animal models in the 1980s, intravitreal triamcinolone acetonide (IVTA) was first used in human eyes at the Save Sight Institute in Sydney for exudative macular degeneration. When early observations suggested that its effect on macular disease was more marked against exudation than neovascularisation, it was used for diabetic macular edema with remarkable effects that could be appreciated particularly using optical coherence tomography. Early placebo-controlled randomised clinical trials performed by us and others reported a beneficial effect of IVTA treatment on best-corrected visual acuity and central macular thickness that persisted out to 2 years. Local adverse events, especially elevated intraocular pressure and cataract are manageable but very common with IVTA. Subsequent studies by DRCR.net investigators found firstly that IVTA, at least in the cases they selected, might be inferior to laser, and then that it was inferior to anti-VEGF therapy for DME, although not, significantly, in pseudophakic eyes. New formulations of steroid being tested for DME include Ozurdex and Iluvien.

Intravitreal steroid therapy can still be considered for example in eyes with macular edema secondary to focal parafoveal or severe diffuse leak, prior to cataract surgery, or in eyes with macular edema and high risk proliferative diabetic retinopathy for which immediate pan-retinal photocoagulation is required. Further research is warranted to determine into how ocular steroid therapy can be combined with both retinal laser treatment and the new anti-Vascular Endothelial Growth Factor treatments for the safest and most efficacious outcomes for our patients.

Neuroprotection Update

M. Gillies
Save Sight Institute, Australia

While neuroprotective strategies have been sought to prevent ganglion cell loss in glaucoma for years, neuroprotection of the outer retina, especially the photoreceptors, is a relatively new field. Diseases in which photoreceptor degeneration leads to loss of vision include retinitis pigmentosa, idiopathic macular telangiectasia type 2 and, possibly, diabetic retinopathy. Neurons usually die by pre-programmed cell death, or apoptosis. A number of potential neuroprotective agents have been proposed based on in vitro and in vivo studies. Two agents have progressed to the level of clinical trials: Ciliary Neurotrophic factor (CNTF), which is delivered as a pellet manufactured by Neurotech that contains retinal pigment epithlial cells engineered to produce CNTF contuuously, has shown some evidence of efficacy in preliminary clinical trials for atrophic macular degeneration and retinitis pigmentosa, where it resulted in some thickening of the retina, some improvement of visual acuity and perhaps recovery of outer segments in diseased areas of a few eyes examined with adaptive optics fundoscopy. Another agent that is being tested in randomised clinical trials for atrophic macular degeneration is the alpha-2 agonist, brimonidine (Allergan), which is delivered in a slow-release biodegradable semipermeable hollow fibre. Neuroprotection of the outer retina offers hope for prevention of vision loss in a number of common macular diseases.

Ozurdex for Retinal Vein Occlusion

M. Gillies
Save Sight Institute, Australia

Ozurdex Geneva Study Group

Objective: To evaluate the safety and efficacy of dexamethasone intravitreal implant (DEX implant; OZURDEX, Allergan, Inc., Irvine, CA) compared with sham in eyes with vision loss due to macular edema (ME) associated with branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO).

Design: Two identical, multicenter, masked, randomized, 6-month, sham-controlled clinical trials (each of which included patients with BRVO and CRVO). Participants: A total of 1267 patients with vision loss due to ME associated with BRVO or CRVO.

Intervention: A single treatment with DEX implant 0.7 mg (n = 427), DEX implant 0.35 mg (n = 414), or sham (n = 426).

Main Outcome Measures: The primary outcome measure for the pooled data from the 2 studies was time to achieve a > or =15-letter improvement in best-corrected visual acuity (BCVA). Secondary end points included BCVA, central retinal thickness, and safety.

Results: After a single administration, the time to achieve a > or =15-letter improvement in BCVA was significantly less in both DEX implant groups compared with sham (P<0.001). The percentage of eyes with a > or =15-letter improvement in BCVA was significantly higher in both DEX implant groups compared with sham at days 30 to 90 (P<0.001). Improvement in mean BCVA was greater in both DEX implant groups compared with sham at all follow-up visits (P< or =0.006). Improvements in BCVA with DEX implant were seen in patients with BRVO and CRVO, although the patterns of response differed. The percentage of DEX implant-treated eyes with intraocular pressure (IOP) of > or =25 mmHg peaked at 16% at day 60 (both doses) and was not different from sham by day 180. There was no significant between-group difference in the occurrence of cataract or cataract surgery.

Conclusions: DEX implant can both reduce the risk of vision loss and improve the speed and incidence of visual improvement in eyes with ME secondary to BRVO or CRVO.

READ 2 - Two-Year Outcomes of the Ranibizumab for Edema of the Macula in Diabetes

M. Goldstein
Tel Aviv University, Israel

Purpose: to evaluate the long term effects of Ranibizumab in patients with Diabetic Macular Edema (DME).

Methods: this is a 2 years prospective randomized multicenter clinical trial. 126 patients with DME were randomized 1:1:1 Treatment groups included: Ranibizumab 0.5mg at baseline and months 1,3,5 (group 1), focal or grid laser at baseline and month 3 if needed (group 2), combination of Ranibizumab and focal/grid laser at baseline and month 3 (group 3). Starting at month 6, all patients could be treated with Ranibizumab if met re-treatment criteria. Primary outcome measure was the change in best corrected visual acuity (BCVA) from baseline to month 24.

Results: 33 patients in group 1, 34 patients in group 2 and 34 patients in group 3 remained in the study for 24 months. After the primary endpoint at month 6 most patients in all groups were treated only with Ranibizumab. Mean number of injections was 5.3, 4.4 and 2.9 during the 18-months follow up period in groups 1,2,3 respectively. Mean improvement in BCVA was 7.7, 5.1 and 6.8 letters at month 24, and the percentage of patients who gained 3 lined or more of BCVA was 21, 0 and 6 at 24 months. The percentage of patients with BCVA 20/40 or better at month 24 was 45% in group 1, 44% in group 2 and 35% in group 3. Mean Foveal thickness at month 24 was 340µ, 286µ and 250µ for groups 1,2,3 respectively.

Conclusion: Intraocular injections with Ranibizumab provided benefit for patients with DME for at least 2 years. Intravitreal Ranibizumab combined with focal/grid laser reduced the amount of residual edema and the frequency of injections needed to control the edema.

VIEW 2 - VEGF Trap-Eye Investigation of Efficacy and Safety in Wet AMD (VIEW 2)

M. Goldstein
Tel Aviv University, Israel

Purpose: to evaluate the safety and efficacy of three treatment regimens of VEGF Trap Eye compared to standard treatment with Ranibizumab for CNV secondary to AMD.

Methods: this is a 2 years prospective randomized double masked control trial. Patients aged >50 with primary or recurrent subfoveal CNV secondary to AMD and BCVA of 20/40-20/320 were included in the study. Participants were randomized to 4 different treatment groups. During the first year patients were treated with 0.5mg VEGF Trap every 4 weeks, or 2mg VEGF Trap every 4 weeks, or 2mg VEGF Trap every 8 weeks or Ranibizumab every 4 weeks. The primary end point was prevention of vision loss of Greater or Equal To 15 letters on the ETDRS chart, compared to baseline, at 52 weeks. Secondary endpoints were; mean change in BCVA from baseline, the proportion of participants who gained 3 lines or more in BCVA, mean change from baseline in total NEI VFQ-25 score, mean change in CNV area and safety.

Results: 1240 patients with SFCNV were included. 17,000 intravitreal injections were given.

Conclusion: the Phase III VIEW 1 and VIEW 2 trials are currently ongoing to determine how prolonged dosing intervals can sustain efficacy at a lower injection burden.

Anti Angiogenic Agents for Other Indications

M. Goldstein ; A. Loewenstein
Tel Aviv Medical Center, Israel

Purpose: to evaluate the efficacy of Anti Angiogenic agents in treating retinal vascular diseases other than Vein occlusion or Diabetic retinopathy

Methods: this is a prospective case series in 1 center. Patients with parafoveal telangiectasis, adult coat's, radiation retinopathy and retinal macroaneurysm. All patients presented with decreased vision. Clinical examination revealed macular edema involving the fovea. All patients were treated with Intravitreal Ranibizumab or Bevacizumab, and some of them received additional focal laser.

Results: There were 6 patients age 27-58 years. Follow up was 4-30 months. Patients received 1-5 injections of Ranibizumab or Bevacizumab. All patients showed a decrease in macular edema demonstrated by SD-OCT. All patients had an improvement in visual acuity. No adverse events were recorded.

Conclusion: Intraocular injections with Ranibizumab or Bevacizumab can improve macular edema and visual acuity in patients with retinal vascular diseases other than Vein Occlusion or Diabetic Retinopathy. Larger randomized trials are needed to establish the benefit if Anti Angiogenic drugs for these indications.

Protein Biomarkers and Tear Film and Dry Eye Disease

F. Grus
Experimental Ophthalmology, Germany

Purpose: The composition of proteins and peptides in tears plays an important role in ocular surface diseases. Proteomic analyses could reveal biomarkers for the health and integrity of the ocular surface. Several studies could demonstrate changes in the tear protein patterns of dry-eye patients compared to controls. The presentation will give a critical state-of-the-art analysis of the relevance of tear film proteomics in the diagnosis of disease and the problems of translating it into clinical routine. Methods: Different proteomic analyses in tear film will be compared such as conventional gel-electrophoresis, micro-array based approaches, and e.g. mass spectrometric profiling (LC-MSMS, Maldi-TOFTOF, Seldi-TOF etc.). Furthermore, different methods for quantification and validation of the biomarkers will be demonstrated. Results: Many studies could reveal protein and peptides biomarkers which are consistently up - or down-regulated in dry-eye disease and could differentiate between different disease subgroups. Some of these biomarkers are even consistent between different analytical methods. The presentation will compare the results of several of those studies and discuss the clinical implications of these biomarkers and possible implications for new treatment options. Conclusions: Proteomic technologies might be a very promising approach in dry-eye disease. In comparison to genetic testing, proteomic biomarkers can describe the actual state of the ocular surface and the ongoing disease processes. However, the application of these technologies in clinical routine is still challenging. Beside of new treatment options, these biomarkers could serve in future to optimize treatments in individual patients in personalized medicine.

Ocular Perfusion Pressure and Hemodynamics in Glaucoma

A. Harris
Indiana University School of Medicine, USA

Treatment of glaucomatous optic neuropathy has been directed at lowering intraocular pressure (IOP) and is currently the only therapeutic strategy available to patients with glaucoma. Studies have demonstrated that some patients show progression of glaucoma despite meeting target IOP. In the Early Manifest Glaucoma Trial (EMGT), despite significant reduction in progression risks in higher and lower baseline IOP (HRs, 0.41 and 0.55), overall progression was 67% when follow-up ended (median, 8 years). Vascular dysregulation is considered to be a major candidate in the pathogenesis of glaucoma.

The strongest evidence of vascular deficiencies in glaucoma comes from numerous population-based studies that link lower than average diastolic ocular perfusion pressure with the prevalence, incidence and progression of glaucoma. Low diastolic blood pressure (below 50-55 mmHg) has been reported to be associated with prevalence of glaucoma. In the Barbados Eye study, which spanned over 9 years of follow-up, low systolic, diastolic and mean ocular perfusion pressure increased the incidence of glaucoma with a relative risk of 2 to 2.6. In the EMGT patients with low systolic perfusion pressure at baseline progressed and exhibited a hazard ratio of 1.5. Recently, fluctuation of mean ocular perfusion pressure has been identified as the most consistent risk factor for clinical severity of both anatomic (retinal nerve fiber layer thickness) and functional (visual field) outcome variables in a cohort of glaucoma patients. Another population-based project, the Thessaloniki Eye Study, associated low diastolic blood pressure with a large cup-to-disc ratio and a narrow rim.

In glaucoma patients, it is thought that defective autoregulation of ocular blood flow results in ischemic damage and reperfusion injury. This mechanism helps explain why low ocular perfusion pressure has been found to be such a consistent risk factor for the development and progression of glaucoma

OCT in Glaucoma

M. He
Zhongshan Ophthalmic Center, Sun Yat-Sen University, China

Primary angle closure glaucoma remains a major cause of blindness particularly in East Asian population. Previous studies have demonstrated that people with narrow drainage angle are at higher risk of developing glaucomatous damage. The anterior segment optical coherence tomography (ASOCT) provides a fast, non-contact method for imaging the anterior chamber. A single image can illustrate the entire cornea, both angles on one meridian, and the anterior portion of the lens. In Guangzhou, we develop software that allows quantitative measurements on ASOCT images. In this symposium, we will briefly summarize the new findings on the anatomical basis and mechanism of angle closure based on OCT quantitative measurements.

Latency and Suppression of Reactivation of HSV

S. Higaki
Kinki University, Japan

Herpes simplex virus type 1 (HSV-1) establishes a latent state in sensory neurons and may reactivate throughout the life of the host. HSV-1 keratitis often recurs and it can be vision threatening.

We detected herpes simplex virus types 1 (HSV-1) and 2 (HSV-2), varicella zoster virus (VZV), and cytomegalovirus (CMV) DNAs in human corneas. Twenty-seven corneal buttons were obtained from 27 patients at the time of penetrating keratoplasty. The detection of HSV-1, HSV-2, VZV, and CMV DNAs was carried out by a nested polymerase chain reaction (PCR). HSV-1, HSV-2, VZV, and CMV DNAs were detected in 10, 1, 9, and 2 of the 27 recipient corneal buttons, respectively. Two cases of CMV-positive patients had ocular pemphigoid. The relationship between CMV in the cornea and the anterior segment disorders should be further evaluated.

The next topic is about the suppression of HSV-1 reactivation. We have shown that bromfenac sodium (cyclooxygenase inhibitor) eye drops, intramuscular adenosine monophosphate (AMP), geldanamycin (heatshock protein inhibitor) are effective for reducing HSV-1 recurrence in a mouse model. Recently we also found that NFKB can suppress HSV-1 reactivation in HSV-1 latently-infected mice. We are going to assess gene expression in the trigeminal ganglia of HSV-1 latently-infected and reactivated mice after treatment with NFKB using microarray analysis.

The Use of the Express Implant in Asian Eyes

C.L. Ho
Singapore National Eye Centre, Singapore

The Ex-PRESS Mini glaucoma shunt (Optonol Limited, Neve Ilan, Israel) is a miniature, non-valved, stainless steel glaucoma device. It was developed as an alternative to trabeculectomy filtration surgery for patients with glaucoma.Implanted under a partial thickness scleral flap, this procedure is similar to standard trabeculectomy without the need for sclerostomy and iridectomy. The use of the device claims to be quicker, simpler and more reproducible to perform as well as less traumatic to the ocular tissue than traditional filtering surgery.

Several studies evaluating the efficacy and safety of the Ex-PRESS device alone and in combination with cataract phacoemulsification have been reported. However all studies were performed for open angle glaucomas, and the majority in Caucasian populations. Primary angle closure glaucoma (PACG) is a prevalent disease in Asia. The safety and efficacy of the device in Asian patients and in PACG is unknown. We describe the findings of combined cataract extraction (CCE) with the Ex-PRESS device in Asian patients and in those with PACG.

Neuroprotective Effects of Agmatine on Various Oxidative Stressed Neurons

S. Hong
Yonsei University College of Medicine, Korea, Republic of

Agmatine is an endogeous metabolite of arginine and has known to act as a putative neuromodulator. For last several years, we investigated whether agmatine protects neurons from the oxidative stress-induced neuronal injury. For in vitro study, the neurons were exposed to hydrogen peroxide or hypoxic environment; for in vivo study, the middle cerebral artery was transiently occluded. As results of these in vitro and in vivo studies, agmatine significantly attenuated the cytotoxicity of retinal ganglion cells, Muller glia, and microglia. Accordingly, agmatine may offer a powerful new neuroprotective agent for the oxidative stress-related diseases including glaucoma.

Protective Effect of GSTT on Retinal Ganglion Cells and Optic Nerve in Rabbits with Chronic Intraocular Hypertension

L-N. Huang
Shen Zhen Eye Hospital, China

Objective: To observe the effects of GSTT protective of retina and optic nerve in rabbit eyes with Hyper-intraocular Pressure (HIOP), explain its mechanism.

Methods: The 24 healthy NewZealand white rabbits were randomly divided into 4 groups: normal control group (A group); HIOP untreated group (B group); HIOP with GSTT treated group (C group); HIOP with EBHM treated group (D group). HIOP was induced by 20g•L-1 methylcellulose injection into the anterior chamber with HIOP and GSTT group and EBHM group. GSTT group was injected 5 mg/kg GSTT and EBHM group was injected 4.5 mg/kg EBHM and measured intraocular pressure with Schiotz tonometer every day. Continuous medication 28 days, before construction of the mode, detection 28 days after modeling experiments on hemorheology and VEP in rabbits, the rabbits were sacrificed and the globles were excavated for study Glutamate and ultrastructure.

Result: Compared with those testing criterions, the statistical significance was found in four groups ($P<0.05$).

Conclusion: GSTT may protect RGCs and optic nerve against HIOP.

A Novel Thermo-Sensitive Biodegradable Hydrogel for Extended Release of Bevacizumab

Y-S. Hwang [1]; Y-S. Chiang [2]; C-C. Lai [1]
[1]Chang Gung Memorial Hospital, Linkou and Taipei, Taiwan; [2]National Tsing Hua University, Taiwan

Background: Anti-VEGF has been nominated as a strategy for proliferative diabetic retinopathy. Short half-life, however, is the major concern of frequent intravitreal injections. Extended release of anti-VEGF biologics could be a new and safer clinical application for the high-prevalent neovascular retinal disorders.

Methods: A novel biodegradable and thermo-sensitive block copolymers consisting of poly(2-ethyl-2-oxzoline) and poly(ε-caprolactone) (PEOz-PCL-PEOz, ECE) were synthesized, and such triblock copolymers have shown a reversible sol (room temperature)–gel (physiological temperature) phase transition for easily carrying and extended release of the protein biologics.

