ARVO
CHAPTER AFFILIATE

האגודה הישראלית לחקר העין והראיה
Israel Society for Vision & Eye Research

PROGRAM

32ND Annual Meeting
Ramat-Gan
March 15-16, 2012

תכנית

הכינוס השנתי ה–32
רמת–גן
16–15 מרץ, 2012

עריכת התוכנית: פרופ' איתי חוברס, פרופ' דרור שרון וד"ר חני לבקוביץ–ורבין

עיצוב והבאה לדפוס: מיכל שפיגל ודבורה מרקס–אוחנה.

ISRAEL SOCIETY FOR VISION AND EYE RESEARCH
32ND ANNUAL MEETING, 2012
PROGRAM AT A GLANCE

Thursday, March 15, 2012			
Session	**Location**	**Time**	**Page**
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Opening Remarks	Lecture Hall	08:30 – 08:35	9
Poster Presentations 1	Lecture Hall	08:35 – 09:30	9
Cornea 1	Lecture Hall	09:30 – 10:40	13
Poster viewing and Coffee	Exhibition Hall	10:40 – 11:10	14
Retina 1	Lecture Hall	11:10 – 12:30	15
Guest Lecture 1	Lecture Hall	12:30 – 13:10	16
Lunch break and Poster viewing	Lecture Hall	13:10 – 14:10	16
Poster Presentations 2	Lecture Hall	14:10 – 15:10	16
Awards and ISVER update	Lecture Hall	15:10 – 15:30	21
Genetics A	Lecture Hall	15:30 – 16:00	21
Poster viewing and Coffee	Exhibition Hall	16:00 – 16:30	21
Genetics B	Lecture Hall	16:30 – 17:20	22
Glaucoma/Neuro-ophthalmology	Lecture Hall	17:20 – 18:40	23
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Friday, March 16, 2012			
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Cornea 2	Lecture Hall	08:30 – 09:50	25
Guest Lecture 2	Lecture Hall	09:50 – 10:20	26
Brunch and Posters	Exhibition Hall	10:20 – 11:00	26
Pediatrics and Visual science	Lecture Hall	11:00 – 12:10	26
Retina 2	Lecture Hall	12:10 – 13:20	28
Concluding Remarks	Lecture Hall	13:20 – 13:25	29

יושבי-ראש של האגודה הישראלית לחקר העין והראיה

CHAIRMEN OF THE ISRAEL SOCIETY FOR VISION AND EYE RESEARCH

Prof. Elaine Berman	1979-1982	פרופ איליין ברמן ז"ל
Prof. Michael Belkin	1983-1985	פרופ' מיכאל בלקין
Prof. Saul Merin	1986-1989	פרופ' שאול מרין
Prof. Shabtay Dikstein	1990-1993	פרופ' שבתאי דיקשטיין
Prof. Fabian Abraham	1994-1996	פרופ' פביאן אברהם ז"ל
Prof. Ido Perlman	1997-1999	פרופ' אידו פרלמן
Prof. Jacob Pe'er	2000-2003	פרופ' יעקב פאר
Prof. Ahuva Dovrat	2004-2006	פרופ' אהובה דברת ז"ל
Prof. Mordechai Rosner	2007-2009	פרופ' מרדכי רוזנר
Prof. Eyal Banin	2010- 2012	פרופ' איל בנין

חברי ועד האגודה הישראלית לחקר העין והראיה

BOARD MEMBERS OF THE ISRAEL SOCIETY FOR VISION AND EYE RESEARCH

Eyal Banin	איל בנין, יו"ר
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Arieh Solomon	אריה סולומון
Ehud Assia	אהוד אסיה

מרצים המקבלים פרס על עבודות שהוצגו בכינוס השנתי ה-31, מרץ 2011

RECIPIENTS OF AWARDS FOR THE BEST POSTERS AND TALKS PRESENTED AT THE 31ST MEETING, MARCH 2011

1st prize: research talk: SAFURI SHADI (Technion)
Bestrophin modulates phagocytosis of photoreceptors outer segments by retinal pigment epithelial cells.

2nd prize: research poster: GUETA KEREN (Tel-Aviv University)
The role of lim-domain binding proteins in retinal development.

3rd prize: clinical talk: WUSSUKI-LIOR ORLY (Assaf Harofeh Hospital)
Hematologic biomarkers in childhood cataracts.

4th prize: clinical poster: BACHAR-ZIPORI ANAT (Rambam Hospital)
Hyperglycemia induces microparticles formation and affects their antigenic expression and thrombogenicity.

הפרס הראשון הינו מלגת נסיעה ל-ARVO
על-שמה של פרופסור אהובה דברת, ז"ל

פרסים 2-4 הינם בחסות
"לראות"- העמותה למחקר בריאות העין ומניעת עיוורון בישראל

לראות

העמותה לחקר בריאות העין
ומניעת עיוורון בישראל (ע"ר)

תודה לחברות שתרמו לכינוס:

Many thanks to the sponsoring companies:

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העמותה לחקר בריאות העין
ומניעת עיוורון בישראל (ע"ר)

לראות

העמותה לחקר בריאות העין ומניעת עיוורון בישראל

מטרות לראות

- הגברת המאמץ המחקרי ברפואת עיניים בישראל ובעולם
- העלאת המודעות הציבורית לחשיבות רפואת עיניים מונעת

המועצה המדעית של לראות

מורכבת מהשורה הראשונה של רופאים וחוקרי עיניים בישראל וכן גורמים בכירים מתחומי הבריאות, האקדמיה והתעשייה כולם מתנדבים בעמותה.
משרד הבריאות בחר בעמותה כגוף מייעץ בתחום תרופות וטכנולוגיות חדשות.
המועצה מרכזת פרויקטים מחקריים הקיימים בישראל בתחום רפואת העיניים, בוחנת ומתקצבת אותם במסגרת המשאבים העומדים לרשותה על פי סדר עדיפויות מוגדר. המועצה פועלת לגיוס מיטב החוקרים מתחומים רלוונטיים וכן להקמת רשות מחקרית בינלאומית.

בין יוזמות עמותת לראות בשנת 2011

"**לילה של בריאות בפארק הרצליה**" קיום בדיקות סקר לילדים.
"**כנס רפואי במרכז פרס לשלום**" כנס ראשון מסוגו בשיתוף רופאים פלסטינאיים ורופאים וחוקרים ישראליים "What we can learn from each other"
"**יום בריאות העין – רפואת עיניים בקרב האוכלוסייה הערבית בצפון הארץ**" כנס ראשון מסוגו לאוכלוסייה הערבית בנצרת בשפה הערבית ה לקהל הרחב, לאופטומטריסטים ורופאים.
"**נבדקים היום כדי לראות את המחר**" חודש מודעות בריאות העין השלישי- שכלל כנס מומחים לציבור הרחב, קמפיין תקשורתי ומוסף מיוחד בשיתוף מעריב.