Results: The ECE hydrogel was chemically and molecularly characterized by 1H NMR and FTIR, respectively. The hydrolytic degradation of ECE hydrogel was studied in balanced salt solution for up to 2 months by gel permeation chromatography (GPC), which showed no changes in the molecular weight. Scanning electron microscope (SEM) was utilized to assessing the porosity of the ECE surface, which revealed the erosion and the pores became more numerous within 2 months. There was no in-vitro cytotoxic effect of ECE noted in human retinal pigment epithelial (RPE) cell line co-cultured with ECE. Six-month results of retinal photography and retinal electrophysiology further demonstrated the good in vivo biocompatibility of ECE for ocular tissues in rabbits. The retinal electrophysiology showed comparable a and b waveforms between the study and control eyes, which is further confirmed with no morphology difference in retinal histology analysis. The in-vitro release of bevacizumab from the ECE was extended than control.

Conclusion: The features of noncytotoxicity, intraocular biocompatibility and biodegradability as well as phase-transition make the ECE hydrogel a great potential to be widely used in biomedical applications.

Multicenter Surveillance of Microbial Keratitis in Korea

J. Y. Hyon
Seoul National University Bundang Hospital, Korea, Republic of

Purpose: To investigate the microbial profile of infectious keratitis in Korea.

Methods: Twenty one referral hospitals were participated in this nationwide multicenter surveillance from 2006 to 2008. The patients with clinical diagnosis of bacterial or fungal keratitis were enrolled. Clinical characteristics, microbioligcal profile, and antibiotic susceptibility were investigated.

Results: Out of 235 cases, 202 cases (86%) were bacterial keratitis . Fungal keratitis and acanthamoeba keratitis were 35 cases (14.9%) and 4 cases (1.7%) each. Culture positive rate was 37.0%. The most common causative pathogen was Pseudomonas species (21.8%), followed by coagulase negative Staphylococcus species (19.2%) and Staphylococcus aureus (15.4%). Fusarium species were most common pathogen for fungal keratitis. Ciprofloxacin-resistance Pseudomonas species were not found. Staphylococcus species showed Methicillin-resistance in 80%.

Conclusion: The microbial profile showed similar pattern as in the other literatures. This study raised concerns regarding MRSA ocular infection in Korea.

TA/Steroids for Inhibition of Progression of DR

M. Ip
University of Wisconsin, USA

Objective: Compare effect of intravitreal triamcinolone acetonide with focal/grid photocoagulation on progression of diabetic retinopathy.

Methods: Exploratory analysis performed on subjects with diabetic macular edema (DME) randomly assigned to laser or intravitreal triamcinolone acetonide (1mg or 4mg). Fundus photographs were obtained at baseline, 1, 2 and 3 years. Main Outcome Measures: Progression to proliferative diabetic retinopathy (PDR) or worsening of 2 or more severity levels on reading center masked assessment of 7-field fundus photographs, plus additional eyes that received panretinal photocoagulation (PRP) or had a vitreous hemorrhage.

Results: Cumulative probability of progression of retinopathy at 2 years was 31% (laser), 29% (1mg), and 21% (4mg), (compared with laser group, P=0.65 in 1mg group, and 0.005 in 4mg group). These differences appeared sustained at 3 years.

Conclusions: Intravitreal triamcinolone acetonide (4 mg) appeared to reduce the risk of progression of diabetic retinopathy. Given the exploratory nature of this analysis, and since intravitreal triamcinolone has cataract and glaucoma side effects, use of this treatment just to reduce the rates of progression of PDR or worsening of the level of diabetic retinopathy does not seem warranted at this time.

Targeted Nanocarriers for Therapy of Ocular Neovascularization

J. Penn [1]; A. Jayagopal [2]
[1]Vanderbilt Eye Institute, USA; [2]Vanderbilt University, USA

Background and aims: Cell adhesion molecules (CAMs), particularly ICAM-1 and VCAM-1, are markers of inflammation expressed on retinal endothelial cell surfaces in a broad spectrum of ocular vascular diseases, including uveitis, diabetic retinopathy, and age-related macular degeneration. As CAM expression often precedes development of severe pathology, clinical approaches for early detection of this marker would facilitate timely therapeutic interventions. Furthermore, as these CAMs are often expressed focally on inflamed endothelium, and not the endothelium lining healthy tissues, they constitute potential therapeutic targets. We have developed a series of nanocarriers targeted against CAMs which can bear imaging or therapeutic payloads. The goal of this study was to demonstrate the utility of CAM targeted nanocarriers for intracellular delivery of imaging agents and/or therapeutics in animal models of vascular disease.

Methods: CAM targeted nanocarriers bearing optical imaging agents or siRNAs were characterized to determine optimal size, surface charge, and encapsulation efficiencies. Cytotoxicity, delivery efficiency, and functional knockdown of several molecular targets were determined in retinal microvascular endothelial cells. Homing and biodistribution of nanocarriers in animal models of neovascular age-related macular degeneration, oxygen-induced retinopathy, and atherosclerosis were analyzed using optical imaging.

Results: CAM targeted nanocarriers were capable of specific targeting of the CAMs ICAM-1 and VCAM-1 on inflamed retinal endothelial cells in vitro and in vivo. Specific targeting of inflamed retinal endothelium was observed in animal models of vascular disease. Knockdown of several molecular targets via siRNAs was achieved.

Conclusions: CAM targeted nanocarriers are a promising framework for the delivery of diverse imaging and therapeutic payloads to the cytoplasm of diseased retinal endothelial cells in vivo.

Clinical Observation on the Treatment of Early Diabetic Retinopathy with Compound Danshen Dripping Pills

M. Jin ; W. Yuan ; H. Deng
China-Japan Friendship Hospital, China, Peoples Republic

Objective: To observe the effects of compound danshen dripping pills in treating early diabetic retinopathy (DR).

Methods: All the 58 cases in 1 to 3 periods selected were type 2 DR patients. There were 30 cases (60 eyes) in danshen group, 28 cases (56 eyes) in controlled group. The result of treatment was evaluated by the test of visual acuity, fundus photography, fundus fluorescein angiography and visual field.

Result:

1.The visual acuity changes: No significant difference was seen between the two groups, After the treatment, the total effective of the treated group were both of 65%.and 61%;

2.The defect of visual field: The changes of Mean Defect (MD) of visual field before and after the treatment are showed,MD value of visual field decreased obviously than before in the treated group;3. Fundus fluorescein angiography and fundus photography: both groups had effect in treating microaneurysm and small blood spots. Significant changes were found after the treatment.

Conclusion: To type 2 DR patients, diabetic retinopathy with compound danshen dripping pills could improve the state of hemorrheology and pathological changes of fundus microaneurysm . Compared with calcium dobesilate, compound danshen dripping pills had certain advantage in the control of microaneurysm, bleeding and the improvement of visual acuity and visual field.

Pathogenic Hints for Glaucoma from the Optic Nerve Head

J. Jonas
Medical Faculty Mannheim-Heidelberg, Germany

Purpose: To demonstrate morphological features of the optic nerve head which may help in elucidating the pathogenesis of glaucomatous optic nerve damage.

Methods: A review of previous studies on the appearance of the optic nerve head in normal eyes, eyes with non-glaucomatous optic nerve damage and eyes with glaucomatous optic neuropathy will be presented.

Results: Since there are morphological differences between vascular optic nerve damage and glaucomatous optic neuropathy, the hypothesis is that the retro-lamina cribrosa orbital cerebrospinal fluid pressure as the counter pressure against the intraocular pressure may potentially play a role in the pathogenesis of glaucomatous optic neuropathy.

Conclusions: In future considerations of the pathogenesis of glaucomatous optic neuropathy, n particular in patients with normal (intraocular) pressure glaucoma, the orbital cerebrosopinal fluid pressure may be taken into account.

Intravitreal Cell-Based Production of Glucagon-Like Peptide-1

J. Jonas [1]; R. Zhang [2]; L. Xu [2]; K. Ma [2]; C. Wallrapp [3]
[1]Medical Faculty Mannheim-Heidelberg, Germany; [2]Beijing Tongren Hospital, China; [3]CellMed AG, Germany

Background: To examine efficacy and safety of an intravitreal cell.-based production of glucagon-like peptide-1 (GLP-1) by intravitreally implanted and encapsulated cells.

Methods: The experimental study included 12 Sprague-Dawley rats. Four cell beads with a diameter of 600 µm were intravitreally implanted. Each bead contained 3000 GLP-1 secreting cells which were encapsulated by a barium cross-linked sodium alginate matrix. At baseline and at each of the follow-up examinations at day 3, day 7 and day 14, four, three, three and two animals, respectively, were sacrificed. The concentration of active GLP-1 in the vitreous body samples was determined by ELISA. The retinas were histologically examined.

Results: The active GLP-1 concentration in the vitreous samples increased significantly after baseline (< 5 pM) to a peak at day 3 (287 ± 196 pM) and at day 7 (238 ± 55 pM), before it decreased (day 14: 70 ± 8 pM). The histological examinations did not show signs of apoptosis or tissue destruction.

Conclusion: The intravitreal application of beads containing alginate encapsulated cells producing GLP-1 resulted in an intraocular production of GLP-1 with a significant increase in the intraocular GLP-1 concentration, without observed cytotoxic effects. An intravitreal cell-based drug therapy with GLP-1 appears feasible.

Monocyte Chemoattractant Protein-1 (MCP-1), and Adhesion Molecules ICAM-1 VCAM-1 in Exudative Age-Related Macular Degeneration

J. Jonas [1]; Y. Tao [2]; M. Neumaier [3]; P. Findeisen [1]
[1]Medical Faculty Mannheim-Heidelberg, Germany; [2]People's Hospital, China; [3]Medical Faculty Mannheim, Germany

Objective: To examine intraocular concentrations of monocyte chemoattractant protein-1 (MCP-1), soluble intercellular adhesion molecule-1 (sICAM-1), soluble vascular cell adhesion molecule-1(sVCAM-1) and vascular endothelial growth factor (VEGF) in eyes with exudative age-related macular degeneration (AMD).

Methods: The investigation included a study group of 28 patients (28 eyes) with exudative AMD and a control group of 25 patients (25 eyes) with cataract. The concentrations of MCP-1, sICAM-1, sVCAM-1 and VEGF in aqueous humor samples obtained during surgery were measured using a solid-phase chemiluminescence immunoassay.

Results: The aqueous concentrations of sICAM-1 (844±2073 pg/mL versus 246±206 pg/mL; P<0.001), sVCAM-1 (7978±7120 pg/mL versus 2999±1426 pg/mL; P 0.001) and MCP-1 (587±338 pg/mL versus 435±221 pg/mL;P=0.07) were higher in the study group than in the control group. The concentration of VEGF did not vary significantly (P=0.76) between both groups. The MCP-1 concentration was significantly associated with macular thickness (r=0.40;P=0.004). It decreased significantly (P=0.009) with the type of subfoveal neovascular membrane (classic membrane type - occult membrane - retinal pigment epithelium detachment). The concentrations of sICAM-1, sVCAM-1 and VEGF were not significantly (P>0.25) associated with membrane type and macular thickness.

Conclusions: MCP-1, sICAM-1 and sVCAM-1 are significantly associated with exudative AMD, even in the presence of normal VEGF concentrations. Intraocular MCP-1 concentrations correlated with the subfoveal neovascular membrane type and the amount of macular edema. One may infer that MCP-1, sICAM-1 and sVCAM-1 may potentially be additional target molecules for the therapy

Intraocular VEGF Concentration and Refractive Error

J. Jonas [1]; Y. Tao [2]; M. Neumaier [1]; P. Findeisen [1]
[1]Medical Faculty Mannheim-Heidelberg, Germany; [2]People's Hospital, China

Purpose: Myopia has been shown to be a protective factor against the development of neovascular intraocular diseases such as exudative age-related macular degeneration and proliferative diabetic retinopathy. Since mainly the vascular endothelial growth factor (VEGF), but also other cytokines are mediators of intraocular neovascularization, we examined whether the concentration of cytokines in normal eyes is associated with myopia.

Methods: Sixteen patients without signs of diabetic retinopathy or age-related macular degeneration underwent cataract surgery at the start of which aqueous humor samples were obtained. The mean refractive error was -3.8 ± 5.5 diopters (range, -15.75 to 2.63 diopters). Using a solid-phase chemiluminescence immunoassay, we determined the concentrations of VEGF, monocyte chemoattractant protein-1 (MCP-1), soluble intercellular adhesion molecule-1 (sICAM-1), and soluble vascular cell adhesion molecule-1 (sVCAM-1).

Results: The mean concentration of VEGF, MCP-1, sICAM-1 and sVCAM-1 in the aqueous humor was 38±39 pg/mL, 400±233 pg/mL, 197±163 pg/mL and 2800±1446 pg/mL, respectively. The aqueous humor concentration of VEGF was significantly and positively correlated with refractive error (Pearson's correlation coefficient r=0.53; P=0.04) and significantly and negatively with axial length (r=-0.50; P=0.047). The concentrations of MCP-1, sICAM-1, and sVCAM-1 were not significantly (P>0.05) associated with refractive error nor with axial length.

Conclusions: Intraocular concentrations of VEGF, but not of MCP-1, sICAM-1, and sVCAM-1, were significantly lower in myopic eyes than in hyperopic eyes without signs of intraocular neovascularization. This might be related to the reduced risk for exudative age-related macular degeneration and proliferative diabetic retinopathy in myopic eyes.

Comparison of Antibiotic Effect and Corneal Epithelial Toxicity on Fluoroquinolone Antibiotics

C-K. Joo
College of Medicine, The Catholic University of Korea, South Korea

Purpose: To compare bacterial susceptibility and corneal epithelial toxicity between levofloxacin, moxifloxacin and tosufloxacin in the human corneal epithelial cells (HCEC).

Methods: We used two types of strains, i.e. ATCC strains and resistant strains. The HCEC were incubated with each bacterial population for 1 hour and exposed to both antibiotics for 1 hour. To determine corneal epithelial toxicity, the HCEC were exposed to each antibiotic agent at a concentration of 0.1% for 24 hours. And we observed the wound healing rate of injured HCEC cultured in each antibiotic agent for 24 hours.

Results: In bacterial susceptibility testing of antibiotics, levofloxacin, moxifloxacin and tosufloxacin demonstrated the same efficacy against gram-positive bacteria. Moxifloxacin and tosufloxacin showed a higher toxicity than levofloxacin when the HCEC were exposed to the respective antibiotics for 24 hours. The Moxifloxacin and tosufloxacin inhibited the effect of wound healing in HCEC injury but levofloxacin did not.

Conclusion: In this study, levofloxacin seemed to be safer than moxifloxacin and tosufloxacin in corneal epithelial cells. These results suggest that the selection of antibiotic therapy should be based on the identification of specific bacteria and the condition of the corneal surface.

Biocompatibility of Thermo-Response Hydrogel as Ocular Drug Delivery System

J. Kang-Mieler [1]; W. Mieler [2]
[1]Illinois Institute of Technology, USA; [2]University of Illinois at Chicago, USA

Recently developed thermo-responsive hydrogel has been shown to be effective in encapsulating and releasing active protein in vitro and may have various significant applications for the eye. The main objective of this study was to investigate any potential toxicity, if any, of the thermo-responsive hydrogel in an in vivo animal model. All experiments were performed on anesthetized adult pigmented rats. Thermo-responsive hydrogel was synthesized using poly(N-isopropylacrylamide) (PNIPAAm) and crosslinked with polyethylene glycols-diacrylate (PEG-DA). Approximately 5 µl of sterile hydrogel was injected into the vitreous cavity via a 30 gauge needle. SD-OCT was used to measure the thickness of the retina and injected hydrogel; SLO was used to measure retinal blood flow; and ERG was used to measure the retinal cellular function. Data were acquired at prior to injection and weekly up to 4 weeks post injection. Both the retina and hydrogel were imaged at the same time with SD-OCT. The retinal thickness near the hydrogel was determined to be 259 ± 15 µm compared to the non-exposed area of 247 ± 19 µm. The location and size of the hydrogel remained constant throughout the investigated period. There was a transient small change (~10%) in the retinal blood flow after one week but it recovered to the normal level. A corresponding small change in the a- and b-wave ERG amplitudes were noted after one week but recovered to the normal pre-injection level. The small transient change in blood flow and ERG after the intravitreal injection of the hydrogel fully recovered back to baseline after one week. Current results suggest that thermo-responsive hydrogels appear to be a safe and promising minimally invasive drug delivery platform to the posterior segment of the eye.

Control Sustained Release from Biodegradable Thermo-Responsive Hydrogel

J. Kang-Mieler [1]; W. Mieler [2]
[1]Illinois Institute of Technology, USA; [2]University of Illinois at Chicago, USA

Recently developed non-degradable thermo-responsive hydrogel has been shown to be effective in encapsulating and releasing active protein in vitro and may have various significant applications for the eye. The main objective of this study was to modify thermo-responsive hydrogel to be fully biodegradable and to be able to control release time of active protein. Thermo-responsive hydrogel was synthesized using poly(N-isopropylacrylamide) (PNIPAAm) and crosslinked with polyethylene glycols-diacrylate (PEG-DA) and poly(L-Lactic acid) (PLLA). The poly(NIPAAm)-co-PLLA-b-PEG-b-PLLA hydrogel was modified so that it can be injectable below the VPTT. To control release, two methods were used: (a) addition of chain transfer agents (CTA)s to the precursor (b) PEGylation and tethering of the encapsulated proteins to the degrading polymer chains. By modifying CTA concentration, the degradation time was varied from one day to several weeks. By PEGylation, the burst of initial release at temperature transition was reduced and the release of protein occurred as the degradation linker degraded over time. Current results suggest that it is possible to control release time of active protein over time. The hydrogel system appears to be a promising sustained drug delivery platform to the posterior segment of the eye.

Trabecular Meshwork Outflow / Gene Therapy / Cochlin Update

P. Kaufman
University of Wisconsin, Madison, USA

Background: Cytoskeleton modulating proteins and small molecules can affect the structural and functional biology of the trabecular meshwork (TM) by altering the actin cytoskeleton and the dynamics of cell-cell and cell-matrix adhesions and contractility. Perturbations of the actomyosin system can affect the tissue geometry of the trabecular meshwork (TM) and/or inner wall of Schlemm's canal (SC), increasing or decreasing outflow resistance. Gene transfer methods for these compounds may produce long-term effects.

Methods: IOP and outflow facility responses were measured using in vitro organ-cultured anterior segments (human, monkey, porcine) and live animals (monkeys). TM and SC cells were examined for changes in actin stress fibers, focal and cellular adhesions, and protein phosphotyrosine staining.

Results: Manipulation of the actomyosin system by rho kinase inhibitors (Y-27632, AR-12286), compounds that sequester monomeric actin (latrunculin B), inhibitors of actin polymerization (cytochalasins), and broad spectrum protein kinase inhibitors (H-7) led to loss of focal adhesions, disruption of actin filaments, and/or loss of cell-cell adhesions in cells in culture. IOP was decreased and outflow facility increased in vivo and in organ-cultured anterior segments. TGFb2 treatment increased IOP and decreased outflow facility in the organ culture system. The decrease in outflow facility was partially reversed by treatment with latrunculin-B. TGFb2 treatment also resulted in expression of cochlin protein. Cochlin overexpression alone increased IOP and decreased outflow facility.

Conclusions: Perturbation of the TM/SC actomyosin system can increase or decrease outflow resistance. Cytoskeletal agents that decrease resistance are now in clinical trials. Gene therapy strategies specifically targeting the TM may overcome problems of patient adherence. Models that more closely match the actual pathophysiology of human glaucoma could result in development of novel therapeutics.

NEI and FDA Hold Second Glaucoma Endpoints Meeting

P. Kaufman
Univ of Wisconsin Sch of Med & Public HI, USA

On September 24, 2010 the US NEI and FDA jointly held a Glaucoma Clinical Trial Design and Endpoints Symposium that engaged the glaucoma research community and the drug and device approval divisions within the FDA - specifically the Center for Drug Evaluation and Research (CDER) and the Center for Devices and Radiological Health (CDRH). Subtitled Measures of Structural Change and Visual Function, this meeting followed up on an initial March 2008 symposium by reviewing the latest research to examine whether measures of structural change can correlate to visual function and therefore serve as endpoints in clinical studies to support the approval of new drug and device diagnostics and therapies for glaucoma. Additional endpoints could potentially make glaucoma trials more logistically feasible by reducing study length, cost, and number of participants enrolled, thereby getting new therapies to patients sooner.

At the March 2008 meeting, FDA representatives stated that new clinically relevant endpoints could be considered in the regulatory review process if they are properly validated. At the follow-up meeting, noted glaucoma researchers, many funded by the NEI, reported data from studies of several imaging techniques to determine structural changes to the optic nerve head or retinal nerve fiber layer that may be correlated to visual function changes in glaucoma progression. For each imaging technique, speakers addressed the optimal criteria for measuring the rate of tissue loss and defining structural events, the statistically significant extent of structural change considering known variability of the imaging technique, and how structure predicts clinically relevant functional outcomes.

The Symposium, managed by ARVO, is the fourth in a series of collaborative meetings between the NEI and FDA, following the November 2006 Ophthalmic Clinical Trial Design and Endpoints Symposium, focusing on AMD and Diabetic Retinopathy and the September 2009 Patient Reported Outcomes meeting.

Vascular Changes in the Retina of Hypoxic Neonatal Rats

C. Kaur
National University of Singapore, Singapore

The immature retina is extremely susceptible to hypoxic-ischemic conditions resulting in the development of retinopathy. Hypoxia is an underlying factor in many conditions such as compromised pulmonary function and cyanotic heart disease which are important aetiological factors in the development of retinopathy. This study aimed to examine vascular changes in the retina of neonatal rats subjected to hypoxia. One-day old Wistar rats were subjected to hypoxia (5% oxygen+95% nitrogen) for 2 h. The expression of vascular factors such as endothelial nitric oxide synthase (eNOS) and vascular endothelial growth factor (VEGF) was examined in the retina along with ultrastructure of the blood vessels. Increased mRNA and protein expression of VEGF and eNOS was observed in hypoxic retinas. Specific localization of VEGF was observed in the astrocytes closely associated with the blood vessels. The blood vessels expressed eNOS immunoreactivity and appeared to be dilated as compared to the vessels in the controls but the tight junctions between the endothelial cells remained intact. Vascular endothelial cells often showed membrane bound vacuoles and multivesicular aggregations in the cytoplasm following the hypoxic injury. Increased leakage of intraperitoneally administered fluorescent tracer rhodamine isothiocyanate was detected in the retina of hypoxic rats suggesting that hypoxia induces increased permeability of the blood vessels which may be mediated by VEGF and eNOS. The structural changes in the endothelial cells may reflect impairment of transendothelial transport in the developing retina. We suggest that vascular changes, as observed in this study, may be a major factor contributing to degenerative changes such as retinal ganglion cell (RGC) death following a hypoxic injury. Administration of melatonin, an antioxidant drug, was beneficial in suppressing the production of VEGF and vascular permeability as well reversing the structural changes in the blood vessels and RGC.

The Ocular Surface in Health and Diseases

S. Kinoshita
Kyoto Prefectural University of Medicine, Japan

The ocular surface serves a critical function as the defensive front line of the cornea, which mostly maintains the corneal transparency. The health and disease of the ocular surface rely upon tear-fluid function, ocular surface epithelial integrity, ocular surface innate immunity, commensal and/or pathogenic bacteria, etc. Among them, since the basic understanding of ocular surface mucosal innate immunity on interaction with commensal and/or pathogenic bacteria is one of the enlightening scientific fields of the ocular surface, this presentation will be focused on this subject.

The ability of cells to recognize pathogen-associated molecular patterns depends on the expression of a family of TLRs, RIG-1, MDA5, etc. In fact, immune competent cells such as macrophages could recognize various microbial components and induce the inflammation and then exclude the microbes. Ocular surface epithelial cells are, however, selectively respond to microbial components and induce limited inflammation probably because of the unique innate immune response to the coexistence with commensal bacteria on the ocular surface.

Based upon the evidence mentioned above, it is reasonable to consider that there is an association between ocular surface inflammatory diseases and a disordered innate immune response. In fact, we have documented the association with TLR3 and IL4R gene polymorphisms in Japanese SJS/TEN patients with ocular surface complications, suggesting genetic background involvement in this syndrome. A similar event may be considered in patients with meibomitis-related keratoconjunctivitis, a similar form of acne rosacea. Therefore, it is the possibility that sustained, inflamed ocular surface diseases may be closely related to a disorderd mucosal innate immunity, its incidence may be higher than we have expected.

Diabetic Retinopathy and Inihibitors of RAF Kinase

R. Kowluru ; G. Mohammad
Kresge Eye Institute, Wayne State University, USA

Diabetic retinopathy is a slow progressing disease faced by almost 90% of patients after 20 years of diabetes. Many metabolic pathways, including oxidative stress, protein kinase C, and polyol pathway have been implicated in the development of diabetic retinopathy, but, despite extensive research, its pathogenesis remains unclear. Experimental studies have demonstrated the role of small molecular weight G-protein (H-Ras)-mediated signaling pathway in its development. The key effector protein of Ras function is a threonine/serine kinase-Raf kinase, and this kinase is involved in a variety of functions, including cell cycle and proliferation and apoptosis. In animal models of diabetic retinopathy, Raf kinase is activated in the retina and its microvasculature. Activated Raf kinase is associated with increased apoptosis of retinal capillary cells, the process which precedes the development of retinal histopathology, and inhibition of Raf kinase ameliorates apoptosis. Inhibitors of Raf kinase have shown promising results in cancer treatment, and a second-generation Raf kinase antisense oligonucleotides, iCo 007, is in phase I trial for macular edema, another chronic ocular disease. The use of Raf kinase targeted antisense oligonucleotides for macular degeneration, and the recent advances in the drug delivery to the targeted area, paves a path for future testing of Raf kinase-antisense oligonucleotides for diabetic retinopathy, a blinding complication that a diabetic patient fears the most.

Fundus Autofluorescence Imaging of Chorioretinal Inflammatory Diseases

M. Kramer [1]; S. Brastishevsky [1]; E. Priel [2]
[1]Rabin Medical Center, Israel; [2]Mor Institutes of Diagnosis, Israel

Purpose: To describe the fundus autofluorescence (FAF) imaging findings in chorioretinal inflammatory diseases and to correlate them with disease activity and other imaging modalities.

Methods: Twenty-one patients with various chorioretinal inflammatory diseases were evaluated during the disease course with fluorescein angiography (FA), FAF imaging, indocyanine green angiography (ICGA), and spectral domain optical coherence tomography (SD-OCT).

Results: FAF imaging best distinguished active from nonactive lesions in serpiginous choroiditis (n=4). The transition of the active area from hyper- to hypoautofluorescence corresponded to the degeneration of the photoreceptor-retinal pigment epithelium (RPE) complex on SD-OCT. A similar pattern was noted for syphilitic posterior placoid chorioretinopathy (n=1). In multifocal choroiditis and punctate inner choroidopathy (n=4), scarred foci appeared hypofluorescent whereas active spots were either hyper- or hypoautofluorescent, corresponding with the SD-OCT findings but with no clear distinction between inflammation and choroidal neovascularization. In multiple evanescent white dot syndrome (n=1), hyperautofluorescent spots on FAF corresponded partially to hypofluorescent spots on ICGA. FAF imaging was less informative than FA and ICGA in Vogt-Koyanagi-Harada syndrome (n=7) and birdshot choroidopathy (n=4).

Conclusions: Noninvasive FAF imaging may assist clinicians in assessing disease activity in chorioretinal inflammatory diseases that affect mainly the integrity of the photoreceptor-RPE complex. Further corroborative studies are required.

Levels of Cytokines in the Aqueous Humor of Patients with Age-related Macular Degeneration.

M. Kramer [1]; M. Hasanreisoglu [1]; A. Feldman [2]; R. Axer-Siegel [1]; P. Sonis [2]; I. Maharshak [1]; Y. Monselise [1]; M. Gurevich [2]; D. Weinberger [1]
[1]Rabin Medical Center, Israel; [2]Sheba Medical Center, Israel

Purpose: To investigate the role of inflammation in age-related macular degeneration (AMD) by measuring inflammatory related cytokines in the aqueous humor of AMD patients.

Methods: Aqueous humor samples were obtained from 36 patients with AMD and 16 age-matched control subjects undergoing cataract surgery. AMD stage (AREDS) was determined clinically, before surgery. Multiple cytokines (basic-FGF, IFN-γ, Interleukin(IL)-1β, IL-10, IL-12(p70), IL-4, IL-6, IL-8, IL-17, MCP-1, TNF-α, and VEGF were measured by Luminex X-MAP technology and verified by Western blot.

Results: Four patients had mild AMD, 14 intermediate, and 18 advanced. Advanced AMD was divided into active choroidal neovascularization (CNV) (n=9), disciform scar (n=7), and central geographic atrophy (n=2). Higher than normal MCP-1 levels were associated with advanced AMD (186±138 pg/ml vs 100±61pg/ml; p=0.03), especially active CNV (215±157pg/ml;p=0.02),and higher than normal IL-6 levels, with mild AMD (1459±1793pg/ml vs 351±516pg/ml; p=0.06). Levels of MCP-1 and IL-6 were verified by western blot analysis. Patients with disciform scar showed a trend of abnormally high levels of IL-12(p70) (1.7±2.4 pg/ml vs 0.2±1pg/ml; p=0.07), TNF-α (1.8±2.4 pg/ml vs 0.3±1pg/ml; p=0.06), and IL-8 (4.7±6.4 pg/ml vs 1.2±2.1 pg/ml; p=0.08). VEGF level was low in patients with active CNV.

Conclusion: Elevated levels of inflammatory cytokines in various stages of AMD may suggest the involvement of inflammation in the disease pathogenesis. IL-6 may be present in the early stages, MCP-1 in the angiogenic phase, and IL-12(p70), TNF-α and IL-8 during healing.

Inhibition of α5β1 Integrin in Neovascular AMD - a Phase 1 Study

B. Kuppermann
The Gavin Herbert Eye Institute, University of California, Irvine, USA

Purpose: To assess the safety and pharmacokinetic profile of intravitreal volociximab, an α5β1 integrin antagonist, in combination with ranibizumab in wet age-related macular degeneration (AMD). Alpha5 Beta1 (α5β1) integrins are transmembrane receptors which bind to fibronectin in the extracellular matrix. This leads to intracellular signal transduction controlling critical events involved in angiogenesis such as cell proliferation, survival and migration. These α5β1 integrin mediated activities are downstream to VEGF and other activators of angiogenesis. α5β1 integrin antagonism has demonstrated potent anti-angiogenic effects in preclinical oncologic and ophthalmic models.

Methods: Phase 1, open label, multicenter, dose escalation study of eyes with all subtypes of choroidal neovascularization secondary to AMD. Patients receive three monthly intravitreal injections of the combination of volociximab, an anti-α5β1 integrin monoclonal antibody (0.5, 1.25 or 2.5 mg) and ranibizumab (0.5 mg). Both anti-VEGF treatment-naive eyes (n=37) and anti-VEGF experienced eyes (n=11) were treated with the experimental regimen. Treatment-experienced eyes were investigator determined to be unresponsive to previous anti-VEGF monotherapy (lack of visual and anatomic response).

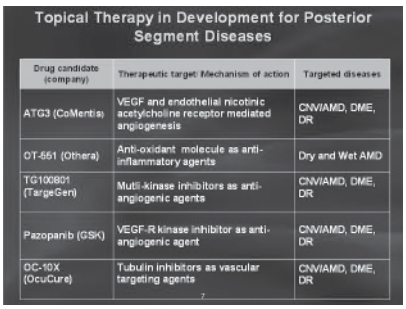
Results: To date, all 37 treatment-naive eyes received 2 doses of volociximab in combination with ranibizumab for wet AMD. Baseline visual acuity and OCT center point thickness (CPT) were 52.4 letters and 343 µm respectively. After 2 doses of combination therapy (week 8) the mean change in VA was +9.5 letters. Twenty-four percent of patients gained ≥3 lines of vision. The mean change in OCT center point thickness was -108 µm. To date, 11 treatment-experienced eyes received 2 doses of volociximab in combination with ranibizumab for wet AMD. Baseline visual acuity and OCT CPT were 56.5 letters and 333 µm respectively. After 2 doses of combination therapy (week 8) the mean change in VA was +5.3 letters. Eighteen percent of patients gained ≥3 lines of vision. The mean change in OCT CPT was -107 µm. Dose escalation was completed without evidence of dose-limiting toxicity.

Conclusions: Preliminary results of this phase 1 study of volociximab combined with ranibizumab suggest a favorable safety profile.

Topical Therapy for CNV/AMD

B. Kuppermann
The Gavin Herbert Eye Institute, University of California, Irvine, USA

An overview of all the agents currently or recently in development will be provided, including the status of all clinical trials, mechanisms of action of specific agents, and general concepts of topical therapy to the posterior segment. An overview slide is provided below.



Topical Therapy in Development for Posterior Segment Diseases

Drug candidate (company)	Therapeutic target/ Mechanism of action	Targeted diseases
ATG3 (CoMentis)	VEGF and endothelial nicotinic acetylcholine receptor mediated angiogenesis	CNV/AMD, DME, DR
OT-551 (Othera)	Anti-oxidant molecule as anti-inflammatory agents	Dry and Wet AMD
TG100801 (TargeGen)	Multi-kinase inhibitors as anti-angiogenic agents	CNV/AMD, DME, DR
Pazopanib (GSK)	VEGF-R kinase inhibitor as anti-angiogenic agent	CNV/AMD, DME, DR
OC-10X (OcuCure)	Tubulin inhibitors as vascular targeting agents	CNV/AMD, DME, DR

Ozurdex™ as Adjunctive Therapy to Lucentis® in Patients With Choroidal Neovascularization Secondary to Age-Related Macular Degeneration

B. Kuppermann [1]; Michael Singer [2]; Dov Weinberger [3]; Michaella Goldstein [4]; Anat Loewenstein [4]; Ching-Chih Liu [5]; Lou Jean [6]; Xiao-Yan Li [6]; Scott Whitcup [6]
[1]The Gavin Herbert Eye Institute, University of California, Irvine, USA; [2]Medical Center Ophthalmology Associates, USA; [3]Rabin Medical Ctr, Israel; [4]Tel-Aviv Medical Center, Israel; [5]Chi Mei Medical Center, Taiwan; [6]Allergan, Inc., USA

Objective: This study was designed to evaluate the efficacy and safety of dexamethasone intravitreal implant as adjunctive therapy to ranibizumab in patients with neovascular age-related macular degeneration.

Purpose: Evaluate the safety and efficacy of Ozurdex™ (dexamethasone intravitreal implant) 0.7 mg when given with Lucentis® (ranibizumab) in patients with choroidal neovascularization (CNV) secondary to exudative age-related macular degeneration (AMD).

Methods: This 6-month, randomized, single-masked, multicenter, sham-controlled study enrolled patients requiring ranibizumab treatment for CNV secondary to AMD. At screening, patients received an intravitreal injection of ranibizumab 0.5 mg. 4 weeks later at the baseline (day 1) visit, patients who met OCT and clinical criteria for ranibizumab retreatment were randomized to receive DEX Implant (n=123) or sham procedure (n=120). Patients were given a second ranibizumab injection 7-14 days after the baseline visit. For patients meeting retreatment criteria, up to 5 additional ranibizumab injections were given prior to study exit (week 25). Primary efficacy outcome measure was injection-free interval.