תכניות לשנת הפעילות 2012

א. פעילויות שוטפות

1. תכנית למימון מחקרים במוסדות מחקר רפואיים
2. סמינר הרצאות וידאו מפי מיטב החוקרים והרופאים בשידור חי באתר העמותה
3. מתן יעוץ רפואי על ידי פורומים של רופאים מומחים ומנהלי מחלקות עיניים
4. ארגון חודש המודעות לבריאות העין הרביעי

ב. פרויקטים מתוכננים

1. ניידת עיניים לבדיקות קשישים נזקקים
2. קידום פעילות סקר ראיה לילדים
3. המשך גיוס משאבים למחקר רפואי בארץ ובחו"ל

מחקרים ממומנים ע"י עמותת לראות 2007-2011

שלוש עשרה הצעות מחקר מצטיינות זכו למימון בגובה מיליון דולר, כתוצאה מפעילותה האינטנסיבית של העמותה

1. **דר' רות אשרי-פדן**, הפקולטה לרפואה ע"ש סאקלר, אוניברסיטת ת"א חקר המנגנונים המולקולאריים המעורבים בבקרת התפתחות תאי הפיגמנט בעין יונקים.
בין השנים 2007-2006: 200,000 ₪

2. **פרופ' איל בנין**, המחלקה למחלות עיניים, בית החולים האוניברסיטאי הדסה והפקולטה לרפואה האוניברסיטה העברית ירושלים
תאי גזע עובריים אנושיים כמקור לתאי אפיתל פיגמנטי ברשתית.
בין השנים 2007-2006: 200,000 ₪

3. **דר' תמר בן יוסף**, המחלקה לגנטיקה, הפקולטה לרפואה ע"ש רפפורט, הטכניון מפוי גנים וזהוי מוטציות בגנים האחראיים לרטיניטיס פיגמנטוזה במשפחות ערביות ויהודיות מצפון הארץ.
בין השנים 2007-2006: 200,000 ₪

4. **דר' דרור שרון**, המרכז למחלות ניוונויות של המקולה והרשתית, בית החולים האוניברסיטאי הדסה ירושלים
אפיון גנטי של מחלות ניוון מקולרי תורשתיות באוכלוסייה הישראלית.
בין השנים 2007-2006: 200,000 ₪

5. **פרופ' אידו פרלמן**, הפקולטה למדעי הרפואה, המחלקה לפיסיולוגיה, הטכניון חיפה התפשטות תהליכים ניוונים מפוטורצפטורים חולים מסוג קנים לפוטורצפטורים בריאים מסוג מדוכים במודל חולדה לרטיניטיס פיגמנטוזה.
שנת 2008: 500,000 ₪

6. **פרופ' אריה סולומון**, הפקולטה לרפואה, אוניברסיטת תל אביב שילוב ננו טכנולוגיות וחומרים ביו-טכנולוגיים חדשים ליצירת טיפול אינטגרטיבי לרפוי עצב הראייה לאחר חבלה או מחלה.
שנת 2008: 500,000 ₪

7. **פרופ' איתי חוברס**, מחלקת עיניים, המרכז הרפואי הדסה עין כרם, ירושלים אפיון מעורבות תתי אוכלוסיות של תאי דם לבנים והרצפטורים לכמוקינים CCR2 ו-CXECR בפתוגנזה של ניוון מקולרי גילי (נמ"ג)
שנת 2008: 300,000 ₪

8. **דר' ניצה גולדנברג-כהן**, מרכז רפואי שניידר לרפואת ילדים בישראל הזרקה תוך עינית של תאי גזע ממח עצם בוגר לרשתית מתפתחת בעין של עכברים בני יומם.
שנת 2008: 300,000 ₪

9. **דר' מיכאל ויסבורד**, מחלקת עיניים, המרכז הרפואי איכילוב, ת"א שימוש טופיקלי באבסטין למחלות עיניים.
שנת 2008: 300,000 ₪

10. **פרופ' עופרי רון**, האוניברסיטה העברית, ירושלים מודל חדשני לעיוורון יום. מחקר היתכנות לקראת טיפול גנטי בחולי אכרומטופסיה.
שנת 2010: 200,000 ₪

11. **ד"ר שחר פרנקל**, מ"ר הדסה עין-כרם גרורות ממלנומה של הענביה: עיכוב גורמי התיעתוק NFkB ו-USF2 כטיפול נגד מיקרו-גרורות.
שנת 2010: 200,000 ₪

12. **ד"ר דרור שרון**, מ"ר הדסה עין-כרם אפיון גנטי ותפקודי של גן חדש שהינו גורם עיקרי לרטיניטיס פיגמנטוזה באוכלוסיה הישראלית.
שנת 2010: 200,000 ₪

13. **ד"ר ערן פרס**, מחלקת עיניים, מ"ר אסף הרופא איפיון קליני וגנטי של ירוד (קטרקט) משפחתי בישראל.
שנת 2010: 150,000 ₪

Moderators and committee members please note: you should select two presentations for the young investigator award for the best oral and the best poster presentations. The candidates are marked by AC (AC: Award Candidate).

The page number refers to the location of the full abstract.

PROGRAM

Thursday, March 15, 2012

Registration and Coffee 08:00–08:30

Opening Remarks: Prof. Eyal Banin 08:30–08:35

Session I - Poster Presentations 1 08:35–09:30

Moderators: Prof. Ehud Assia, Dr. Nitza Goldenberg-Cohen

10. **TLR4 KNOCK-OUT MICE ARE RESISTANT TO OPTIC NERVE CRUSH DAMAGE** **39**

AC

Dana Morzaev (1,4), Shirel Weiss (1,4), Bat Chen R. Avraham-Lubin (1,4), Edith Hochhauser (2,4), Nitza Goldenberg-Cohen (1,3,4).
(1) The Krieger Eye Research Laboratory. (2) Laboratory of Cardiac Research, Felsenstein Medical Research Center, Petah Tiqwa. (3) Department of Ophthalmology, Rabin Medical Center, Petah Tiqwa. (4) Sackler School of Medicine, Tel Aviv University, Tel Aviv; Israel.

11. **ISOTOPIC CO2 LASER ASSISTED SCLERECTOMY SURGERY FOR TREATING GLAUCOMA** **40**

Shai Assia (1,2), Joshua Degani, PhD (2).
(1) Tel Aviv University, Faculty of Engineering, Bio-Medical Department.
(2) IOPtima Ltd. Tel Aviv.

12. **PHOSPHOPROTEOMICS OF AXONAL SIGNALING IN GLAUCOMA** **41**

Marek Rajman (2), Michal Pardo (1), Juan A Oses-Prieto (3), Katalin F. Medzihradszky (3), Alma Burlingame (3), Mike Fainzilber (2), and Hani Levkovitch-Verbin (1).
(1) Goldschleger Eye Institute, Sheba Medical Center, Tel-Hashomer, Israel, affiliated to the Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel. (2) Dept.of Biological Chemistry, Ullman Building, Weizmann Institute of Science, Rehovot 76100, Israel. (3) Mass Spectrometry Facility, University of California, San Francisco, USA.

13. **GENETIC VARIATIONS IN DIABETIC PATIENTS WITH PROLIFERATIVE AND NON-PROLIFERATIVE RETINOPATHY** **42**

Mohamed Atamney (1), Olga Dratviman-Storobinsky (2), Ruth Axer-Siegel (1,3), Merav Gabbay (4), Uri Gabbay (5), Yoram Cohen (6), and Nitza Goldenberg-Cohen (2,3,7).
(1) Department of Ophthalmology, Rabin Medical Center, Petah Tiqwa. (2) The Krieger Eye Research Laboratory, Felsenstein Medical Research Center-Tel Aviv University, Petah Tiqwa. (3) Sackler School of Medicine, Tel Aviv University, Tel Aviv; Israel. (4) Kiryat Ono Community Health Center, Clalit Health Services, Dan-Petach Tikva District. (5) Epidemiology and Preventive Medicine Department, School of Public Health, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv; Israel. (6) Department of Gynecology, The Gynecology Research Laboratory, Sheba Medical Center, Tel Hashomer. (7) Pediatric Ophthalmology Unit, Schneider Children's Medical Center of Israel, Petach Tikva.

14. **MUTATIONS IN A TRANSIENT RECEPTOR POTENTIAL CHANNEL GENE (TRPM1) ARE A MAJOR CAUSE OF CSNB IN THE ISRAELI POPULATION** **43**

Lina Zelinger, Eyal Banin, Dror Sharon.
Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem.

22. **LIGHT INTENSITY DRIVEN RETINAL TYROSINE HYDROXYLASE EXPRESSION, AND REFRACTIVE DEVELOPMENT OF THE CHICK'S EYES** **51**

Yuval Cohen (1), Mary Safrin (1), Anat Nizan (1), Edna Peleg (2), and Arieh S. Solomon (1).
(1) Goldschleger Eye Research Institute, Tel Aviv University, Tel Hashomer, Israel. (2) Hypertension Unit, Department of Internal Medicine, Chaim Sheba Medical Center, Tel Hashomer, Israel.

23. **MONOCYTE-DERIVED MACROPHAGE DIVERSITY IN EAU** **52**

AC

Inbal Benhar (1), Anat London (1), Rachel R. Caspi (2), Michal Schwartz (1).
(1) Department of Neurobiology, Weizmann Institute of Science, Rehovot, Israel. (2) Laboratory of Immunology, National Eye Inst/NIH, Bethesda, MD.

24. **RETINAL BLOOD VESSELS DIAMETER IN A HEALTHY COHORT AS MEASURED BY THE SPECTRAL DOMAIN OCT (SD OCT)** **53**

Dafna Goldenberg, Jonathan Shahar, Anat Loewenstein, Michaella Goldstein.
Department of ophthalmology, Tel Aviv medical center, Tel Aviv, Israel and Sackler faculty of medicine, Tel Aviv University, Tel Aviv, Israel.

Session II - Cornea 1 09:30–10:40

Moderators: Prof. Abraham Solomon, Dr. Irina Barequet

Time	Title	Page
09:30-09:40	**HIGH ORDER ABERRATIONS & TOPOGRAPHY IN NORMAL, KERATOCONUS-SUSPECT & KERATOCONIC EYES** Ariela Gordon-Shaag (1), Michel Millodot (2), Reut Ifrah (1), and Einat Shneor (1) (1) Department of Optometry and Vision Science, Hadassah Academic College, Jerusalem, Israel. (2) School of Optometry, The Hong Kong polytechnic University, Hong Kong, China.	**54**
09:40-09:50 AC	**IL-17 AND VEGF IN OCULAR SURFACE EPITHELIAL DISORDERS** Basel Jabarin, Abraham Solomon, Radgonde Amer. Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem.	**55**

09:50-10:00 **PPM1A REGULATES ANGIOGENESIS IN MOUSE CORNEA THROUGH P38** **56**

AC

Dvashi Z. (1), Jacobi H. (1), Shohat M. (1), Ben-Meir D. (1), Ashery-Padan R. (2), Rosner M. (3), Solomon A.S. (3) and Sara Lavi (1).
(1) Department of Cell Research and Immunology, George S. Wise Faculty of Life Sciences, Tel Aviv University, Tel Aviv, Israel. (2) Human Genetics Faculty of Medicine Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.
(3) Goldschleger Eye Research Institute, Sheba Medical Center, Tel Hashomer, Israel.

10:00-10:10 **CLINICAL AND BIOCHEMICAL BENEFICIAL EFFECTS OF PROLONGED TREATMENT WITH THE MMP INHIBITOR, DOXYCYCLINE, FOLLOWING OCULAR CHEMICAL INJURY IN RABBITS** **57**

Vered Horwitz, Shlomit Dachir, Maayan Cohen, Hila Gutman, Liat Cohen, Eliezer Fishbine, Rachel Brandeis, Ariel Gore, Joseph Turetz, and Tamar Kadar.
Israel Institute for Biological Research.

10:10-10:20 **THE EXPRESSION OF TOLL-LIKE RECEPTORS ON HUMAN CORNEAL EPITHELIAL CELLS AND CONJUNCTIVAL FIBROBLASTS** **58**

AC

Gal Aviel (1), Nir Erdinest (1), Eli Moallem (2), Haim Ovadia (3), Abraham Solomon (1).
(1) Department of Ophthalmology, Hadassah University Hospital, Jerusalem, Israel.
(2) Department of Immunology, Hadassah University Hospital, Jerusalem, Israel.
(3) Department of Neurology, Hadassah University Hospital, Jerusalem, Israel.

10:20-10:30 **A NOVEL CORNEAL ANATOMY OBSERVED IN THE FLORIDA MANATEE** **59**

AC

Gil Ben-Shlomo (1), Dennis Brooks (2), Caryn Plummer (2), Kathleen Barrie (2), Don Samuelson (2)
(1) Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Iowa State University, United States of America. (2) Department of Small and Large Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, United States of America.

10:30-10:40 **THE INHIBITORY EFFECTS OF ALPHA-LINOLEIC ACID ON NITRIC OXIDE SECRETION BY HUMAN OCULAR SURFACE CELLS** **60**

AC

Noam Shohat, Nir Erdinest, Eli Moallem, Abraham Solomon.
Department of Ophthalmology Hadassah University Hospital Ein Karem, Jerusalem.

Poster viewing and Coffee 10:40–11:10

Session III - Retina 1 11:10–12:20

Moderators: Dr. Ygal Rotenstreich, Dr. Michaella Goldstein

12:00-12:10 **THE RELATIONSHIP BETWEEN LIGHT PERCEPTION AND PAIN PERCEPTION IN SIMULTANEOUS STIMULUS** **66**

Orit Ezra Nimni (1), Joseph R Ferencz (2), Gila Gilady (3), Isaac Glass (4).
(1) Meir Medical Center (currenly working at Sheba Medical Center). (2) Meir Medical Center. (3) Meir Medical Center. (4) Loewenstein Hospital Rehabilitation Center.

12:10-12:20 **RETINAL BREAKS IN SMALL GAUGE VITRECTOMY** **67**

Rita Ehrlich (1), Nadeem Ahmad (2), Philip Polkinghorne (2).
(1) Rabin Medical Center, Israel. (2) University of Auckland, New Zealand.

Session IV - Keynote Guest Lecture 1: 12:30–13:10

Prof. Anand Swaroop, PhD

Senior Investigator and Chief, Neurobiology-Neurodegeneration and Repair Laboratory (N-NRL)
National Eye Institute, NIH Bethesda, Maryland, USA

Title: How to make a photoreceptor? From basic biology to treatment paradigms

Lunch break and Poster viewing 13:10–14:10

Session V -Poster Presentations 2 14:10–15:10

Moderators: Prof. Jacob Pe'er, Dr. Tamar Ben-Yosef

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26. AC	**INFLAMMATORY EFFECTS OF CONTACT LENS MULTIPURPOSE SOLUTIONS ON HUMAN CORNEAL EPITHELIAL CELLS** Nir Erdinest (1), Abraham Solomon (1). (1) Department of Ophthalmology, Hadassah University Hospital, Jerusalem, Israel.	**69**

27. **REPEATABILITY AND INTRA-SESSION REPRODUCIBILITY OBTAINED BY THE SIRIUS ANTERIOR SEGMENT ANALYSIS SYSTEM** **70**

Muhannad Masoud (1), Irit Bahar (1,2,3).
(1) Ophthalmology Department, Rabin Medical Center, Petah-Tikva, Israel.
(2) Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel. (3) Assuta Optic Laser Center, Tel Aviv, Israel.

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Eitan Livny (1), Tami Livnat (2), Muhanad Masoud (3), Max Yakimov (4), Irit Bahar (1).
(1) Ophthalmology Department, Rabin Medical Center, Petach Tiqva, Israel.
(2) Ophthalmology Eye Lab, Felsenstein Institute, Rabin Medical Center, Petach Tiqva, Israel. (3) Ophthalmology Department, Ziv Medical Center, Safed, Israel.
(4) Pathology Department, Rabin Medical Center, Petach Tiqva, Israel.