Results: Adjunctive therapy with DEX Implant significantly delayed first as-needed ranibizumab injection based on Kaplan-Meier product-limit method (P=.016). The 75th percentile of injection-free interval was 12 weeks in DEX Implant group vs 8 weeks in control group. Relative risk of not requiring additional as-needed ranibizumab injection was 3.28 (DEX Implant vs sham, P=.048). No significant between-group differences in visual acuity or improvement in central retinal thickness was noted. Treatment-related adverse events were similar between groups, except increased IOP (9.9% vs 3.4%) and conjunctival hemorrhage (6.6% vs 0.8%) in the DEX Implant group vs control group (P ≤ .044).

Conclusions: DEX Implant delayed the time to as-needed injection of ranibizumab and reduced the need for repeated ranibizumab treatment in patients with CNV secondary to AMD.

Ophthalmic Medication Adherence Behaviors among Asian Patients in America

S. Kwok [1]; A. Tam [2]
[1]University of California, Berkeley, USA; [2]Univeristy of California, Berkeley, USA

Purpose: To determine Asian patients' adherence to ophthalmic medication in the United States and to systematically identify the various barriers to medication adherence for these patients.

Method: 300 Asian-American patients in an ophthalmology practice were interviewed by a trained intern-assistant in a non-confrontation way. The pattern of medication use was noted. Reasons for not using medication as prescribed were reviewed.

Results: 25% (26/104) chronic glaucoma patients, 26% (43/168) patients with dysfunctional tear syndrome/dry eyes and 71% (20/28) patients with allergic conjunctivitis reported to have used eye medication as prescribed. Patients' barriers to medication adherence included cognitive and psychological problems, e.g. forgetfulness (40%), emotional factors(5%); cost(10%); side effect of medication (7%); lack of symptoms (20%); lack of information (9%); and other priorities (5%). Physician's contributions (10%) included failure to explain benefits and side effects of medication adequately; and failure to consider patients' life styles. The health care system barriers (15%) were the high cost of medication; the co-payments for the physician office visits; and the restrictive formularies of medication.

Conclusion: Asian-American patients have poor adherence to eye medication as compared to other ethnic groups. This study offers insight into these patients' eye medication behaviors. Questions may be raised as to whether similar adherence behaviors are found in other medical treatments for the Asian-American patients. Solution is likely to be multi-dimensional and individualized. Baseline screening for adherence predictors, and more importantly, a focused intervention in addressing the modifiable risk behaviors for poor adherence should be implemented in each physician-patient encounter.

Statins and Glaucoma

D. Leung
Hong Kong Eye Hospital, The Chinese University of Hong Kong, Hong Kong

Purpose: To investigate whether simvastatin use is associated with visual field (VF) stabilization in patients with normal tension glaucoma (NTG).

Design: Prospective cohort study (ClinicalTrials.gov Identifier: NCT00321386).

Participants: A total of 256 eyes from 256 Chinese subjects with NTG.

Methods: Patients were followed up at 4-month intervals for 36 months for VF progression per Anderson's criteria. Clinical parameters were checked for association with progression in multivariate analysis.

Main Outcome Measures: The primary outcome was the association between simvastatin use and VF progression.

Results: Thirty-one patients (12.1%) were taking simvastatin (statin+), and 225 patients (87.9%) were not taking simvastatin (statin-). Baseline age, gender, untreated intraocular pressure, VF indices, vertical cup-to-disc ratio, and central corneal thickness (CCT) were comparable between the 2 groups. There were significantly more patients with a history of hypercholesterolemia, systemic hypertension, and ischemic heart disease in the statin+ group. A total of 121 patients (47.3%) showed evidence of VF progression (mean rate of mean deviation loss was -0.30 decibel per year) during the 36 months of follow-up. Simvastatin use was among 8 of 121 patients (6.6%) who progressed compared with 23 of 135 patients (17.0%) who did not progress (P=0.011). Logistic regression revealed that history of disc hemorrhage (relative risk [RR] 3.26; 95% confidence interval [CI], 1.21-8.76; P=0.019), history of cerebrovascular accidents (RR 2.28; 95% CI, 1.03-5.06; P=0.043), and baseline age (per 10 years older; RR 1.38; 95% CI, 1.08-1.76; P=0.009) were significant risk factors for VF progression, whereas simvastatin use conferred a protective effect (RR 0.36; 95% CI, 0.14-0.91; P=0.030).

Conclusions: Simvastatin use may be associated with VF stabilization in patients with NTG. A larger scale randomized controlled trial and cost-effectiveness analyses seem warranted.

Applications of Ocular Response Analyzer in Normal Tension Glaucoma

D. Leung
Hong Kong Eye Hospital, The Chinese University of Hong Kong, Hong Kong

Purpose: To investigate whether corneal hysteresis, corneal resistance factor, and central corneal thickness are related to progression in normal-tension glaucoma (NTG).

Design: Prospective longitudinal cohort study.

Methods: We analyzed 118 eyes from 118 Chinese NTG subjects. Corneal hysteresis and corneal resistance factor were measured with ocular response analyzer. Patients were followed for 36 months to detect field progression. Clinical parameters were checked for association with progression by multivariate analysis. Performance of corneal hysteresis, corneal resistance factor, and central corneal thickness in predicting progression were investigated with receiver-operator-characteristic curves and area-under-curve (AUC).

Results: Fifty-five subjects (46.6%) experienced field progression and 63 (53.4%) were stable. In univariate analysis, corneas were thinner in progressed than that in stable group (528.6 ± 31.2µm vs.542.8 ± 31.8µm, p= 0.017). Corneal hysteresis was lower in progressed than that in stable group (8.83 ± 1.48mmHg vs.9.62 ± 1.61mmHg, p= 0.012). Corneal resistance factor was also lower (9.38 ± 1.45mmHg vs.10.08 ± 1.67mmHg, p = 0.026, in progressed vs. stable group). In multivariate analysis, lower hysteresis (relative risk [RR] = 1.44 for every mmHg decrease, 95% confidence interval [CI] = 1.09-1.89, p=0.010), thinner corneas (RR = 1.12 for every 10µm decrease, 95% CI = 1.01–1.32; p = 0.033), and disc hemorrhage (RR= 2.52, 95% CI = 1.10–7.46; p = 0.041) were significantly associated with progression. The AUC for corneal hysteresis, corneal resistance factor, and central corneal thickness were 0.637, 0.641 and 0.603 respectively, indicating average, but not good, stand-alone performance for predicting progression.

Conclusion: Low corneal hysteresis and thin central cornea are risk factors associated with field progression in NTG. Neither of them are good stand-alone predictors of progression.

Dry Eye Disease Management in the Community

D.A. Schaumberg [1]; J. Li [2]
[1]Brigham and Women's Hospital Harvard Medical School, USA; [2]Pfizer, Inc., USA

Background: Limited information is available on treatment of patients with dry eye disease (DED) in the community.

Methods: We surveyed 4000 participants of the Women's Health Study and Physicians' Health Studies on their DED symptoms, diagnosis, comorbidities, treatments, patient satisfaction, and impact of disease. Data from the first 1925 respondents who reported a DED diagnosis are reported here and analyzed using stepwise logistic regression.

Results: The study sample comprised 1390 women and 535 men (mean ages 70.7 and 76.7 years; mean DED duration 10.5 and 10.1 years, respectively). Using the OSDI© 56.3%, 14.9%, and 28.8% of the respondents were classified as having mild, moderate, or severe DED, respectively. Comorbidities included blepharitis (14.4%), rosacea (12.7%), corneal ulcer (6.0%), Sjogren's syndrome (4.0%), and meibomian gland dysfunction (2.4%). Common treatments included artificial tears (77.4%), lubricating ointments (17.4%), oral omega-3 fatty acid supplements (16.3%), punctual occlusion (15.6%), and topical cyclosporine (11.6%). Patients on ≥ level 2 treatments (eg cyclosporine; punctual occlusion) were more likely to have: rosacea (p=0.002); Sjogren's syndrome (p=0.002); report more severe symptoms (p=0.002); and report more limitations of everyday activities (p=0.002). Treatment dissatisfaction was expressed by 9.1% (mild DED), 18.4% (moderate DED), and 36.9% (severe DED) of patients. Factors associated with dissatisfaction included: more frequent symptoms (p<0.0001), greater limitations in everyday activities (p<0.0001), more frequent fluctuating vision (p=0.002), and severe symptoms (p=0.01).

Conclusions: Patients with severe DED are more likely to receive ≥ level 2 treatments. However, persistence of severe symptoms, impact on everyday activities, and a high level of patient dissatisfaction in patients with severe DED suggests the need for development of additional treatment strategies to improve quality of life in these patients.

The Treatment of ROP Type1: Laser or Anti-VEGF

X. Li
Peking University People's Hospital, China

Object: To determine the anti- VEGF (bevacizumab) alone is effective? It can replace laser ablation? One injection is enough for the regression? How high is the complication in compare to Laser?

Methods: We choice the 12 ROP Type I babys with the same severity of the ROP in both eye, after Informed consents one eye completely ablate the peripheral avascular retina with 810 nm laser, another eye treated by inactivating VEGF.

Results: Bevacizumab is effective to facilitate plus disease regression, faster than laser. The normal retina vascularization is going slowly towards ora serrata. Retina hemorrhages absorped slower than laser. Laser treatment induced fibrosis formation in 50% (6 eyes) in compare to Bevacizumab only 16.7%.

Conclusion: Anti-VEGF shows a better prognosis to aggressive ROP, but slower retina vessel growth.

Lucentis (Ranibizumab) versus Avastin (Bevacizumab) for CNV/AMD

N. Fischer ; U. Soiberman ; R. Jung ; G. Heilweil ; D. Varssano ; M. Goldstein ; A. Barak ; S. Shulman ; A. Loewenstein
Tel Aviv Medical Center, Israel

Purpose: Intravitreal ranibizumab (Lucentis) is the current standard of care in treating subfoveal choroidal neovascularization (CNV) in age-related macular degeneration (AMD) based on randomized multi-center trial evidence. In addition, a vast amount of clinical experience as well as case series regarding the use of bevacizumab (Avastin) has accumulated. The difference in efficacy and safety between the two drugs is still unknown. This presentation aims to show our comparative findings of ranibizumab to bevacizumab as well as that in the available literature.

Methods: Retrospective data was collected for patients receiving either drug for naive CNV secondary to AMD follow-up of 3-12 months. Visual acuity and central macular thickness (CMT), number of injections required and adverse events were analyzed.

Results: According to our study, visual acuity and CMT results are similar for both drugs with no statistically significant difference. Visual acuity and CMT results will be presented. Ocular and systemic side effects were rare for both drugs.

Conclusions: Bevacizumab and Ranibizumab showed similar efficiency and safety in our retrospective study. Different pharmacokinetics of the drugs, which may affect their dosing profiles, as well as on going multi-center trials will be discussed.

Lucentis (Ranibizumab) for Central Retinal Vein Occlusion with Macular Edema: The CRUISE Study

N. Fischer ; M. Goldstein ; U. Soiberman ; S. Shulman ; A. Loewenstein
Tel Aviv Medical Center, Israel

Purpose: Central retinal vein occlusion (CRVO) is a common vascular retinal disorder. The main reason for visual loss is secondary development of macular edema (ME) and ischemia for which there is no proven management. Up regulation of vascular endothelial growth factor (VEGF) has been observed in these patients. The CRUISE study aimed to study the efficacy and safety of intravitreal ranibizumab, an anti-VEGF agent, in patients with macular edema secondary to CRVO.

Aims: To quantify the change from baseline in best-corrected visual acuity (BCVA) score. Secondary aims included, among others, the change in central foveal thickness as measured by optical coherence tomography (OCT).

Methods: A prospective, phase III, multicenter, randomized, double-masked controlled study. Patients were randomized into groups receiving 6 monthly injections of either 0.3 mg or 0.5 mg ranibizumab or sham injections. Eligibility criteria included: adult patients with macular edema of at least 250 microns secondary to CRVO and BVCA of 20/40-20/320. Some of the ocular exclusion criteria included: CRVO diagnosed more than 12 months earlier or prior RVO, prior anti-VEGF or intravitreal corticosteroid treatment within 3 months and laser photocoagulation for macular edema within 4 months.

Results: The study included 392 subjects. At 6 months, vision improvement of 15 letters or more was observed in 46.2% and 47.7% of the ranibizumab treated patients (0.3mg and 0.5mg, respectively), compared to 16.9% for sham injections. Mean gain in BCVA was observed beginning at day seven, with an 8.8 and 9.3 letter gain in the 0.3 mg and 0.5 mg study arms of ranibizumab respectively (1.1 letters in the sham injection arm). The six month safety profile was consistent with previous ranibizumab trials in neovascular age-related macular degeneration.

Conclusions: Ranibizumab appears to be effective and safe in the treatment of CRVO with ME. Further follow up is needed to establish long-term effects.

Lucentis (Ranibizumab) for Branch Retinal Vein Occlusion: BRAVO

N. Fischer ; M. Goldstein ; U. Soiberman ; S. Shulman ; A. Loewenstein
Tel Aviv Medical Center, Israel

Purpose: Branch retinal vein occlusion (BRVO) is a common retinal vascular disorder. Primary visual handicap is often secondary to chronic macular edema (ME). New modalities such as steroids and anti-vascular endothelial growth factor (anti-VEGF) aim to inhibit inflammatory factors. Data for the steroid Ozurdex shows safety and efficacy. BRAVO studies efficacy and safety of intravitreal ranibizumab in patients with ME secondary to BRVO in terms of: visual acuity (BCVA), central foveal thickness (CFT), visual functioning assessed by the National Eye Institute Visual Functioning Questionnaire (NEI VFQ-25) and adverse events.

Methods: BRAVO is a prospective, phase III, multi-center, double-masked controlled study. Inclusion criteria include: new BRVO, BCVA 20/40-20/320, ME >m. Patients are randomized into monthly: 0.3mg, 0.5mg, or sham 250 injections for 6 months. Exclusion criteria include laser photocoagulation ≤4 months prior to study.

Results: Six month results for 397 subjects show ≥15 letter improvement in: 55.2% (74/134) 0.3mg arm, 61.1% (80/131) 0.5mg arm versus 28.8% (38/132) receiving sham injections. Mean BCVA improvement begins day seven (7.6 and 7.4 letter gain in 0.3mg and 0.5 mg arms respectively compared with 1.9 for sham). Safety profile is consistent with previous ranibizumab phase III trials. Common ocular adverse events are more frequent in the ranibizumab arm but serious events are rare. Non-ocular adverse events are uncommon.

Conclusions: Ranibizumab appears to be effective, safe treatment for BRVO with ME. Further follow up and comparison to other available treatments such as slow release steroids and to combination treatment is needed to establish treatment regimens.

Protective Effects of Gingko Biloba Extract on Glaucoma with IOP Controlled: A Multicenter Randomized Double-Blind Controlled Clinical Trial

X. Lu [1]; J. Duan [2]; H. Zhou [1]; J. Zeng [1]; L. Cheng [3]
[1]Sichuan Provincial Hospital of T.C.M., China, Peoples Republic; [2]The Teaching Hospital of Chengdu University of T. C.M., China, Peoples Republic; [3]Chengdu University of Traditional Chinese Medicine, China, Peoples Republic

Objective: To evaluate the protective effects of gingko biloba extract on glaucoma with IOP controlled by means of visual field mean deviation (MD).

Methods: A multicenter randomized double-blind placebo-controlled clinical trial was carried. 284 glaucoma patients with IOP controlled were involved according to inclusive criteria. All cases were divided into Gingko Group and Placebo Group with 142 patients both. MD were compared after treatment of 3 and 6 months.

Results: The average MD in Gingko Group were dropped 0.75¡À2.92dB and 1.02¡À2.78dB 3 and 6 months post-treatment respectively, compared with 10.60¡À6.89dB pre-treatment (P£¼0.01).No significant difference of MD were showed in Placebo Group, with 0.29¡À2.91dB and 0.21¡À3.29dB dropped 3 and 6 months post-treatment (P£¾0.05£©.The average difference in dropped MD was significant between two groups After 6 months£¨P£¼0.01£©.

Conclusion: The gingko biloba extract could improve the visual field of glaucoma with IOP controlled, and protect the optic nerve.

Study on Yang Deficiency Mechanism of Diabetic Retinopathy Based on Metabonomics

X. Luo [1]; J. Duan [2]
[1]Gansu Provincial Hospital of T.C.M., China, Peoples Republic; [2]The Teaching Hospital of Chengdu University of T. C.M., China, Peoples Republic

Objective: To explore metabonomics material and relationship of DR and the Yang deficiency pathogenesis, and then to explain the Chinese medicine mechanism theory that the Yang deficiency pathogenesis leads of the DR progress.

Methods: Patients with type 2 diabetes mellitus and healthy volunteer were collected in same living district, finally, 89 DR and 30 normal subjects were screened under the inclusive criterion and its information database including the special questionnaire and experimental tests was recorded. These patients were divided in 2 groups as the difference of Yang deficiency.(yes\no). GC\TOFMS and multivariate statistical £¨OPLS and OSC-PLS £©analysis has been used for the analysis of blood serum metabolic profiling.

Results: The discrimination of metabonomics outcomes among the different groups showed that DR drew off from normal group completely, Yang and non-Yang deficiency groups were basically separated with few overlap, DR preclinical and non-proliferative phase was overlap and hard to classify, but proliferative could divided from these phases in score plot. The potential biological markers for Yang deficiency and PDR stage classification belonged to amino acids and organic acids which correlated with human energy metabolism.

Conclusion: Both supervised OPLS and OSC-PLS have been classified successfully Yang deficiency (yes\no) in DR and control, further, to discover potential biomarkers that can be identified by MS/MS. and the essence might be organism energy metabolism diversity, induce the gene expression of new vessels factors by affecting the energy metabolism and internal environment great changes. Yang deficiency pathogenesis was the key influence to DR progress.