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Adi Einan-Lifshitz, Izaac Avni, Shay Gotfroind, David Zadok.
Assaf Harofeh medical center.

30. AC **COMPARISON OF DIFFERENT CONTACT LENSES AND SURFACES AS CARRIERS FOR HUMAN CORNEAL LIMBAL EPITHELIAL CELLS** **73**

Noam Shohat, Nir Erdinest, Abraham Solomon.
Department of Ophthalmology Hadassah University Hospital Ein Karem, Jerusalem.

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Alexey Obolensky (1), Itzhak Hemo (1), Devora Marks-Ohana (1), Malka Sela (1), Esther Yamin (1), Israel Barzel (1), William W. Hauswirth (2), Samuel G. Jacobson (3), Dror Sharon (1), and Eyal Banin (1).
(1) Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel. (2) Department of Ophthalmology, University of Florida, Gainesville, FL. USA. (3) Scheie Eye Institute, University of Pennsylvania, Philadelphia, PA. USA.

38. **PREVALENCE OF MAJOR RISK POLYMORPHISMS FOR NEOVASCULAR AGE-RELATED MACULAR DEGENERATION IN ETHNIC SUBGROUPS COMPRISING THE ISRAELI POPULATION** **81**

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Gala Beykin-Khasin, Michelle Grunin, Shira Hagbi-Levi, Michal Lederman, Itay Chowers.
Hadassah - Hebrew University Medical Center.

39. **FAM161A PRODUCES TWO PROTEIN ISOFORMS WITH A DIFFERENTIAL RETINAL EXPRESSION PATTERN** **82**

Dikla Bandah-Rozenfeld (1), Alexey Obolensky (1), Eyal Banin (1), Shahar Frenkel (1), Adi Inbal (2), Dror Sharon (1).
(1) Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel. (2) Department of Medical Neurobiology, IMRIC, The Hebrew University-Hadassah Medical School, Jerusalem, Israel.

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Shirel Weiss (1,4), Eran Eyal (2), Mali Salmon-Divon (2), Nitza Goldenberg-Cohen (1,3,4), Yoram Cohen (4,5).
(1) The Krieger Eye Research Laboratory, Felsenstein Medical Research Center, Tel Aviv University, Petah Tiqwa. (2) Bioinformatics Laboratory, Cancer Research Center, Chaim Sheba Medical Center. (3) Pediatric Ophthalmology Unit, Schneider Children's Medical Center of Israel, Petach Tikva. (4) Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel. (5) Department of Gynecology, The Gynecology Research Laboratory, Sheba Medical Center, Tel Hashomer.

41. **SUB-RETINAL INJECTION OF HUMAN ADULT STEM CELLS PRESERVES ERG RESPONSE IN RCS RATS** **84**

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(1) Sheba Medical Center, Goldschleger Eye Research Institute (2) Tel-Aviv University. (3) Sheba Medical Center, Cancer Reserch Center. (4) Sheba Medical Center, Hematology Division.

42. **THE EFFECT OF INTRAOCULAR OR SYSTEMIC INJECTION OF REVATIO (SILDENAFIL) ON MOUSE OCULAR BLOOD VESSELS AND NEURONS** **85**

Cornelius Nasser (2), Bat-Chen R. Avraham-Lubin (1,4), Mark Vieyra (4), Dana Morzaev (1,4), Shirel Weiss (1,4), David Zadok (2), and Nitza Goldenberg-Cohen (1,3,4).
(1) The Krieger Eye Research Laboratory, Felsenstein Medical Research Center. (2) Ophthalmology Department, Assaf Harofe, Zrifin. (3) Pediatric Unit, Ophthalmology Department, Schneider Children's Medical Center of Israel, Petach Tikva, Israel. (4) Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv.

Awards and ISVER update 15:10-15:30

Session VI - Genetics A 15:30-16:00

Moderators: Prof. Ron Ofri, Dr. Eran Pras

Time	Title	Page
15:10-15:20 AC	**A HOMOZYGOUS NULL MUTATION IN THE USH1C GENE CAUSES NON-SYNDROMIC AUTOSOMAL-RECESSIVE RETINITIS PIGMENTOSA** Samer Khateb (1), Lina Zelinger (1), Tamar Ben-Yosef (2), Saul Merin (1), Ornit Kristal-Shalit (3), Menahem Gross (4), Eyal Banin (1), and Dror Sharon (1). (1) Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem. (2) Genetics Department, Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa. (3) Department of Ophthalmology, Rabin Medical Center, Beilinson Campus, Tel Aviv. (4) Department of Otolaryngology - Head and Neck Surgery, Hadassah Hebrew-University Medical Center, Jerusalem	**91**
15:20-15:30	**GUCY2F ZEBRAFISH KNOCKDOWN - A MODEL FOR GUCY2D-RELATED LEBER CONGENITAL AMAUROSIS** Hadas Stiebel-Kalish (1,2,6), Ehud Reich* (2,6), Nir Rainy* (3), Gad Vatine (3), Yael Nisgav (4), Anna Tovar (5), Yoav Gothilf (3), and Michael Bach (7). (1) Neuro-Ophthalmology Unit, Department of Ophthalmology, Rabin Medical Center, Petah Tikva, Israel. (2) Sackler Faculty of Medicine, Tel Aviv University, Israel. (3) Department of Neurobiology, George S. Wise Faculty of Life Sciences, Tel Aviv University, Israel. (4) Felsenstein Medical Research Center Israel, Laboratory of Eye Research, Petah Tikva, Israel. (5) Department of Pathology, Rabin Medical Center, Petah Tikva, Israel. (6) Department of Ophthalmology, Rabin Medical Center, Petah Tikva, Israel. (7) Department of Ophthalmology, University of Freiburg, Killianstraße 5, 79106 Freiburg, Germany. *equal contribution second authors	**92**
15:30-15:40 AC	**PRCD IS A SECRETED PROTEIN WHICH INTERACTS WITH OTHER RETINAL DEGENERATION CAUSATIVE PROTEINS** Lital Remez, Ben Cohen, Judith M. Nevet, Tamar Ben-Yosef. Department of Genetics, Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel.	**93**

Poster viewing and Coffee 16:00-16:30

Session VII - Genetics B 16:30-17:20

Moderators: Prof. Ron Ofri, Dr. Eran Pras

Session VIII - Glaucoma/Neuro-ophthalmology 17:20 -18:40

Moderators: Dr. Yehoshua Almog, Prof. Michael Belkin

18:20-18:30 **DO HIGHER VISUAL AREAS HAVE A ROLE IN THE RECOVERY FROM OPTIC NEURITIS?** **105**

AC

Raz N. (1), Dotan S. (2), Chokron S. (3), Ben-Hur T. (1) and Levin N. (1).
(1) Department of Neurology, Hadassah Hebrew University Medical Center.
(2) Department of Ophthalmology, Hadassah Hebrew-University Medical Center.
(3) Service de Neurologie, Fondation Ophtalmologique Rothschild.

18:30-18:40 **NOVEL TECHNIQUE: A PUPILLOMETER-BASED OBJECTIVE CHROMATIC PERIMETRY** **106**

Ygal Rotenstreich (1), Alon Skaat (1), Andru Kolker (2), Shlomo Melamed (1), Michael Belkin (1)
(1) Sheba Medical Center, Goldschleger Eye Research Institute ,Israel. (2) George Washington University, Depratment of Opthalmology.

Dinner (optional)

Friday, March 16, 2012

Poster viewing and Coffee 08:00 - 08:30

Session IX - Cornea 2 08:30 - 09:50

Moderators: Dr. Irit Bahar, Dr. David Zadok

09:20-09:30 **LATE ONSET TOXIC ANTERIOR SEGMENT SYNDROME: INVESTIGATING A QUIET OUTBREAK** **112**
Shay Ofir (1). Coauthors: Ehud Assia (1), Yokrat Ton (2).
(1) Meir Medical Center, Kfar Saba, Israel. (2) Sir Charles Gairdner Hospital, Perth, Australia.