Experimental Research on Compound Danshen Dripping Pills Treating Early Diabetic Retinopathy

J. Ma [1]; X. Shen [2]; J. Hu [2]; F. Yang [1]; Y. Zhu [3]
[1]Tianjin Tasly Institute, China, Peoples Republic; [2]Tianjin Institute of Pharmaceutical Research, China, Peoples Republic; [3]Tianjin Tasly Institue, China, Peoples Republic

0bjective: To study the therapeutic effect and mechanism of Compound Danshen Dripping Pills on early experimental diabetic retinopathy.

Methods: Diabetic rats induced by streptozotocin(STZ) were randomly divided into normal group and model group which were then divided into model group ,control group and treated groups with Compound Danshen Dripping Pills with three dosages. For at 3 months the blood flow velocity of CRA ,the resistance index(RI),the hemodynamic, the activity of superoxide dismutase(SOD), malondialdehyde (MDA)and GSH-PX in retinal tissue, the content of nitrogen onoxidum(NO) in serum were tested.

Results: There is a significant increase in blood flow velocity of CRA in treated groups£¬however that is decreased in model group compared with the normal group. The content of MDA in retina was decreased evidently£¬the activity of SOD in retina and the content of NO in serum were increased distinctly in treated groups£¬there was a statistic significant difference between them (P <0.01).

Conclusion: Compound Danshen Dripping Pills can enhance capability of diabetic rats in antioxidation and reduce damage of retina from oxidation.

Compound Danshen Dripping Pills is a compound Chinese medicine consisting of ingredients extracted from Salvia miltiorrhiza (SM),Panax notoginseng (PN), and Borneol. It has been widely used in China for more than 16 years, for the prevention and management of coronary arteriosclerosis, angina pectoris. We found it also gets very good effect on clinical application of early diabetic retinopathy. This effect may be associated with the effect of Compound Danshen Dripping Pills¡'s radical scavenging, retinal microcirculation improving and lipid metabolism improving. In the present experiment, the pharmacodynamics experiment of treating early diabetic retinopathy is studied on Diabetic rats.

Bacteriologic Profile of the Conjunctiva and Susceptibility to Fluoroquinolones

N. Maeda
Osaka University, Japan

Purpose: To understand the bacteriological profile of the conjunctive and the susceptibility to fluoroquinolones in patients having ocular surgery and in patients with dry eye.

Methods: The subjects included 200 eyes of pre-operative patients and 71 eyes of dry eye patients. The efficacy of fluoroquinolones was calculated.

Results: For the pre-operative eyes, 81.5% had positive bacterial growth. 39.7% of coagulase-negative Staphylococcus (CNS), 40% of Staphylococcus aureus (SA), and 20.7% of Corynebacterium were fluoroquinolones resistant. On the other hand, 94.0% had positive bacterial growth for eyes with dry eye. 64.5% of coagulase-negative CNS and 33.3% of SA were fluoroquinolones resistant.

Conclusions: As many fluoroquinolones-resistant strains were isolated from the conjunctiva preoperatively and from the eye with dry eye, clinicians should be mindful of the infections associated with these strains.

Quantitative and Qualitative Use of Anterior Segment OCT in Corneal Surgery

J. Mehta
Singapore Eye Research Institute, Singapore

Background Anterior Segment OCT is a non-invasive real-time imaging device of the anterior segment that offers high resolution images. With the aid of new imaging software, quantitative analysis is able to be performed to give more information from the images obtained. Methods Presentation of studies using new software techniques for quantitative analysis of images of patients undergoing corneal surgery e.g. ZAP and COLGATE Results The results from quantitative analysis provide in depth analysis of the cornea following surgery Conclusion Newer softwares available with OCT devices offer in depth analysis of patients undergoing anterior segment surgery.

The Intraocular Pressure-reducing Effect of Oral Paracetamol – a Pilot Study

D. Meyer ; N. Mohamed
University of Stellenbosch, South Africa

Background: Several studies have confirmed the ability of cannabinoids to reduce intraocular pressure (IOP). Experimental data recently unequivocally demonstrated that the analgesic effect of paracetamol is due to its indirect action on cannabinoid CB1 receptors. The question then arises as to whether paracetamol can reduce IOP via its effect on intraocular cannabinoid receptors.

Methods: A two-week, prospective, randomized, controlled, single centre, parallel group pilot study was carried out to determine the efficacy and safety of orally administered paracetamol 1g every 6 hours in adult patients with primary or secondary open angle glaucoma as compared to topical levobunolol 0.5% twice a day. Patient well-being was closely monitored throughout the study and focused on hepatic safety.

Results: Eighteen adult patients were enrolled in the study, nine in the topical levobunolol group and nine in the oral paracetamol group. In the levobunolol group the mean IOP reduction at day 7 was 7.5 mmHg ($p<0.008$) and at day 14 was 9.1 mmHg ($p<0.005$) from a mean IOP baseline of 29.6 mmHg. The corresponding figures for the paracetamol group were 8.8 mmHg ($p<0.0004$) at day 7 and 6.5 mmHg ($p<0.004$) at day 14 from a mean IOP baseline of 29.4 mmHg. A mean IOP reduction of 20% or more from baseline was achieved in 78% of patients in the levobunolol group compared with 63% of patients in the paracetamol group at week 2 of the study. Both study regimens were well tolerated. No serious treatment-related adverse events were reported in either of the two treatment groups. Liver function tests, systolic/diastolic blood pressures and heart rates remained unchanged during the two weeks of the study in both groups.

Conclusion: The results of this study suggest that paracetamol taken orally, 1g every 6 hours, reduces IOP in patients with open angle glaucoma and/or angle recession glaucoma in a comparable way to a topical beta-adrenergic receptor antagonist.

Treatment and Prevention of Endophthalmitis 2011

W.F. Mieler
University of Illinois at Chicago, USA

The treatment of endophthalmitis, along with the prophylaxis against the development of infection, continues to evolve. There have been numerous changes since the recommendations of the Endophthalmitis Vitrectomy Study (EVS) were published over a decade ago. The majority of changes have involved the introduction of new generation antimicrobials, which offer better penetration of the agents into the eye, even when administered orally. Additionally, these newer antimicrobials, have a very good spectrum of activity against the commonly encountered organisms.

This presentation will review the use of oral and topical fourth generation fluoroquinolones (gatifloxacin, moxifloxacin, besafloxacin) in the treatment of endophthalmitis, and will also discuss their use in the prophylaxis against infection. Data will also be presented regarding the use of intravitreal moxifloxacin, along with clearance of the antibiotic from the eye following intravitreal administration.

The treatment of fungal endophthalmitis has also changed considerably over the past five years with the introduction of voriconazole and posaconazole. Data will be reviewed regarding the use of these agents topically, orally, and intravitreally, both in animal models, as well as in humans.

The ongoing controversy regarding the risk and/or benefit of intravitreal corticosteroids will also be discussed. Potential benefit seems to be dependent upon the specific organism that is being treated, along with the timing of administration. The impact of systemic disease on the response to treatment of infection will also be reviewed.

Additionally, prophylactic measures attempting to minimize the risk of infection will be discussed when performing intravitreal injections. Finally, a review of prophylactic treatment from the standpoint of the cataract surgeon will be reviewed, including the use of antibiotics in the infusion solution along with the use of intracameral antibiotics.

Update Regarding Use and Benefit of NSAIDs in Ophthalmology

W.F. Mieler
University of Illinois at Chicago, USA

Non-steroidal anti-inflammatory drugs (NSAIDs) are one of the most widely prescribed classes of medications worldwide. From the ophthalmic standpoint, they are employed to enhance mydriasis, reduce postoperative inflammation, and prevent and treat postoperative cystoid macular edema (CME). Other possible indications for usage include decreasing pain and photophobia following refractive surgery, and alleviating itching associated with allergic conjunctivitis. There may also be possible roles in the treatment of diabetic retinopathy, age-related macular degeneration (AMD), and in various ocular tumors as well.

NSAIDs are potent inhibitors of cyclo-oxygenase (COX), an important group of enzymes active in the inflammatory process. Through this mechanism of action, they reduce the synthesis of prostaglandins (PGs). Commercially available drugs include diclofenac, ketorolac, bromfenac, nepafenac, and flurbiprofen. These agents are quite commonly employed as singular treatments, or in combination with corticosteroids.

This presentation will thoroughly review the use and benefit of the NSAIDs in the prevention and treatment of postoperative inflammation and CME in both the setting of cataract surgery, as well as in vitreoretinal surgery. Potential toxicity will also be reviewed.

New Monitoring Guidelines for Hydroxychloroquine

W.F. Mieler
University of Illinois at Chicago, USA

The American Academy of Ophthalmology (AAO) recommendations for screening of chloroquine (CQ) and hydroxychloroquine (HCQ) retinopathy were published in 2002, but new knowledge about the prevalence of toxicity, and improved screening tools, have appeared in the ensuing years. No treatment exists as yet for this disorder, so it is imperative that patients and their physicians be aware of the best practices for minimizing toxic damage.

Risk of Toxicity: New data has shown that the risk of toxicity rises sharply towards 1% after 5-7 years of usage, or a cumulative dose of 1000 gms of HCQ. The risk increases further with continued usage of the drugs.

Dosage: The prior recommendation emphasized dosing by weight. However, most patients are routinely given 400 mg of HCQ daily (or 250 mg CQ). This dose is now considered acceptable, except for individuals of short stature who should be dosed on the basis of ideal body weight. Screening Schedule: Baseline examination is advised for patients starting these drugs, to serve as a reference point and to rule out maculopathy that might be a contraindication to their use. Annual screening should begin after 5 years, or sooner if other risk factors exist.

Screening Tests: Newer objective tests such as spectral domain ocular coherence tomography (SD-OCT), fundus autofluorescence (FAF), and the multifocal electroretinogram (mfERG) appear to be more sensitive than Humphrey Visual Fields (HVF). If any abnormality is detected on HVF, then at least one of these additional tests should be employed. Even a subtle change on HVF should be taken seriously, and are an indication for evaluation by objective testing. Since mfERG testing is an objective test which evaluates function it may be used in place of visual fields (recognizing the mfERGs may not be uniformly available).

Counseling: Patients need to be aware of the risk of toxicity and the rationale for screening. The drugs should be stopped if toxicity is recognized.

Clinical Observation on the Treatment of Early Diabetic Retinopathy with Compound Danshen Dripping Pills

J. Ming ; Y. Wei ; D. Hui
China-Japan Friendship Hospital, China, Peoples Republic

Objective: To observe the effects of compound danshen dripping pills in treating early diabetic retinopathy (DR).

Methods: All the 58 cases in â… to â…¢ periods selected were type â…¡ DR patients. There were 30 cases (60 eyes) in danshen group, 28 cases (56 eyes) in controlled group. The result of treatment was evaluated by the test of visual acuity, fundus photography, fundus fluorescein angiography and visual field.

Result:

1.The visual acuity changes: No significant difference was seen between the two groups, After the treatment, the total effective of the treated group were both of 65%.and 61%;

2.The defect of visual field: The changes of Mean Defect (MD) of visual field before and after the treatment are showedï¼ŒMD value of visual field decreased obviously than before in the treated group;

3. Fundus fluorescein angiography and fundus photography: both groups had effect in treating microaneurysm and small blood spots. Significant changes were found after the treatment.

Conclusion: To type â…¡ DR patients, diabetic retinopathy with compound danshen(ä¸¹å‚,) dripping pills could improve the state of hemorrheology and pathological changes of fundus microaneurysm . Compared with calcium dobesilate, compound danshen dripping pills had certain advantage in the control of microaneurysm, bleeding and the improvement of visual acuity and visual field.

Targeting the GAPDH Nuclear Translocation Pathway as a Potential New Strategy to Prevent Hyperglycemia-Induced Retinal Damage

S. Mohr
Michigan State University, USA

Background: Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) nuclear translocation and accumulation seem to play an important role in the development of various degenerative diseases including diabetic retinopathy. The translocation to and accumulation of GAPDH within the nucleus has closely been associated with cell death induction.

Methods: Transformed rat (rMC-1) and human (HMC) Muller cells as well as diabetic mice were used for the studies to identify mechanisms of GAPDH nuclear translocation. The effect of inhibition of this pathway on Muller cells viability was determined using an IL-1 receptor blocker, a caspase-1 inhibitor, IL-6, siah-1 antisense, and R-(-) deprenyl.

Results: Hyperglycemia induces GAPDH nuclear accumulation in retinal Muller cells in vitro and in vivo. Our in vitro results reveal a novel mechanism for high glucose-induced cellular damage in retinal Muller cells through production and autocrine stimulation by interleukin-1beta (IL-1β).This autocrine IL-1β feed-back loop leads to the upregulation of the E3 ubiquitin ligase seven in absentia homolog-1 (siah-1), a protein essential for the transport of GAPDH to the nucleus. We have identified several targets by which GAPDH nuclear translocation and accumulation can be prevented, such as interference in the IL-1β signaling, the use of the drug R-(-)-deprenyl, the use of siah-1 antisense, or the restoration of a healthy cytokine ratio. Inhibition of GAPDH nuclear translocation and accumulation prevents hyperglycemia-induced cellular damage of retinal Muller cells in vitro and in vivo.

Conclusion: Therefore, targeting GAPDH nuclear translocation pathway might present a novel strategy to prevent retinal damage and subsequently the development of diabetic retinopathy.

Retinal Circulation in Diabetes

T. Nagaoka
Asahikawa Medical University, Japan

Although diabetic retinopathy is a leading cause of blindness in Western countries, the etiology and development of vascular and visual pathology in this disease is not fully understood. Because retinal vascular dysfunction precedes the clinical histopathology in retinal findings, early surrogate clinical markers are needed to diagnose and quantitate the presence of preclinical lesions in diabetic retinopathy that would allow initiation of treatment at the beginning of the disease. Substantial evidence indicates that vasodilation mediated by endothelium-derived nitric oxide (NO) is impaired in animal models of diabetes and in patients with types 1 or 2 diabetes. This impairment can result in decreased regional blood flow and consequently lead to development of retinopathy. Therefore, it has been suggested that the pathogenesis of diabetic vascular disease, including diabetic retinopathy, in the early stage may involve endothelial dysfunction, resulting in a reduced bioavailability of endothelium-derived NO. A study of endothelial function in the retinal microcirculation seems particularly appropriate, because endothelial dysfunction has emerged as an independent predictor of clinical events.

Wound Modulation in Glaucoma Surgery

K. Nagpal
Retina Foundation, India

Success of glaucoma filtering surgery depends upon modification of wound healing. Aim is to limit the healing process &avoid fibrous tissue formation. Risk factors include age, race, type of glaucoma, inflammation, prolonged use of topical medication, aphakia, etc. Stages of wound healing include injury, inflammation, coagulation, cell migration& proliferation, angiogenesis & scar formation. Strategies to interfere with wound healing include meticulous surgical technique, topical steroids (Inflammation stage), thrombolytic drugs, t-PA (Coagulation stage), mitomycin C & 5FU (Cellular migration stage) and colchicine (Scar formation stage). Clinico-pathologic correlations of glaucoma surgical site in context of wound healing and surgical success will be discussed. Methodology and results of conventional and novel wound modulating agents (space maintainers, anti VEGFs) will be discussed.

DME and VEGF Trap-Eye Phase 2: DA VINCI Study

R. Narayanan
L.V. Prasad Eye Institute, India

Purpose: VEGF Trap-Eye is a fusion protein which blocks all isoforms of vascular endothelial growth factor (VEGF A) and placental growth factor (PlGF). It binds to the factors with more affinity than the native receptors. The purpose of the study was to determine the efficacy and safety of VEGF Trap-Eye in diabetic macular edema (DME).

Methods: A prospective, randomized, multicenter trial was conducted to assess the safety and efficacy of VEGF Trap-Eye in center involving DME compared to focal laser. Patients were randomized 1:1:1:1:1 to a) VEGF Trap-Eye 0.5 mg q 4 weeks b) VEGF Trap-Eye 2.0 mg q 4 weeks c) VEGF Trap-Eye 2.0 mg q 8 weeks d) VEGF Trap-Eye 2.0 mg PRN or e) Focal laser. The primary endpoint was the mean change in best correct visual acuity (BCVA) at 24 weeks and the secondary endpoint was the mean change in retinal thickness.

Results: All the groups randomized to receive VEGF Trap-Eye had statistically significant gain in mean BCVA compared to the focal laser group. The maximum gain in mean BCVA was 11.4 letters in the 0.5 mg q 4 weeks group. Thirty four percent of patients receiving 0.5 mg q 4 weeks had a gain of 15 or more letters, compared to 32%, 17%, 27% and 20% of patients in the 2 mg q 4 weeks, 2 mg q 8 weeks, 2 mg PRN and focal laser groups respectively. Endophthalmitis occurred in 2 (1.1%) patients.

Conclusion: VEGF Trap-Eye appears to be effective in the treatment of DME. Phase 3 trials are currently ongoing.

Anti-Vascular Endothelial Growth Factor Plus Laser in Diabetic Macular Edema

R. Narayanan
L.V. Prasad Eye Institute, India

Purpose: To present the various levels of evidence in support of the role of anti-vascular endothelial growth factor (VEGF) in diabetic macular edema. Methods: Literature review Results: There is level 1 evidence to support the use of anti-VEGF agents in the management of diabetic macular edema. The major concern is the need for multiple intravitreal injections, inspite of supplemental laser treatment. Results of prospective randomized studies will be presented.