09:30-09:40 **POST OPERATIVE ENDOPHTHALMITIS PREVENTION BY DIFFERENT MOXIFLOXACIN PROPHYLAXIS PROTOCOLS** **113**
Oren S. Yovel, Guy Kleinmann.
Ophthalmology Department, Kaplan Medical Center.

09:40-09:50 **THE EFFECT OF FIBRIN SEALANT ON CORNEAL ENDOTHELIAL LAYER EX-VIVO** **114**
AC
Tsvi Sheleg, Amir Kuperman, Valery Bersudsky.
Western Galilee Hospital - Naharia, Faculty of Medicine in the Galilee, Bar Ilan University.

Session X - Keynote Guest Lecture 2: 09:50–10:20

Prof. Anand Swaroop, PhD
Senior Investigator and Chief, Neurobiology-Neurodegeneration and Repair Laboratory (N-NRL)
National Eye Institute, NIH Bethesda, Maryland, USA

Title: Cep290, photoreceptor cilium and retinal degeneration

Brunch and Posters 10:20 - 11:00

Session XI - Pediatrics and Visual Science 11:00 - 12:10

Moderators: Prof. Abraham Spierer, Dr. Moshe Snir

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11:00-11:10	**SPLIT EYES, SPLIT BRAIN AND SPLIT ATTENTION IN THE COMMON CHAMELEON**	**115**

Hadas Ketter Katz (1), and Gadi Katzir (2,3).
(1) Department of Neurobiology and Ethology, University of Haifa, Mount Carmel, Haifa 31905. (2) Department of Evolutionary and Environmental Biology, University of Haifa, Haifa 31905. (3) Department of Marine Biology, University of Haifa, Haifa 31905.

11:10-11:20 **AMBIENT LIGHT INTENSITY OF FLUORESCENT VERSUS INCANDESCENT LIGHT AND THE EMMETROPIZATION PROCESS OF THE CHICK'S EYE.** **116**

Yuval Cohen (1), Richard A Stone (2), Arieh S Solomon (1).
(1) Goldschleger Eye Research Institute, Tel Aviv University, 52621 Tel Hashomer, Israel. (2) Department of Ophthalmology, University of Pennsylvania School of Medicine, Scheie Eye Institute, Philadelphia, PA, USA.

11:20-11:30 **VISUO-MOTOR "STATION-KEEPING" AND LATERALIZED DETOUR BEHAVIOUR IN THE COMMON CHAMELEON** **117**

Avichai Lustig
Dept. of Neurobiology & Ethology, University of Haifa, Haifa 31905

11:30-11:40 **LATE PROPRANOLOL TREATMENT OF INFANTILE PERIOCULR CAPILLARY HEMANGIOMA BEYOND PROLIFERATIVE STAGE: FUNCTIONAL AND STRUCTURAL CHANGES** **118**

Moshe Snir* (1,2,4), Ehud Reich* (3,4), Alex Zvulunov (2), Ruth Siegel-Axer (3,4), Ronit Friling (1,4), Nitza Goldenberg-Cohen (1,4), Yonina Ron (1), Dan Ben-Amitai (2,4).
(1) Units of Pediatric Ophthalmology and (2) Pediatric Dermatology, Schneider Children's Medical Center, Petah Tikva. (3) Department of Ophthalmology, Rabin Medical Center, Beilinson Campus, Petah Tikva. (4) Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv; Israel.
*The first two authors contributed equally to this work

11:40-11:50 **HIGH MYOPIA CAUSED BY A MUTATION IN LEPREL1, ENCODING PROLYL 3-HYDROXYLASE 2** **119**

Shikma Mordechai (1,5), Libe Gradstein* (2,5), Annika Pasanen (3), Rivka Ofir (1), Khalil El Amour (4), Jaime Levy (2), Nadav Belfair (2), Tova Lifshitz (2), Sara Joshua (1), Ginat Narkis (1,4), Khalil Elbedour (4), Johanna Myllyharju (3), Ohad S. Birk (1,4).
(1) The Morris Kahn Laboratory of Human Genetics, National Institute for Biotechnology in the Negev, Ben Gurion University. (2) Department of Ophthalmology, Soroka Medical Center and Clalit Health Services, Faculty of Health Sciences, Ben-Gurion University. (3) Biocenter Oulu and Oulu Centre for Cell-Matrix Research, Department of Medical Biochemistry and Molecular Biology, University of Oulu, Finland. (4) Genetics Institute, Soroka Medical Center. (5) SM and LG contributed equally to this study.
*Presenting author

11:50-12:00 **THE EFFICACY OF TINTED CONTACT LENSES IMPROVING PHOTOPHOBIA AND VISUAL FUNCTION IN PATIENTS SUFFERING FROM LOW VISION** **120**

Tatiana Florescu Sebok (1,2), Boris Severinsky (1), Veronica Tzur (2), Claudia Yahalom (1,2).
(1) Ophthalmology Department, Hadassah- Hebrew University Medical Center, Jerusalem, Israel. (2) Michaelson Institute for the rehabilitation of vision, Hadassah-Hebrew University Medical Center, Jerusalem, Israel.

12:00-12:10 **HANG-BACK VERSUS CONVENTIONAL MEDIAL RECTUS RECESSION FOR THE CORRECTION OF INFANTILE ESOTROPIA** **121**

Oriel Spierer (1), and Abraham Spierer (2).
(1) Ophthalmology Department, Tel-Aviv Sourasky Medical Center, Israel.
(2) Goldschleger Eye Institute, Sheba Medical Center, Tel-Hashomer, Israel.

Session XII - Retina 2 12:10 - 13:20

Moderators: Prof. Dov Weinberger, Dr. Ruth Ashery-Padan

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12:10-12:20 AC	**IN VITRO CONTROL OF AN OPTOGENETIC NEURAL PROSTHETIC FOR A BLIND RETINA**	**122**

Reutsky-Gefen I., Tsur L. and Shoham S.
Faculty of Biomedical Engineering, Technion - Israel Institute of Technology, Haifa, Israel.

12:20-12:30 AC **THE FUNCTIONAL ROLE OF CONTACTIN ASSOCIATED PROTEIN IN THE MOUSE RETINA** **123**

S. Sandalon (1), V. Bar (2), E. Peles (2), R. Ofri (1).
(1) Koret School of Veterinary Medicine, The R.H. Smith Faculty of Agriculture, Food and Environment, The Hebrew University of Jerusalem. (2) Molecular Cell Biology, Weizmann Institute of Science, Rehovot, Israel.

12:30-12:40 **ROLES FOR PAX6 IN THE MELANOGENESIS OF THE RETINAL PIGMENTED EPITHELIUM IN MICE** **124**

Shauli Raviv (1), Kapil Bharti (2), Chen Farhy(1), Heinz Arnheiter (2), and Ruth Ashery-Padan (1).
(1) Department of Human Molecular Genetics and Biochemistry, Sackler School of Medicine, Tel-Aviv University, Israel. (2) Mammalian Development Section, National Institute of Neurological Disorders and Stroke, National Institute of Health, Bethesda, MD, USA.

12:40-12:50 **THE ROLES OF PAX6 DURING LATE STAGES OF MAMMALIAN RETINOGENESIS** **125**

Lena Remizova, Ruth Ashery-Padan.
Department of Human Molecular Genetics and Biochemistry, Sackler School of Medicine, Tel Aviv University.

12:50-13:00 **THROMBIN AND ACTIVATED PROTEIN C (APC) INDUCE OPPOSITE EFFECTS ON RPE PERMEABILITY** **126**

AC

Omer Bialer, Tami Livnat, Yael Nisgav, Rima Dardik Dov Weinberger.
Department of Ophthalmology and Laboratory of Eye Research, Felsenstein Medical Research Center, (FMRC) Rabin Medical Center, Petah Tiqwa, Israel; Tel-Aviv University School of Medicine, Tel-Aviv, Israel.

13:00-13:10 **A NEW TECHNIQUE FOR EXPERIMENTAL CREATION OF CHOROIDAL NEOVASCULARIZATION (CNV) IN PIGMENTED MICE USING INDIRECT DIODE LASER** **127**

AC

Elite Bor (1,2), Tami Livnat (3), Yael Nisgav (3), Dov Weinberger (1,2).
(1) Department of Ophthalmology, Rabin Medical Center (RMC), Petach Tikva, Israel. (2) Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel.
(3) Laboratory of Eye Research, Felsenstein Medical Research Center (FMRC), Petach Tikva, Israel.

13:10-13:20 **PREVALENCE AND RISK FACTORS FOR CHOROIDAL NEVI USING OPTOS SCANNING LASER OPHTHALMOSCOPE** **128**

AC

Ariela Gordon-Shaag (1), Simon Barnard (1,2), Liat Gantz (1), Rima Pinchasov (1), Zoya Gosman (1), Gabrielle Chiche (1), Elbaz Vanessa (1), Wolff Ruth (1), and Einat Shneor* (1).
(1) Department of Optometry, Hadassah Academic College, Jerusalem. (2) Institute of Optometry, London, YK.

Concluding Remarks: Prof. Eyal Banin 13:20 - 13:25

HO/05/09 A NOVEL DRUG CANDIDATE FOR ACCELERATED CORNEAL WOUND CLOSURE

Sagiv Y. (1), Lavie Y. (2), Solomon A. (3), Storovinsky O. (1), Benhamou M. (1), Brener E. (1), Hammer L. (1), Mandil Levin R. (1), Braiman Wiksman L. (1).
(1) HealOr Ltd., 3 Pekeris St., Rehovot 76702. (2) Harlan Biotech Israel Ltd, Rehovot, Israel.
(3) Department of Opthalmology, Sackler Faculty of Medicine,
Tel Aviv University.

Introduction and Purpose: Mechanical injury and inflammation of the cornea can cause severe loss of vision and blindness. Treatment involves antibiotics and anti inflammatory agents, however no drug promotes corneal re-epithelialization and wound closure. Our study examined the effect of HO/05/09, a drug containing a specific PKCα inhibitor (MPDY-1), that promotes epithelial closure and reduces inflammation, on corneal healing.

Patients / Methods: Superficial mechanical and chemical corneal erosion models were used. Mechanical erosion of the corneal epithelium was performed on rabbit's eyes (6 per group), creating a central corneal erosion of 6 mm in diameter and 50 microns depth. Eyes were treated for 3 days with HO/05/09 or Balanced Salt Solution as control. Chemically induced injury in rabbit and mice eyes (6-8 per group) were done by Alkali burn using NaOH or silver nitrate applicator stick (respectively). Eyes were treated for 7 days with HO/05/09, Strerodex & Oflox (standard of care), or left untreated.

Results: In the mechanical model, HO/05/09 reduced the time to full healing by 30-40%, as assessed by fluorescein staining. At 48 hours post wounding, 60% of treated wounds were fully closed versus none in the control group. 60 hours post wounding, all treated wounds exhibited full closure compared to 30% in control. Similar results were obtained in the chemical burn models. In rabbit eyes, 48 hours post wounding, 60% of wounds demonstrated 98% closure in the HO/05/09-treated group versus none in control. A slit lamp morphological assessment demonstrated reduced inflammatory response of HO/05/09, as expressed by a decrease in corneal edema, conjunctival erythema and edema, and discharge. In the mice model, at 7 days post wounding, 60% of wounds were closed in the HO/05/09 group, versus only 20% in the control group. Histological analysis reveals less infiltrating cells and reduced edema in HO/05/09 treated eyes, further demonstrating the drug anti-inflammatory activity.

Conclusions: HO/05/09 accelerates re-epithelialization in eye injuries. It reduces inflammation and "time to heal", and significantly protecting the eye from infections. HO/05/09 is a novel ophthalmic drug that promotes rapid and effective healing in cases such as corneal injuries and post surgery, and may benefit chronic conditions such as dry eye.

PHENOTYPIC CHARACTERIZATION OF RABBIT LIMBAL EPITHELIAL CELL EXPANSION ON CONTACT LENSES WITH A 3T3 FEEDER LAYER

Gore A., Horwitz V., Gutman H., Tveria L., Dachir S., Kadar T.
Department of Pharmacology, Israel Institute for Biological Research, Ness- Ziona, Israel.

Introduction and Purpose: Limbal epithelial cell sheets co-cultivated with 3T3 feeder layer are used in order to promote corneal reconstruction following limbal epithelial stem cell deficiency (LSCD). To date, stem cell cultivated sheets are transferred to damaged ocular surfaces mainly by using biological carriers such as collagen, fibrin and amniotic membranes or by using temperature-responsive polymers as carriers. The aim of the present study was to evaluate the potential use of contact lenses (CL) as a carrier of limbal cells grown on a feeder layer. This novel method may provide a cheap, available, easy handling and non-immunogenic carrier substrate of the engineered construct.

Patients / Methods: Limbal or corneal epithelial cells were isolated from rabbit cornea and cultured with or without 3T3 fibroblast cell line in plastic wells or on CL. Positive stem cell markers p63, p63α and ABCG2 and negative markers CK3, CK19 were used to characterize the culture phenotype. Colony forming efficacy (CFE) assay was performed in order to evaluate the percent of stem cells in corneal and limbal tissues.

Results: Expression of the stem cell markers p63, p63α, ABCG2 with no stain of CK3 was observed in cultures of limbal cells with 3T3 feeder layer opposed to corneal culture or limbal culture with no feeder layer. In addition, a higher percentage of colonies were observed in limbal cultures compared to corneal cultures. No difference in colony percentage was observed between the four limbal regions examined. Finally, a proliferation and migration of single seeded limbal cells were observed on contact lenses with 3T3 feeder layer, showing retention of viable stem and/or progenitor cell population.

Conclusions: Cultivation of limbal cells with 3T3 fibroblasts on the simple handling CL carrier, showed a proliferation and preservation of stem and/or progenitor cells. This technique may provide a non-immunogenic, simple and useful carrier for transferring stem cells to ocular surface of LSCD patients, reconstructing ocular surface.

THE ANTIBACTERIAL EFFECTIVENESS OF ULTRAVIOLET A/RIBOFLAVIN CORNEAL CROSS-LINKING IN DIFFERENT PATHOGENIC INFECTIOUS KERATITIS

Alon Skaat, Yakov Goldich, David Versano,Yoav Berger, Orit Ezra-Nimni, David Zadok, Irina S. Barequet.
(1) Goldschleger Eye Institute, Sheba Medical Center, Tel Aviv University, Tel Hashomer, Israel. (2) Department of Ophthalmology, Assaf Harofe Medical Center, Zerifin, Israel. (3) Department of Ophthalmology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel.

Introduction and Purpose: To describe the antibacterial effect of Ultraviolet A/Riboflavin Collagen Cross-linking (CXL) in cases of severe infectious keratitis unresponsive to medical treatment.

Methods: Retrospective analysis of interventional case series. Five eyes of five patients with severe infectious keratitis, which were all refractive to multi-drug conventional therapy, were treated with corneal CXL. The procedure was conducted according to the standardized protocol of CXL for keratoconus. Best spectacle-corrected visual acuity and clinical outcomes were evaluated before and during the follow-up period.