Tear Film and Ocular Surface Society: A Report from the International Workshop on Meibomian Gland Dysfunction

P. Asbell [1]; C. Baudouin [2]; K.K. Nichols [3]; M. Rolando [4]; D.A. Sullivan [5]
[1]Mount Sinai School of Medicine, USA; [2]Quninze-Vingts Hospital AP-HP Univ Paris, France; [3]The Ohio State University, USA; [4]Eye Clinic, University of Genoa, Italy; [5]Schepens Eye Research Institute/Harvard Medical School, USA

Purpose: Meibomian gland dysfunction (MGD) may be the leading cause of dry eye syndrome in the world. However, although this condition impacts the health and well being of millions of people, there is no global consensus on the definition, classification, diagnosis or therapy of MGD. To obtain such a consensus, the Tear Film & Ocular Surface Society (TFOS; http://www.TearFilm.org), a non-profit organization, launched the International Workshop on Meibomian Gland Dysfunction (www.tearfilm.org/mgdworkshop/index.html). The goals of the MGD Workshop were to:

(1) perform an evidence-based evaluation of meibomian gland structure and function in health and disease;

(2) develop a contemporary understanding of the definition and classification of MGD;

(3) assess methods of diagnosis, evaluation and grading of severity of MGD;

(4) develop appropriate norms of clinical trial design to evaluate pharmaceutical interventions for the treatment of MGD;

(5) develop recommendations for the management and therapy of MGD; and

(6) create an executive summary of recommendations for future research in MGD.

Methods: The Workshop, which finalized its report in September 2010, required almost 2 years to complete and involved the efforts of 50 leading clinical and basic research experts from around the world. These experts were assigned to Subcommittees, reviewed published data and analyzed the levels of supporting evidence. Subcommittee reports were circulated among all Workshop members, presented in open forum and discussed in an interactive manner.

Results & Conclusions: This ISOPT session will communicate the conclusions and recommendations of the TFOS International MGD Workshop.

Macular Pigment Changes in Pseudophakic Eyes Quantified with Resonance Raman Spectroscopy

A. Obana [1]; M. Tanito [2]; Y. Gohto [1]; W. Gellermann [3]; S. Okazaki [4]; A. Ohira [2]
[1]Seirei Hamamatsu General Hospital, Japan; [2]Shimane University Faculty of Medicine, Japan; [3]University of Utah, USA; [4]Photon Medical Research Center, Hamamatsu University School of Medicine, Japan

Purpose: Removal of the crystalline lens by cataract surgery enhances the exposure of the retina to phototoxic, short-wavelength blue light, and could be a risk factor in the development of age-related macular degeneration (AMD). Yellow-tinted intraocular lenses (IOLs) that absorb blue light have been recommended for the protection of the retina from phototoxic blue light, although their usefulness has not yet been proved. The healthy human retina contains macular pigment that absorbs blue light, and therefore contributes to the protection from phototoxic damage. We quantified changes in macular pigment optical density (MPOD) after cataract surgery, comparing subjects with clear IOLs versus relative to yellow-tinted IOLs.

Patients and methods: 259 eyes of 259 Japanese patients (clear IOL group: 121 eyes; yellow-tinted IOL group: 138 eyes) were included. Eyes with poor post-operative visual acuity (<0.8) and any fundus diseases were excluded. MPOD levels were measured by resonance Raman spectroscopy for the duration of two years after surgery.

Results: There were no statistically significant differences in base-line characteristics investigated between the two groups. Until 6 months after the surgery, MPOD levels were not significantly different between both IOL groups. After one year and later, levels were significantly higher in the yellow-tinted IOL group relative to the clear IOL group. One day after surgery, the parameters of older age and diabetes correlated with lower MPOD levels; one year after surgery and later, lower MPOD levels correlated with clear IOL implants.

Conclusion: Cataract surgery with clear IOLs induced a higher decrease of macular pigment relative to yellow-tinted IOLs in a longer follow-up time period. The present results do not establish the domination of yellow IOLs, and further investigations are still needed concerning the prophylactic effect of yellow-tinted IOLs against AMD development.

Changes of Macular Pigment Optical Density Before and After Photodynamic Therapy in Age Related Macular Degeneration

A. Ohira [1]; Y. Koyama [1]; M. Tanito [1]; A. Obana [2]
[1]Shimane University School of Medicine, Japan; [2]Seirei Hamamatsu General Hospital, Hamamatsu University School of Medicine, Japan

Purpose: To evaluate effect of photodynamic therapy (PDT) on macular pigment optical density (MPOD) in eyes with age-related macular degeneration (AMD).

Participants: Forty-eight patients aged from 50 to 88 years of age were evaluated for MPOD levels by resonance Raman spectroscopy. The case excluded the person who had received previously the treatment of PDT and of the laser photocoagulation before in this study.

Methods: The MPOD level was measured with resonance Raman spectroscopy before and 1 month after PDT treatment, and at 3, 6, 12, 18and 24 months after treatment. Patients who were diagnosed with AMD also were evaluated by fluorescein and indocyanine green angiography after Raman measurements were complete. Optical coherence tomography (OCT) was used to determine the thickness of a 1-mm central retinal area using 6 diagonal fast and slow 6-mm scans.

Results: The mean age of the patients recruited into the study was 72.8 years from 50-88 years of age. Thirty-three patients were male and 15 were female. The mean follow-up periods were 21.8 months from 12-24 months. The mean (+/-standard deviation [SD]) MPOD level before and 12, 18, 24 months after PDT were 390+/-260, 762+/-460, 704+/-366, and 700+/-304 Raman counts, respectively; the level of MPOD was significantly higher in every post-PDT follow-up periods compared to pre-PDT MPOD level ($p<0.0083$ for each comparisons). By linear regression analyses, LogMAR VA was negatively correlated with MPOD levels at 1, 3, 6, and 12 months after PDT. On the other hand, significant correlation between foveal thickness and MPOD levels were observed by quadratic regression analysis before and 3, 6, and 18 months after PDT, suggesting that both thinner and thicker foveal thickness than normal thickness correlate with lower MPOD levels in eyes with AMD.

Conclusion: MPOD level measured by Raman spectroscopy increases after PDT in AMD. Its level correlates well with foveal morphology and visual function.

Establishment and Evaluation of the High Throughput Screening

System for Antagonistic Agents of Dry Eye Based on TGF-A1 and Bcl-2

Q. Peng ; X. Yao ; H. Tan
The First Affiliated Hospital of Hunan University of Traditional Chinese Medicine, China

Objectives: Through the establishment of the high throughput screening system for antagonistic Herbs of dry eye based on TGF-A1 and Bcl-2, It provided an technology platform of study for antagonistic herbs of dry dye.

Methods: The reporter plasmid p4GCbox-ZsGreen1DR and p3p53BS-ZsGreen1DR were prepared with PCR and genetic engineering method. The 2 kinds of plasmid p4GCbox-ZsGreen1DR were transfected into the rat lacrimal gland epithelial cells (LGEC). After selected with G418, 2 kinds of reporter cell line which were based on TGF-A1 and Bcl-2 were gained and named LGEC-ZsGreen1DR. TGF-A1 or p53 was added to LGEC-ZsGreen1DR cell line separately. The expression of ZsGreen1DR in LGEC-ZsGreen1DR cell line among different time points was detected through fluorescence microscope. The cell lines had been resuscitation culture for one month, after one month of cryopreservation. Then, repeated experiments and the expression of ZsGreen1DR in different time points were detected.

Results: Results of DNA sequencing and PCR identification showed that 2 kinds of report cell lines contained the corresponding plasmid. The reaction of the reported cell lines was successfully constructed. Induced experimental results showed that the average optical density of fluorescence expression peaked at 12 h, then decreased.

The cells were frozen for 30 days, recovery and subcultured 1 month later, fluorescent mean optical density of expression were consistent with the previous.

Conclusions: 2 report cell lines LGEC-ZsGreen1DR which contained eukaryotic expression vector p4GCbox-ZsGreen1DR and p3p53BS-ZsGreen1DR were constructed successfully. These 2 report cell lines had a good responsibility and stability.

Keywords: TGF-A1; Sp-1; GCbox motif; bcl-2; p53; p53 binding site motif; Dry eye; ZsGreen1-DR; Buddleja; Chinese component library; High-throughput screening

Switching to Bimatoprost/Timolol Fixed Combination From Bimatoprost, Latanoprost or Travoprost Significantly Reduces Intraocular Pressure

S Pfennigsdorf [1]; G Brief [2]; T Lammich [3]; E Nagel [4]; C Spraul [5]; S Ho [6]
[1]Praxis Dr. med Pfennigsdorf, Germany; [2]Institution Praxis Dr. Brief, Germany; [3]Praxis Dipl. Med. Lammich, Germany; [4]Praxis PD Dr. med. habil. Edgar Nagel, Germany; [5]Gemeinschaftspraxis Dres. Haupt, Germany; [6]Allergan Limited, UK

The efficacy and tolerability of a fixed combination of bimatoprost and timolol (BTFC) in routine clinical care was previously demonstrated overall in 1862 patients (Brief et al. Clin Ophthalmol 2010, in press), with significant reductions in IOP from baseline to month 3 (mean 5.7 mmHg; $p < 0.0001$). This analysis focuses on the subset previously treated with a topical prostaglandin monotherapy (n = 352). This was a multicentre, observational, non-controlled, open-label study of patients with primary open-angle glaucoma (POAG) or ocular hypertension (OH) treated with BTFC over 3 months. This post hoc analysis examines IOP reductions from baseline in the subset of patients previously treated only with either latanoprost (n = 172), bimatoprost (n = 87) or travoprost (n = 93). Significant mean reductions in IOP from baseline to month 3 ($p < 0.0001$, paired t-test) were seen in both right and left eyes, in patients previously receiving bimatoprost (-4.39 and -4.60 mmHg, respectively), latanoprost (-5.98 and -5.56 mmHg), and travoprost (-6.28 and -6.00 mmHg). The smallest reduction in IOP was seen in patients previously receiving bimatoprost ($p < 0.05$ vs travoprost or latanoprost), probably because baseline IOP was lower in the bimatoprost group (right eye: 20.70 mmHg vs 21.73 mmHg with travoprost and 21.62 mmHg with latanoprost). In these 352 patients, treatment with BTFC was well tolerated (overall incidence of adverse events 5.1%) and the incidence of hyperaemia was low (0.85%). In this subgroup analysis, BTFC treatment in patients with POAG or OH resulted in significant IOP reductions from baseline to month 3, regardless of prior prostaglandin monotherapy.

Switching to Bimatoprost 0.01% Reduces Intraocular Pressure in Patients with Glaucoma: Preliminary Findings From an Observational Study

S. Pfennigsdorf [1]; M. Froboese [2]; B. Maeder [3]; P. Eschstruth [4]
[1]Polch Ophthalmology, Germany; [2]Gemeinschaftspraxis Dr.med. Froboese, Germany; [3]Dr. Birgit Mader Medical Eye Centre, Germany; [4]Lamcke Eckstruth, Germany

In a multicentre, observational, non-controlled, open-label study, patients with primary open-angle glaucoma (POAG) or ocular hypertension (OH) were treated with bimatoprost 0.01% once-daily for 3 months.

Preliminary data are available from 1050 patients with a mean follow-up of 7.6 weeks. Most patients (82.1%) had previously been receiving intraocular pressure (IOP)-lowering therapies; 69% on monotherapy and the remainder on multiple therapy. The most common prior therapy was timolol. In most cases, switching to bimatoprost 0.01% took place because of insufficient IOP control on prior therapy.

In patients with complete data, there was a significant reduction in mean IOP (mean of right and left eyes) from baseline to final visit of 4.31 mmHg ($p < 0.0001$; paired Student's t-test). Most patients met (59.9%) or exceeded (13.2%) target IOP. The largest reduction from baseline in mean IOP occurred in 188 patients with no recorded previous therapy (6.45 mmHg; baseline 22.76 mmHg to final visit 16.31 mmHg), and 78% of these patients reached or exceeded their target IOP.

Patients (n = 193) previously receiving β-blocker monotherapy showed a 5.25 mmHg mean IOP reduction from baseline and 86% of these patients reached or exceeded their target IOP. Mean IOP reduction from baseline was 2.08 mmHg for patients previously receiving latanoprost monotherapy (n = 36); 72% reached or exceeded their target IOP. Most patients (94.8%) experienced no adverse events. The incidence of hyperaemia was 1.5% overall, 1.1% in patients with no recorded previous therapy and 0% in the prior latanoprost group. Most patients (89.6%) continued with bimatoprost 0.01% therapy.

In summary, bimatoprost 0.01% significantly reduced IOP in patients with POAG or OH. Bimatoprost 0.01% was well-tolerated and associated with low rates of hyperaemia.

Keratitis in Vietnam: A Study of Clinical and Microbiological Characteristics and Treatment during 10 years (1998-2007)

T.M.C. Hoang [1]; A.T. Le [2]; T.K.V. Pham [2]
[1]Vietnam National Institute of Ophthalmology, Vietnam; [2]Vietnam National Institute of Ophthalmology, Hanoi Medical University, Vietnam

Purpose: To review the clinical and microbiological characteristics,diagnosis and outcome in hospitalized patients with keratitis during ten years (1998-2007) in Vietnam National Institute of Ophthalmology(VNIO).

Method: A retrospective review was undertaken of the medical and microbiology records of 3210 hospitalized patients (3237 eyes) presenting with keratitis at VNIO during 10 years(from 1998 to 2010).

Results: Keratitis may occur at any age, but mostly seen at middle age (41-60) accounting for 41.5% and the first frequent risk factor was corneal trauma. The common type of keratitis was corneal ulcer (95.8%), others type were corneal abscess(2.59%, mainly by fungal infection)and stromal keratitis (1.61%, mainly by viral infection). Corneal scrapes from 2135 eyes grew positive cultures in 949 eyes. Fungus accounted for 742 (43.75%)with the prominance of Fusarium (318 cases, 42.86%), bacteria accounted for 205 (71.1%) with 80 cases of pseudomonas aeruginosa (39.1%). None of 44 patients with Acanthamoeba keratitis were contact lens wears. Most patients came to hospital quite late with 88.8% blindness (VA less than FC 3m). Patients with history of using steroids were more severe keratitis and had to be treated in hospital longer time. 283 eyes (8.74%) had to be eviscerated. 2882 eyes (89.03%) were recovered with medical treatment (topical eye drops, eye drop continuously, anterior chamber's injection, systemic medicine) or surgery (debridement, hypopion lavage, AMT,PKP).

Conclusion: Keratitis in VNIO was quite severe because of coming hospital late and wrong self-treatment. History of using steroids made keratitis more severe and easy getting complication.

Preservative-Free Tafluprost 0.0015% in the Treatment of Patients with Ocular Hypertension and Glaucoma - Results of an Observational Study

L.E. Pillunat [1]; F. Kimmich [2]
[1]University Eye Clinic Dresden, Germany; [2]eyecons, Germany

Background: Efficacy, tolerability and safety of preservative-free tafluprost 0.0015% were investigated in a broad patient population.

Methods: Data were collected in a non-interventional prospective multi-center observational open label study. IOP readings were recorded for each eye at baseline (previous therapy or without treatment) and 12 weeks after changing medical treatment to or initiating medication with preservative-free tafluprost once-daily. Change in IOP was evaluated over the study period for all patients as well as for specific pre-treatment subgroups. Local comfort was measured using a 5 step scale. Change in IOP was evaluated for all patients and for specific pre-treatment subgroups. All adverse events were recorded.

Results: Data from 2123 patients with glaucoma or ocular hypertension were eligible for the final evaluation. Preservative-free tafluprost 0.0015% lowered IOP in all patients from 19.5±4.4 mmHg at baseline to 16.4±2.9 mmHg after 12 weeks. In total 2077 patients (97.8%) completed the 12 week period. Preservative-free tafluprost lowered IOP in all monotherapy-subgroups: Naúve patients (n=440): 22.6±3.9 mmHg (baseline) to 16.7±2.7mmHg (week 12); betablockers (n=307): 20.3±3.5 mmHg (baseline) to 16.7±2.6 mmHg (week 12); CAI's (n=158): 19.0±3.6 mmHg (baseline) to 16.0±2.6 mmHg (week 12); Prostaglandins (n=447): 16.8±2.9 mmHg (baseline) to 15.8±2.6 mmHg (week 12). Local comfort of preservative-free tafluprost was rated as 'very good' or 'good' by 85.6% of patients. Only few adverse events occurred during the treatment period.

Conclusion: Preservative-free tafluprost 0.0015% was effective, well tolerated and safe in a broad patient population. IOP was controlled effectively, local comfort and patient satisfaction improved in the vast majority of patients.

Thymosin β4 Acts as an Antagonistic Factor of NFkB Subunit RelA/p65 in Suppressing IL-8 Gene Activation by Pro-inflammatory Factor TNF-α

P. Qiu [1]; Y. Qiu [2]; M. Kurpakus-Wheater [3]; G. Sosne [1]
[1]Wayne State University School of Medicine, USA; [2]Dartmouth College, USA; [3]University of Detroit Mercy School of Dentistry, USA

Thymosin beta-4 (Tβ4),a 43-amino acid polypeptide, is ubiquitously expressed and highly conserved across species. Although historically considered solely function as intracellular G-actin sequestering protein, Tβ4 is now known to act as a moonlighting molecule in promoting stem cell migration,cytoprotection, tissue regeneration and wound healing in cornea, heart,skin, and nervous system. Also, growing number evidence has shown Tβ4's novel function in anti-inflammation and septic shock as well as anti-microbials and anti-staphylococcal biofilm. To clarify the anti-inflammatory properties of Tβ4, we herein focused on the specific target of Tβ4 on NFkB signaling, a primary cellular signaling that relays extracellular pro-inflammatory stimuli to cell's inflammatory responses. Using the model of immortalized human corneal epithelial cells (HCET) in response to TNF-α stimulation, we provide first evidence that only Tβ4, but not another actin sequestering protein profilin-1, directly targets NFkB RelA/p65 subunit by co-localization in cytoplasm and nuclei. Topic treatment or enforced expression of Tβ4 in HCET efficiently interferes with TNF-α-induced RelA/p65 nuclear translocation, phosphorylation, kB site binding and IL-8 promoter targeting. Similar treatments of Tβ4 also suppressed TNF-α-induced IL-8 transcription and secretion in primary human cornea epithelial cells(HCEC) and HCET. Tβ4 antagonizes the activity of RelA/p65 without the need to bind to G-actin and other intra-cellular binding partners, such as focal adhesion protein PINCH-1 and ILK. Enforced expression of Tβ4 compromised the sensitizing effects of PINCH-1and ILK on TNF-α-mediated NFkB activation. The identification of a functional regulatory role by Tβ4 and the focal adhesion proteins PINCH-1 and ILK on NFkB signaling opens a new window for scientific exploration of how Tβ4 modulates inflammation. The results of this study also serve as a foundation for developing Tβ4 as a new anti-inflammatory therapy.

OCT - From Morphology to Function

L. Schmetterer
Medical University of Vienna, Austria

Optical coherence tomography (OCT) has become a standard tool in imaging the tissues of the human eye. For retinal diseases OCT plays a key role in diagnosis, treatment decision and treatment guidance. In glaucoma OCT has gained much interest to study the morphology of the optic nerve head. Clinical applications have, however, so far focused on the morphology of ocular tissues. In the recent years much effort was directed to also assess functional parameters using OCT. In Doppler OCT information on the perfusion of the tissues is obtained. Nowadays, most of these systems use Fourier Domain OCT and extract velocity information by phase-sensitive measurements. Using this technique absolute measurements of retinal blood flow become possible. In addition, insight into the retinal and choroidal microvasculature can be gained. Another approach is to use polarization sensitive OCT. This allows to measure phase retardation and birefringence of the human retinal nerve fiber layer (RNFL) in vivo. Comparison with scanning laser polarimetry shows satisfactory results. Finally spectroscopic OCT may be used to assess the oxygen tension in the human retina.

Interaction Between Intraocular Pressure and Blood Flow: Relevance for Glaucoma

L. Schmetterer
Medical University of Vienna, Austria

Glaucoma is an optic neuropathy of unknown origin. The most important risk factor for the disease is an increased intraocular pressure (IOP). Reducing IOP is associated with reduced progression in glaucoma. Several recent large scale trials have indicated that low ocular perfusion pressure (OPP) is a risk factor for the incidence, prevalence and progression of the disease. This is a strong indicator that vascular factors are involved in the pathogenesis of the disease, a hypothesis that was formulated 150 years ago. The relation between OPP and blood flow to the posterior pole of the eye is, however, complex, because of a phenomenon called autoregulation. Autoregulatory processes attempt to keep blood flow constant despite changes in OPP. Although autoregulation has been observed in many experiments in the ocular vasculature the mechanisms underlying the vasodilator and vasoconstrictor responses in face of changes in OPP remain largely unknown. There is, however, recent evidence that the human choroid regulates its blood flow better during changes in blood pressure induced by isometric exercise than during changes in IOP induced by a suction cup. This may have consequences for our understanding of glaucoma, because it indicates that blood flow regulation is strongly dependent not only on OPP, but also on the level of IOP itself. Indeed there is data indicating that reduction of IOP by pharmacological intervention improves optic nerve head blood flow regulation independently of an ocular vasodilator effect.

Optimization of Ocular Drug Delivery Profile of Tasocitinib (CP-690,550) to Support Clinical Success

M. Shiue ; W. Collette III ; W. Huang
Pfizer Global Research and Development, USA

Background: Janus kinase (JAK) is a tyrosine kinase that acts as a signaling protein in cytokine-mediated inflammatory responses. Tasocitinib (CP-690,550) is a potent, selective inhibitor of JAKs. JAK inhibition on multiple cytokine pathways provides the rationale for developing tasocitinib as treatment for ocular diseases that are inflammatory in nature.

Methods: Pharmacokinetics of tasocitinib were assessed in various ocular tissues following oral/topical dosing in pigmented rabbits. The ocular exposure of 3, 30, or 60 µg/eye/day topical tasocitinib was examined in a 5-day multidose study. Ocular exposure was also monitored for 24 hours following a single oral dose of 1 or 10 mg/kg tasocitinib. All studies were conducted at either the Pfizer Global Research and Development La Jolla Laboratories or Covance Laboratories, Inc., in accordance with the Animal Welfare Act, the Guide for the Care and Use of Laboratory Animals and the Office of Animal Welfare. Sample analyses were performed using a LC-MS/MS method.

Results: Anterior and posterior ocular tasocitinib exposure was demonstrated following topical doses. At the 60 µg dose, a decrease in exposure was observed by Day 5, possibly due to compound precipitation in the dosing solution. Reduction in exposure was not seen in pigmented tissues, potentially due to compound accumulation. Ocular exposure was also shown following oral administration. With the exception of the cornea, these exposures were significantly higher than levels achievable by topical administration. All doses were well tolerated.

Conclusions: These results characterize the ocular disposition profile of tasocitinib following topical and oral administration routes. Nevertheless, the pharmacological implication of the individual tissue exposure would be based on specific disease targets. The broad ocular tissue distribution of tasocitinib provides possibilities for treating a wide range of inflammatory ocular diseases with flexible dosing route options.

βA3/A1-crystallin is Essential for the Remodeling of the Retinal Vasculature

D. Sinha
The Johns Hopkins University School of Medicine, USA

We have recently reported that a major lens protein, βA3/A1-crystallin, is also expressed in astrocytes. βA3/A1-crystallin is observed as early as E12.5 in the lens vesicle. Interestingly, expression in the retina, particularly in the astrocytes is induced only in the first few days of post-natal development with no expression detected during embryonic stages. In previous studies we reported a spontaneous mutation, Nuc1, in Cryba1, which causes developmental defects in astrocytes (Molecular and Cellular Neuroscience 37:85-95, 2008). This developmental defect in Nuc1 astrocytes is associated with abnormal retinal vascular patterning and remodeling, perhaps due to weakened astrocyte-blood vessel interactions. Our recent data indicate that βA3/A1-crystallin in astrocytes is important for Notch signaling between astrocytes and endothelial cells and contributes to vessel patterning in the retina. The mutant retina appears to be fully vascularized by one month of age; however, gross abnormalities in blood flow, with microaneurysm formation, blockage in some vessels and increased vessel leakage are found. Our studies provide evidence that βA3/A1-crystallin affects both the initial patterning of retinal vessels during development, as well as the subsequent remodeling which provides the mature vascular architecture. In order to confirm and extend these findings, we have now established transgenic mice that overexpress the mutant βA3/A1-crystallin protein, specifically in astrocytes. These abnormal astrocytes show bundle-like structures with abnormal patterning and short, thickened processes compared to the compact stellate structure of astrocytes in wild type retina. Moreover, these transgenic mice also show changes in the vascular remodeling of the retina. It is tempting to speculate; based on our studies, that βA3/A1-crystallin may be a relevant therapeutic target for retinal vascular diseases.

Neuroprotection in Glaucoma Using Gouqizi (Wolfberry)

KF. So
The University of Hong Kong, Hong Kong, China

Aging is an important risk factor for various neurodegenerative diseases such as glaucoma and Alzheimer's disease (AD). Glaucoma is a common eye disease that may lead to irreversible blindness. Recent studies suggest that development of anti-aging drugs from Chinese medicinal herbs may be one of the possible interventions. The fruits of Lycium barbarum (or commonly known as Gou Qi Zi, or wolfberry), has been used for thousands of years in China and is believed to be effective as an anti-aging agent as well as nourishment of eyes, livers and kidneys. We have shown that aqueous extract of wolfberry provides neuroprotection to the eyes against degeneration in an experimental model of glaucoma.

Using a rat glaucoma model, we have shown that oral administration of L. barbarum polysaccharides (LBP) significantly reduced the retinal ganglion cells (RGCs) loss against elevated intraocular ocular pressure. One to 100mg/Kg LBP exerted the best neuroprotection of RGCs. We have also shown that the neuroprotective effects were, partly, mediated by modulating the activation status of microglia, 2) via direct up-regulation of neuronal survival signal £]2-crystallin, and 3) by regulating the Endothelin-1 (ET-1) biological effects.

In summary, our results show that wolfberry represents a potential neuroprotective agent which deserved to be further explored for preventing neurodegeneration in glaucoma.

The Evaluation of Antibiotics in the Prophylaxis or Treatment of Endophthalmitis Using Animal Model

T. Suzuki
Ehime University, Graduate School of Medicine, Japan

Background: Bacterial endophthalmitis secondary to cataract surgery, results in significant vision loss, and antibiotics are often used empirically for the prophylaxis or treatment of endophthalmitis. However, little is known about the efficacy of new antibiotics for endophthalmitis or suitable drug delivery system. This study was designed to evaluate antibiotics in the prophylaxis or treatment of endophthalmitis using animal model.

Methods: New compound (1835F03) that inhibits Staphylococcus aureus wall teichoic acids biosynthesis and growth bacteriostatically was evaluated using a mice endophthalmitis. In order to evaluate drug delivery systems for endophthalmitis, we examined the effect of intravitreous injection, intracameral injection, or eye drops of various kinds of antibiotics on Enterococcus faecalis endophthalmitis using an aphakic rabbit endophthalmitis model we established. Changes in electroretinography (ERG) and numbers of organisms were determined and compared throughout the infection.

Results: Eyes infected with non-treated S. aureus resulted in a significantly greater reduction of B-wave amplitude of ERG than eyes inoculated by 1835F03 treated strain. Furthermore we found that intravitreous injection of vancomycin, intracameral injection of levofloxacin, and eye drops of moxifloxacin were able to suppress the progression of E. faecalis endophthalmitis.

Conclusions: Animal endophthalmitis model appears to be useful for evaluation of antibiotics in the prophylaxis or treatment of endophthalmitis.

Success in Public Private Partnerships in Collaborative Research

M. Tabiin
Exploit Technologies Pte Ltd, Singapore

Academia has historically focused on ground-breaking basic research in Science & Technology with a focus on creating new knowledge. This knowledge was then disseminated via quality publications to spawn more research effort that built on these results.

However, there has been a global emphasis lately on generating tangible economic value from the knowledge created. This has generated more linkages between Academia to Industry partners that translate the knowledge into applications across products and services for the consumer or end-user.

Research institutions and universities now play a very big role for meeting strategic innovation needs in large established multinational as well as small medium enterprises/spin-off companies which must continue to develop novel innovative products year after year. This talk discusses models for successful partnerships in general and with A*STAR Research Institutes in particular, based on our accumulated knowledge of such partnerships in Singapore.

Phase 2 Studies of Encapsulated CNTF Secreting Cell Implant (NT-501) in Patients with Geographic Atrophy or Retinitis Pigmentosa

W. Tao
Neurotech, USA

Objective: To investigate whether CNTF, delivered via an encapsulated cell implant, preserves vision in subjects with geographic atrophy (GA) or retinitis pigmentosa (RP).

Purpose: NT-501 has shown potential efficacy in a phase 1 trial in patients with late-stage RP. The present study is to evaluate the safety and efficacy of NT-501 in a multi-center, double-masked, controlled, dose-ranging and randomized phase 2 trial for GA (CNTF2) and phase 2 trials for late RP (CNTF3) or early RP (CNTF4) in the U.S.

Method: The CNTF2 study consists of 48 participants that were randomized to the higher or lower CNTF output implant, or to sham surgery in a 2:1:1 ratio. The CNTF3 and CNTF4 studies each consist of 60 participants that were randomized to the higher CNTF output implant and the lower CNTF output implant in a 2:1 ratio. The contralateral eye received sham surgery. These studies will allow safety information to be compiled to develop the safety profile of the implant, and allow the evaluation of primary and secondary efficacy outcomes that may be used in future studies.

Results: To date, the results obtained from these studies suggest that the NT-501 implant and the implant procedure are well tolerated and safe. There is an increase in thickness of the photoreceptor layers of the retina in CNTF treated eyes in all three studies. In addition, visual function stabilization was observed, as measured by 15-letter loss, in the high dose-treated group compared to sham and low dose groups at 12 months in the GA study.

Conclusion: CNTF delivered by intraocular ECT implant increased retinal thickness without serious adverse events in eyes of GA and RP patients. The structural change was accompanied by the corresponding stabilization of visual acuity in the GA patients. For the RP patients, it remains to be determined whether this structural change presages a functional benefit for patients over a longer treatment duration.

Corticosteroid Drug Delivery Systems for Inflammatory Eye Disease

H. Uy ; J. Francisco, III ; F.M. Cruz ; P.S. Chan
Asian Eye Institute, Philippines

Background: Corticosteroids (CS) are potent, mainstay treatments for autoimmune, inflammatory eye disease. A widening range of CS delivery systems now allow for customized treatments resulting in less risk for complications from systemic immunomodulatory drugs.

Methods: A review of key clinical studies reporting the efficacy and safety of different CS drug delivery systems used for ocular inflammation was conducted.

Results: Topical, systemic, transeptal, intravitreal, and implanted CS provide effective, rapid reduction of ocular inflammation. Novel drug delivery systems such as intravitreal fluocinolone acetonide and dexamethasone implants provide long-term, sight-saving, and localized immunosuppressive effects and largely eliminate systemic complications. Cataract formation and increased intraocular pressure remain potential ocular complications of CS use.

Conclusions: CS remain effective primary treatments for autoimmune ocular inflammation. Current and novel routes of CS administration now provide more effective and safer solutions for patients with ocular inflammatory disorders.

Transeptal Triamcinolone Acetonide Injection in the Management of Non-Infectious Uveitis

H. Uy ; F.M. Cruz ; J. Francisco III ; P.S. Chan
Asian Eye Institute, Philippines

Background: Periocular injection of corticosteroids is a potential method for delivering immunosuppressive medications to the inflamed eye. The purpose of this study is to determine the efficacy and safety of transeptal injection of triamcinolone acetonide (TA) in the management of non-infectious uveitis.

Methodology: This is a noncomparative, nonrandomized, uncontrolled, interventional case series involving 18 eyes of 13 patients with acute non-infectious uveitis of which 11 eyes had cystoid macular edema. Each received a single transeptal injection of 40 mg/1 ml of TA. Main outcome measures include logMAR BCVA, improvement in inflammation scores and complications.

Results: The mean follow-up was 17 months (range, 1-52). The mean number of transeptal TA injections received was 2.7 (range, 1-6). The mean VA significantly improved from logMAR 1.03 to logMAR 0.65 after transeptal TA ($p=0.01$). Intraocular inflammation scores improved in 14 eyes. Six eyes developed IOP rise and 4 eyes underwent subsequent cataract surgery. There were no globe perforations or retrobulbar hemorrhage.

Conclusions: Transeptal injection of TA is a safe, easy and effective route for administering periocular corticosteroid in the management of non-infectious uveitis. IOP elevation and cataract progression are expected sequelae.

Glaucoma Screening with a Self-Operated, Inexpensive, Comprehensive Instrument: Can it be done?

A. Walsh
Doheny Eye Institute, USA

Diagnostic technologies exist today that can decrease the cost, increase the efficiency and improve the quality of eyecare and screening around the world. A simple, handheld, automated, patient-operated binocular device containing miniature swept source optical coherence tomography imaging systems has the potential to make the eye exam more objective, consistent, quantitative, documented and efficient. Since this instrument can be made available 24 hours per day in convenient locations, it also has the potential to be able to provide affordable, accessible, comprehensive screening.

OCT images of the entire central axis of the eye from the cornea to the choroid, so-called OCT biomicroscopy, may be able to replace many of the functions of a slit lamp biomicroscope with permanently recorded, quantifiable, high resolution cross-sections of transparent ocular tissues. This handheld OCT device, which should be as easy to operate as any binoculars, should also be able to measure IOP, corneal thickness, refractive error, anterior chamber depth, angle geometry, pupillometrics, NFL thickness, and optic disc topography. Equipped with internal display screens, button inputs and voice recognition, it should also be able to measure visual field deficits, visual acuity, extraocular motility, ocular alignment, central kinetic perimetry, color vision, reading speed, contrast sensitivity, stereo acuity, foveal suppression, and exophthalmometry.

The combination of patient-administered OCT biomicroscopy and a full suite of clinical tests may enable remote examinations of patients outside of a clinical setting. Automated versions of this device should be capable of providing point-of-care risk assessments directly to the subject within minutes without the need for a photographer or expert interpreter. The question remains: will the comprehensive suite of glaucoma tests listed above enable this device to screen for glaucoma with acceptable levels of false positives and false negatives?

Physical therapy and Neuroprotection for Glaucoma

N. Wang
Beijing Tongren Hospital, China

Purpose:

1. Observe short-term and long-term hypotensive effect of exercise on intraocular pressure (abbreviate IOP) of naturopathy combined with Spa-exercise.

2. To study whether the method is beneficial to the ongoing treatment of glaucoma.

Methods: A randomized controlled polycentric clinic trial was designed. 240 patients with primary open-angle glaucoma or ocular hypertension aged between18 and 65 years, will be chosen from outpatients at the Department of Ophthalmology in three centers of Beijing TongRen Hospital, Guanganmen Hospital of China Academy of Chinese Medical Sciences, Peking University First Hospital. All subjects are divided into two groups , group one receives naturopathy and 0.004% travoprost one time a day (Alcon, America), group two only receives 0.004% travoprost one time a day. Before clinical test, all enrolled patients perform exercises at the levels of 20% maximum power (Pmax) for 10minutes, then 60% Pmax for 5minutes of bicycle ergometry. Intraocular pressure is measured by Goldmann applanation tonometer before exercise, immediately after exercise, at the time of 0.5h, 1h, 2h, 3h, 4h of post-exercise. We observe IOP for 3 months mainly, and visual acuity,visual field,retinal nerve fiber layer, heat shock protein 27and 70, TNF-a, VEGF, are measured as secondary items.

Results: We primarily observed 40 subjects. The IOP reduced 1¡«3mmHg (millimetre(s) of mercury) after 10-minute-exercise at 20% Pmax, 3¡«14mmHg after 5-minute-exercise at 60% Pmax, lasting for 0.5 to 4 hours.