Results: Four of five patients showed a rapid reduction in their symptoms and decreased ulcer size after the CXL treatment. Signs of infection and inflammation mostly resolved within 1-2 weeks after the treatment. One patient continued to deteriorate despite the CXL and penetrating keratoplasty was performed. No complications were described during or in the follow up period.

Conclusions: Ultraviolet A-Riboflavin corneal collagen CXL has a positive effect of and on refractory infectious keratitis with a satisfactory final visual outcome. The treatment seems to be safe and effective and should be considered even earlier as part of the first line therapy in severe cases of infectious keratitis or ulceration.

THE L80 WAVE+ KERATOMETER: A VALIDITY STUDY

Einat Shneor (1), Michel Millodot (2), Meira Zyroff (1), and Ariela Gordon-Shaag (1).
(1) Department of Optometry and Vision Science, Hadassah Academic College, Jerusalem, Israel. (2) School of Optometry, The Hong Kong Polytechnic University, Hong Kong, China.

Introduction and Purpose: A clinical evaluation of the L80 videokeratographer (Visionix Luneau, Chartres, France) was performed to assess its validity and repeatability compared with a traditional Bausch and Lomb (B & L) keratometer. The keratometric function of the L80 videokeratographer, a new instrument, is based on the Placido disc. The instrument can also measure refraction, corneal topography and higher-order aberrations.

Patients / Methods: 87 right eyes of 87 subjects, (mean age 23.72 ± 3.62 years, 70 women and 17 men), participated in this study. Corneal curvature was measured using the L80 instrument by one practitioner and by a different practitioner with the manual B & L keratometer. Intratest (measured at the same time) and intertest (measured on different days) repeatability was also assessed on 24 subjects.

Results: Corneal curvature was found to be statistically different in both the horizontal meridian and in the vertical meridian ($p < 0.001$), with the L80 providing a slightly steeper bias of 0.05mm and 0.07mm, respectively than the Bausch and Lomb keratometer. Intratest repeatability was the same for both instruments. Intertest repeatability was better for the L80 videokeratographer than the B & L keratometer and showed no significant difference between the two sessions.

Conclusions: The L80 videokeratographer is a reliable objective instrument comparable to other autokeratometers which, in addition combines many other useful clinical features. It produced somewhat steeper radii of curvature than the Bausch and Lomb keratometer, although an offset incorporated into the instrument could render the two instruments interchangeable.

ANTI-INFLAMMATORY EFFECTS OF ALPHA LINOLENIC ACID ON HUMAN CORNEAL EPITHELIAL CELLS VIA NUCLEAR FACTOR-KB (NF-KB) AND PEROXISOME PROLIFERATOR-ACTIVATED RECEPTORS-ALPHA (PPARA) AND GAMMA (PPARΓ) PATHWAYS

Nir Erdinest (1), Or Shmueli (1), Haim Ovadia (2), Abraham Solomon (1).
(1) Department of Ophthalmology, Hadassah University Hospital, Jerusalem, Israel.(2) Department of Neurology, Hadassah University Hospital, Jerusalem, Israel.

Purpose: Recent studies showed that systemic polyunsaturated fatty acids (PUFAs) may improve the symptoms of dry eye syndrome due to their anti-inflammatory effects. We have evaluated the anti-inflammatory effects of PUFAs and characterized their mechanism of action on human corneal epithelial (HCE) cells in-vitro.

Methods: HCE cells were incubated for 3 hours with different concentrations of three PUFAs: Alpha-linolenic acid (ALA), Gamma-linolenic acid (GLA) and Linolenic acid (LA). Oleic acid (OA) and Dexamethasone (DM) served as negative and positive controls, respectively. Cells were stimulated with either polyinosinic:polycytidylic acid (poly I:C) or lipopolysaccharide (LPS) complex. The protein contents levels of Interleukin (IL)-6, IL-8, IL-1β, Tumor necrosis factor-α (TNF-α) were examined with multiplex fluorescent bead immunoassay and the mRNA expression of IL-6, IL-8, IL-1β, TNF-α, Inhibitory factor-κBα (I-κBα), Peroxisome proliferator-activated receptors alpha (PPARα) and gamma (PPARγ) were examined by real time-PCR,

Results: The protein contents and mRNA expression levels of IL-6, IL-8, IL-1β and TNF-α were significantly increased after stimulation with LPS or poly I:C. These levels were dramatically decreased following treatment with ALA as compared to OA or bovine serum albumin ($p < 0.05$). HCE cells incubation with LPS complex stimulation elicited up to 4.5-fold higher levels of IL-6 ($P<0.001$), 4.35-fold IL-1β ($P<0.001$), 20.9-fold TNFα ($P<0.001$) and 2.5-fold IL-8 ($P<0.001$) compared to cells incubated in medium alone. Following treatment with ALA, a significant decrease was demonstrated in the protein content of TNF-α to 23.81% ($P<0.001$), IL-6 to 46.71% ($P<0.001$), IL-1β to 20.86% ($P<0.05$) and IL-8 to 52.21% ($P<0.001$). Similar results were demonstrated at the mRNA level, as measured by real time PCR. The anti-inflammatory effects of ALA were similar to those of DM for all of the pro-inflammatory cytokines. The ALA inhibition of the LPS-induced pro-inflammatory cytokines was associated with a significant reduction of the mRNA expression level of I-κBα and elevation of the mRNA expression level of PPARα and PPARγ.

Conclusions: ALA may serve as a potent anti-inflammatory agent in ocular surface inflammation, as evaluated in cultured HCE. The anti-inflammatory effects of ALA are comparable to those of the DM, and are mediated through nuclear factor κB (NF-κB, Peroxisome proliferator-activated receptors alpha (PPARα) and gamma (PPARγ).

BIOMETRIC PARAMETERS BEFORE AND AFTER PUPIL DILATATION

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Introduction: Intraocular lens (IOL) power calculation using the IOL Master requires fixation. Mydriasis may cause loss of fixation to some degree. The aim of this study was to evaluate biometric parameters in IOL Master examination before and after mydriasis.

Patients / Methods: Patients were pre-cataract surgery and underwent an IOL master examination pre and post mydriasis . Exclusion criteria were mydriasis >5.5 mm, macular edema or hemorrhage, corneal pathology influencing keratometric (K) values, eyes post trauma/intraocular surgery, inability to fixate and best corrected visual acuity <20/100 before dilatation.

Results: 101 eyes were included (73 patients). The average ±Standard deviation (SD) axial length (AL) and K value differences (pre - post dilatation) were -0.0011 ±0.03901mm and -0.028 ±0.5647 diopters (D) respectively. Right eyes were found with an average ±SD AL and K values difference of -0.0077 ±0.037 mm and 0.002 ±0.169D respectively. Left eyes' average AL and K values difference was 0.005±0.04 mm and -0.056 ±0.772 D respectively. Eyes of males had an average ±SD AL and K values difference of -0.0055 ±0.055 mm and-0.0828 ±0.8566 D respectively, while in females average AL and K values difference were0.0018 ±0.0226 mm and 0.009 ±0.205D respectively.

Conclusions: The average AL differences in our study were<0.1 mm and the average K values <1 in all groups, thus not clinically significant. This implies that an IOL Master examination can be done pre and post mydriasis without a clinically significant change in the calculated IOL power.

OBJECTIVE VS. SUBJECTIVE ACCOMMODATION MEASUREMENTS USING THE L- 80 WAVE+

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Introduction and Purpose: The standard ways of measuring amplitude of accommodation (AA) use subjective methods such as Push-Up (PU) and the Push-Away (PA). Visionix (Luneau, Chartres, France) has recently developed an instrument to objectively measure accommodation using wavefront technology. We tested the precision of the L-80 wave+ accommodation program, using different fixation targets, and its validity by comparing it to the PU and PA methods.