Conclusions:

1. Our study shows that the ocular hypotensive effect of strenuous exercise on the IOP;

2 The greater the exercises workload are given, the lower the IOP reduces;

3. The reduction of IOP depends on the IOP baseline. The higher IOP baseline is, the lower the IOP reduces.

Dynamic Blood Flow Autoregulation in Experimental Glaucoma

L. Wang [1]; G. Cull [1]; C.F. Burgoyne [1]; Y. Liang [1]; K. Rittenhouse [2]
[1]Devers Eye Institute, USA; [2]Pfizer Inc., USA

Background: Autoregulation (AR) dysfunction has been proposed as a cause of circulatory aberration within optic nerve head (ONH) in glaucoma. Solid evidence is however absent. This study investigated an early phase of blood flow (BF) response to a sudden perfusion pressure change, known as dynamic autoregulation (dAR), to determine the effect of chronic IOP elevation on the ONH AR in an experimental glaucoma model and compared with classic static autoregulation (sAR).

Methods: Chronic glaucoma was induced in one eye of each 5 monkeys after multiple lasering of trabecular meshwork. dAR was assessed by continuous measuring of ONH BF with a laser speckle flowgraphy device when the IOP was manometrically increased from 10 to 40 mmHg rapidly; sAR was assessed by measuring BF before and 5 min after multiple-level IOP changes. Retinal nerve fiber layer thickness (NFLT) and ONH surface topography were measured with optical coherence tomography and confocal scanning laser tomography, respectively, to assess in vivo structure. The tests were repeated biweekly on both eyes until NFLT in glaucoma eyes were reduced by 30-40%. Regional ONH BF was measured by microsphere method at IOP 40 mmHg at the end of the experiment.

Results: In the glaucoma eyes, IOP was increased to 27.6 ±2.5 mmHg (12.2 ±7.7 in control); NFLT was reduced significantly up to 40%. Descending slope of dAR response to the IOP challenge was significantly reduced in glaucoma eyes; three out of the 5 animals showed significantly reduced magnitude (Fig 1). No significant sAR changes were observed (Fig 2) except at endpoint measured by microsphere method and a tendency of reduced basal BF.

Conclusion: Chronic IOP elevation impairs AR capacity in the ONH of experimental glaucoma manifested by abnormal dAR responses and affects sAR within seemly the entire region of ONH during late stage. dAR change may be a potential diagnostic target for the hemodynamic change in glaucoma. Support: Translational Medicine, Pfizer Inc.

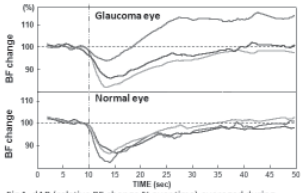


Fig 1. dAR (relative BF change % over time) averaged during baseline (green), post-laser (blue) and late stage (red) in an animal. Vertical line crossing 10th sec indicates the onset of IOP challenge.

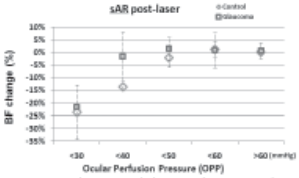


Fig 2. Autoregulation curve (relative BF change vs. OPP) constituted by sAR measurements in glaucoma and control eyes after laser treatment. sAR was grouped by the level of OPP for each animal.

Clinical and Mechanism Research about the Treatment of Xeroma used Runmuling

Y. Wang ; K. Li
Nanjing University of Chinese Medicine, China, Peoples Republic

We have found in the literature of traditional Chinese medicine that Bidens Bipinnata L. has ¡°a side effect of inducing excessive tear¡±, which inspired us to develop Runmuling, an oral granule preparation composed of Bidens Bipinnata L., medlar and chrysanthemum. The remedium cardinale in the prescription, Bidens Bipinnata L., can clear away heat and toxic material, detumescence and eliminate stasis to activate blood circulation; chrysanthemum is for lung and liver channel tropism, which can remove heat, eliminate toxins and nourish the liver to improve eyesight; Medlar is for liver and kidney channel tropism, which can invigorate the liver and kidney and nourish the Yin to improve eyesight. The mixture of the three of them can have a combined effect of treating and curing xeroma. Clinical experiments have proved its quite good curative effect. To further our understanding of the prescription, the following clinical and animal experiments have been conducted to verify its curative effect, and to explore its mechanism.

Conclusion:

Runmuling can promote SIT, lengthen BUT, and alleviate eye dryness, and has an obvious therapeutical effect on xeroma.

One Year Follow-Up of Selective Laser Trabeculoplasty in Primary Open-Angle Glaucoma

T. Wang ; W. Ningli
Beijing TongRen Eye Center, China

Objective: To investigate the safety and efficacy of selective laser trabeculoplasty (SLT) in primary open-angle glaucoma (POAG).

Design: Retrospective case report.

Participants: 47 cases (62 eyes) POAG patients.

Methods: 62 eyes of 47 patients with primary open-angle glaucoma were treated with frequency doubled ND:YAG laser SLT (Selecta Duet). A total of approximately 50 non-overlapping spots were placed over 180 degrees of the trabecular meshwork at energy levels ranging from 0.5 to 1.4 mJ per pulse. After surgery, patients were maintained with the drug regimen identical to that before treatment. The average follow-up was 12 months.

Main Outcome Measures: Intraocular Pressure (IOP) and Complications.

Results: After 1 year the average reduction in intraocular pressure (IOP) from the baseline was 5.2 mmHg. The IOP of 72.5% eyes were controlled well. The slight inflammation of anterior chamber occurred in all the cases 1 hour later after SLT and disappeared 3 days later automatically.

Conclusions: SLT is an effective and safe method to lower IOP in primary open-angle glaucoma in the one year follow up.

Endpoints in Ophthalmology Trials – A Regulatory Perspective from Europe

K. Wickstrom
Medical Products Agency, Sweden

In a clinical trial, the primary endpoint should be the variable capable of providing the most clinically relevant and convincing evidence directly related to the primary objective of the trial while secondary endpoints assess other aspects of the efficacy (or safety) of a drug. Since a direct assessment of the clinical benefit may not be feasible, the use of indirect criteria such as biomarkers may be an option. The regulatory requirements on biomarkers depend on the weight they are given and the associated claims. If used as a tool to, for example, aid in dose selection in exploratory trials, regulatory requirements may be very limited. If used as a primary endpoint in a pivotal trial, the link to and relevance for a true clinical outcome must be established. Regulatory considerations on biomarkers including examples on those discussed to early identify future progression of vision are given together with a discussion on a recently established pathway to qualify such tools for a specific intended use within the EU.

Options for Localized Drug Delivery in Glaucoma

T. Wong
Singapore National Eye Centre, Singapore

Ocular drug delivery development has led to a multitude of approaches and systems that vary in mode of administration, implantation site, composition and vehicles. Biodegradable polymers, or biopolymers, are proven vehicles for drug delivery found to be biocompatible, easily fabricated and useful for sustained drug delivery with predictable biodegradation kinetics. The biocompatibility and use of various biopolymer microfilms to load drugs for treating post-operative inflammation following glaucoma filtration surgery in an animal will be described.

Optically transparent nanosized sustained delivery systems can be delivered in a viscous aqueous vehicle, allowing it to be retained in the eye for longer without clearance. The use of one such carrier system for delivery of anti-glaucoma medication will be discussed.

The Activation and Modulation of Astrocyte in Glaucoma

J. Wu
EYE & ENT Hospital of Fudan University, China, Peoples Republic

The optic neuropathy of glaucoma is characterized by progressive retinal ganglion cell (RGC) death and their axons degeneration. The specific pathogenic mechanisms of glaucomatous neurodegeneration still remained unclear. However, increasing evidence now show that not only the intrinsic events to RGC but also RGC-astrocyte intercommunication are critically important for glaucomatous neurodegeneration. In the retina injured by IOP elevation or other glaucomatous stress, astrocytes exhibited hypertrophic morphology, upregulation of glial fibrilary acidic protein and many alterations of gene expressions in the process referred as to glial activation. In corresponding optic nerve head, normal arrangement of astrocytes was disrupted and migration occurred with morphologic alterations such as hypertrophy, hyperplasia, and increasing expression of GFAP protein. Moreover the reactive astrocytes displayed profound changes in glaucoma as supported by re-expressions of developmental proteins such as vimentin, nestin and Ephrin. In addition to this, many gene expression alterations involved in signal transduction, cell proliferation, cell-cell interaction, cell adhesion, extracellular matrix, and immune response. Altogether, the activated astrocytes played a significant role in the remodeling of the ONH, and eventually formed astrocytic scar.

The Protection of Compound Chinese Medicine MingMuWuZi on Rat Model of Light-Induced Retinal Injury

H. Ye
Chengdu University of Traditional Chinese Medicine, China, Peoples Republic

Objective: To observe the effect of compound Chinese medicine MingMuWuZi on rat model of light-induced retinal injury and to explore its mechanism.

Methods: Sprague-Dawley (SD) rats were exposed to green fluorescent light for 24 hours. MingMuWuZi was given at high, low dosage before light exposure and lasted for 14 days. The control group and the model group were installed, 10 rats each group. MfERG was observed with standard stimulus and record method, thickness of the outer nuclear layer and cells apoptosis labeled by TUNEL were measured. The expression of basic fibroblast growth factor (bFGF), glial fibrillary acidic protein (GFAP) in retinal, content of N.O. and free amino acids were detected.

Results: Compared with the control group, the high dose group of MingMuWuZi had lower retinal cell apoptosis, less retinal GFAP expression, and more expression of bFGF (P <0.01). Meanwhile, compared with the model group, the level of amino acid in high dosage group was decreased (P<0.05) and the level of retinal NO was increased (P <0.01 ~ 0.05). MfERG test showed that the response density of N1 and P1 waves in the high dose group was significantly higher, but decreased obviously in the model group which keep abnormal after test.

Conclusion: The compound Chinese medicine MingMuWuZi could protect retina from light damage effectively, it could also promote repair and improve visual function. This may be related to the inhibition of retinal cell apoptosis and glial cell proliferation, and higher expression of retinal bFGF may contributed to it as well.

TRPC6: A Potential Target for Human Glaucoma

X. Zhang
Zhongshan Ophthalmic Center, China, Peoples Republic

Background: The transient receptor potential (TRP) are Ca2+ permeable non-selective cation channels. TRPCs, who own the most structural similarity to Drosophila TRP channel, are widely distributed and exert multiple functions in the CNS. TRPC6 subfamily is recently reported to play an important role in promoting neuronal survival in brain with growing evidences. This presentation presents the potential role of TRPC6 in the survival of retinal ganglion cells (RGCs) and in patients with primary open-angle glaucoma (POAG).

Methods:

1) The mRNA of TRPC6 in the peripheral blood from patients with POAG was analyzed by quantitative real-time PCR;

2) TRPC6 expression in normal rat retina was analyzed by RT-PCR, western blotting, in situ hybridization, and immunohistochemistry;

3) The TRPC6 mRNA was examined in rat retina from laser-induced hypertensive animal model and in rat retinal ischemic-reperfusion (IR) model. Pharmacological experiments were conducted. The expression of brain-derived neurotrophic factor (BDNF) was measured in the retinal IR model.

Results: The high expression of the TRPC6 gene in POAG was identified comparing to the normal controls. TRPC6 mRNA and protein are selectively enriched in the RGC layer of the retina. TRPC6 mRNA was increased in retina from pressure injury. The pattern of TRPC6 expression was induced in the retinal IR model. Activating TRPC channels prior to ischemia has early neuroprotective effects on RGCs in vivo. The protection of TRPC6 is BDNF-mediated and the proBDNF-p75NTR signaling may contribute to the death of RGCs in retinal ischemia injury.

Conclusions: Studies provide evidence that there is a potential role of TRPC6 in the survival of RGCs. TRPC6 gene highly expressed in POAG may serve a useful biomarker for the disease. TRPC6 may become a potential therapeutic target for the treatment of glaucoma.

Research of QiDengMingMu Capsule Therapy Effect on STZ Induced Diabetic Rat fs Blood-Retinal Barrier and Visual Function Damage

F. Zhang [1]; J. Duan [2]; X. Lu [1]; H. Ye [3]
[1]Visual Physiology Laboratory of State Administration of TCM, China, Peoples Republic; [2]Key Laboratory of Visual Function Protection of State Administration of TCM, China, Peoples Republic; [3]Key Laboratory of Eye Disease Prevention and Visual Function Protection of Sichuan Province, China, Peoples Republic

Purpose: To observe retinal vessel leakage and visual function damage of Streptozotocin (STZ) induced diabetic rat C and effect of traditional Chinese medicine Qi Deng Ming Mu Capsule(QiDeng) on the retinal vessel leakage and visual function damage of STZ induced diabetic rat.

Methods: We reproduced diabetic animal model by peritoneal injectionintra of STZ, in the six months after the blood glucose rised, we used Evans blue to trace the leakage of blood-retina barrier and evaluated the visual function by recorded mfERG. After blood glucose rised three month, we treated the Chinese medicine group diabetic rat with QIDENG capsule and treated the control group with Calcium dobesilate. After three month treated by medicine we evalued the leakage of blood-retina barrier and the visual function.

Results: The damage of BRB and visual function occurented at two week after the blood glucose rised, and the diabetic rat model fs BRB and visual function damage got worse as the hyperglycemia keep on. But after the Chinese medicine treated three month, the rat fs retina vessel leakage was reduced and the Chinese medicine can protected @visual function in the hyperglycemia by recover the P1 wave fs amplitude and the protracted peak latency.

Conclusion: The STZ diabetic rat occurrence BRB break down and visual function damage in early phase and get worse as the hyperglycaemia keep on. The Chinese medicine QIDENG capsule can prevent the vessel leakage by damage of BRB, and QIDENG capsule can protect the visual function of the STZ diabetic rat.

Immune-Mediated Injury and the Retinal Ganglion Cell Survival

C. Zhang [1]; P. Huang [1]; S. Zhang [2]
[1]Peking University Third Hospital, China; [2]Penn State University, USA

Purpose: To examine the cell survival rates of retinal ganglion cells (RGCs) in several immunological conditions in response to ischemic insults.

Methods: Intraocular pressure of the right eyes was raised to create retinal ischemia for 1 hour. All left eyes served as control. To evaluate the effects of lymphocyte T and B cells on RGC survival, we examined the retinas from C57BL/6 mice, SCID mice, and SCID mice adoptively pre-transferred with an enriched CD4+T cell population, which were obtained from splenocytes of C57BL/6 mice by flow cytometry after insult. The RGCs were retrogradely labelled by fluorescence dye Fluorogold. Eyes were harvested 21 days after insult. Cell survival was determined by counting labeled RGCs in the whole-mounted retinas. The eyes from STAT6(−/−) mice were enucleated at 48 hours after insult and processed for morphometric study.

Results: The numbers of surviving RGCs were strikingly declined in C57BL/6 eyes in response to ischemia (n=5, 78±4% of survival cells in contralateral control eyes), while in SCID mice, there was no differences between ischemic and control eyes (n=7, 93±5% of the survival cells in contralateral eye). The RGCs from the immunologically deficient animals showed significantly resistance to ischemic injury compared the RGCs from wild type controls (P<0.01). An adoptive transfer of CD4+T lymphocytes derived from C57BL/6 into SCID mice caused significantly loss of RGCs similar to C57BL/6. We further observed that the RGCs from STAT6(-/-) animals also showed significantly resistance to ischemic injury compared with the RGCs from C57BL/6 controls 48 hours after I/R insults (P<0.05).

Conclusions: Our results supported that the survival of RGCs in response to I/R may be associated with immunological functions.

Preoperative Use of Intravitreal Bevacizumab for Severe Retinopathy of Prematurity

P-Q. Zhao ; Y. Xu
Xinhua Hospital, Shanghai Jiaotong University School, China

Purpose: To evaluate the safety and efficacy of bevacizumab pretreatment in vitrectomy for severe retinopathy of prematurity (ROP).

Methods: In a retrospective, interventional, consecutive case series, the records of 16 eyes of 8 patients presenting with vascularly active Stage 4 ROP who intravitreal injection of bevacizumab from April 2008 to April 2009 were evaluated. An intravitreal injection of 0.625mg bevacizumab was preformed one week prior to planned vitrectomy. Compared the pre and post injection fundus photography and evaluated the vascular activity. The outcomes studied at the final follow-up visit were the retinal status, lens clarity and visual acuity.

Results: In all patients, six were males (12 eyes) and two were females (4 eyes). Gestational age ranged from 27 to 34 weeks (mean 30.5±2.4 weeks) and birth weight ranged from 1000 to 1750g (mean 1290±272g). All cases showed remarkable regression of fibrovascular membrane with visually absent vascular component after the injection. No adverse events occurred. Lens-sparing vitrectomy was performed in 14 eyes, while vitrectomy combined with lensectomy was performed in 2 eyes. The mean follow-up was 8.5 months, ranging from 3 to 15 months. At the final follow-up, anatomical attachment was achieved in 8 patients 15 eyes (93.75%). One eye (6.25%) had partial attachment. The lens remained clear in all the eyes.

Conclusion: Intravitreal bevacizumab administrated prior to vitrectomy reduced neovascularization, thus facilitating PPV. The safety and efficacy of vitrectomy after bevacizumab injection should be further evaluated.

The Prevalence and Burden of Primary Glaucoma in China

J. Zhao
Peking Union Medical College Hospital, China, Peoples Republic

We conducted the epidemiological studies of glaucoma in Beijing in 2006. The objective of the study was to estimate the prevalence of glaucoma in China. A random sample was obtained through cluster sampling of villages. In this population, the prevalence of primary open angle glaucoma and primary angle closure glaucoma was 1.48% and 1.66%. The prevalence of the variety of glaucoma was increasing by aging. The visual function in 64.0% of glaucoma patients was damaged in some degree. we can confirm that glaucoma is a serious eye disease leading to blindness according to the prevalence and the visual function of the glaucoma patients.

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