Patients / Methods: Accommodation was measured monocularly on 35 non-presbyopic subjects, with the L-80 wave+ using a non-accommodative (balloon) and an accommodative (the letter E) target and by the Push-Up (PU) and the PA tests. Each test was carried out three times and the average value was used for analysis. The precision and validity were calculated using the correlation-analysis and t-test.

Results: The AA found with the L-80 wave+ was significantly lower than PU or PA ($p< 0.0001$, for both). However, the accommodative target yielded an AA that was closer to the PA method (9.82±0.47D, 9.06±0.44D, 7.59±0.66D, 6.95±1.01D for PU, PA, L-80 non-accommodative target, L-80 accommodative target, respectively). A simultaneous correlation-analysis showed that PU and PA were well correlated with one another ($R=0.82$), however, neither subjective method correlated well with the L-80 ($R= 0.24$ and 0.35 for PU and PA respectively). All methods for measuring accommodation were found to be repeatable (0.47±0.38, 0.44±0.41, 1.01±2.1, 0.66±0.7 for PU, PA, L-80 balloon, L-80 accommodative target, respectively). There was a good positive correlation between the results of the L-80 between the two sessions ($R=0.83$).

Conclusions: The L-80 does not give results that are statistically similar to PA, the gold standard for measuring accommodation. Although it should be noted, that the true value of AA may not be measured by the subjective tests. Further research is essential in order to evaluate the influence of accommodative target on objective accommodative measurements.

HOLOGRAPHIC PHOTO-ABSORBER INDUCED NEURO-THERMAL STIMULATION (PAINTS)

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Introduction and Purpose: Retinal prostheses for people with degenerative diseases of the outer retina could rely on direct activation of the surviving retinal neurons. Direct activation, to date, has relied on electric activation; a method lacking high spatial specificity. More recently methods for photo-stimulation, such as optogenetics and low intensity mid-IR laser pulses have been introduced as a safe and minimally intrusive alternative. Photo-stimulation methods combined with advanced projection systems can result in high resolution activation of retinal neurons. Here we present a new photo-stimulation method based on photo-thermal excitation of exogenous photo-absorbers, an approach tentatively termed Photo Absorber Induced Neural-Thermal Stimulation or PAINTS

Patients / Methods: We dispersed micron-scale carbon particles in several acute and cultured neuronal preparations, including a retina preparation where they were dispersed next to the ganglion cells. To induce thermal activation of the neurons, high intensity light patterns were directed onto particles in the vicinity of the cells using a computer based holographic system developed by our group. To characterize the properties of the induced thermal transients, experiments using the temperature sensitive dye RU were performed and complemented by theoretical analysis. The resulting neural activity was recorded using fluorescent calcium indicators imaging (OGB-AM and Fluo-4-AM and Gcamp3).

Results: Patterned illumination absorbed by the carbon-based photo-absorbers, yielded in rapid thermal transients with a well-defined and highly-localized dynamics which was visualized using temperature-sensitive dyes, and matched theoretical predictions. Using calcium indicators imaging, we observed that thermal transients repeatedly excited neurons in the close vicinity of the absorbers, when the pulse power exceeded a certain threshold.

Conclusions: The new photo-stimulation method presented here is capable of repeatedly stimulating neurons in a highly specific manner in both space and time. This method can be combined with advanced projection systems and may prove to be a powerful technology towards the development of optical retinal neuro-prosthetics.

REGENERATIVE RESPONSE OF OPTIC NERVE AXONS WHILE USING A SPECIFICALLY DESIGNED HYDROGEL

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Introduction and Purpose: To provide a more permissive environment for axonal regeneration following injury to the optic nerve. Regeneration of the CNS in mammals is limited by the generation of physical and chemical inhibitory barriers that are formed following injury and the absence of positive cues that elicit and guide repair. Hydrogels are considered to be good materials for CNS repair because of high oxygen and nutrient permeability and low interfacial tensions. They also offer 3D scaffolds to support the growth of cells and cell processes. Hyaluronic acid (HA) is a natural polymer used as a building block for hydrogel formation. This polymer is appealing for medical use owing to its similarity to the natural extracellular matrix (ECM), which allows cell adhesion while maintaining very good biocompatible and biodegradable qualities. Peptide-based scaffolds represent another very important biocompatible material that can support cell growth.

Methods: Hyaluronic acid (HA) based composite containing self assembled, small peptide nano-tubes (FmocFF) was selected for the in vivo study based on its net-like 3D structure. Cell culture analysis showed that the composite was non-toxic and allowed cell attachment. The right ONs of adult rats were completely transected while sparing the vasculature and the meninges. The HA-FmocFF composite was implanted at the lesion site. The control group was implanted with 2% unmixed HA. Two months after injury, the optic nerves were isolated and prepared for immuno-histochemical analysis. Longitudinal sections were labeled with GAP43 antibody to determine axonal regeneration.

Results: The HA-FmocFF composite was found to be non-toxic and biocompatible to the optic nerve, with no evidence of degeneration. The control group exhibited no axonal regeneration past the scar area. In the experimental group, 5 out of 7 rats showed GAP43 staining beyond the scar, indicating axonal regeneration of retinal ganglion cells.

Conclusions: Mammals require special modulations of the neuronal environment to enable partial regeneration. Such modulation can be achieved with specifically designed hydrogels, which present the regenerating axons with a relatively clear pathway and net-like 3D scaffold to maintain their progress beyond the lesion site.

TLR4 KNOCK-OUT MICE ARE RESISTANT TO OPTIC NERVE CRUSH DAMAGE

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Introduction: Aim: The purpose of the study is to investigate the role of inflammation induced damage following optic nerve crush (ONC) in knockout (KO) mice for toll like receptor 4 (TLR4 KO) gene.

Methods: ONC was induced in 14 TLR4 KO and 14 C57BL6 wild type (WT) mice, by compressing the optic nerve immediately posterior to the globe. Histology and molecular analysis for inflammatory, hypoxic and apoptotic gene expression was performed on days 1,3 and 21. Histological sections of the retina and ON were analyzed to measure the damage and RGCs loss; mRNA expression levels of THY-1 were also analyzed on day 21 using quantitative real-time PCR.

Results: In the optic nerves, molecular analysis revealed the increase of TNF-α (9.0, 2.1) and reduction of CD45 (0.12, 1.23) and GFAP (0.60, 0.25) on day 1 in the TLR4 KO mice and WT controls, respectively (NS). On day 3, CD45 reverted to baseline while GFAP remained low. On day 21, baseline levels of expression of GFAP, CD45 and TNF-α in the TLR4 KO group were noted, while increased levels were measured in the WT (12.3, 11.6, and 7.4, respectively). Histological analysis showed mean 50% cell loss in ONC-injured retina of the WT while only 20% loss was detected in the TLR4 KO mice. TUNEL staining revealed the reduced apoptosis in the retina and optic nerve 1 and 3 days post injury, in the TLR4 KO compared to the WT mice.

Conclusions: Inflammatory reaction plays a role in ONC damage, as shown in the WT. Reduced levels of inflammation and improved RGCs preservation was observed in TLR4 KO mice. However, the increased expression mightαTNF- bypass the CD45 inflammatory pathway, leading to the 20% RGC apoptosis and loss.

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ISOTOPIC CO2 LASER ASSISTED SCLERECTOMY SURGERY FOR TREATING GLAUCOMA

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Introduction: BACKGROUND: CO2 Laser Assisted Sclerectomy Surgery (CLASS) is a novel filtration surgery for treating glaucoma. Its goal is to reduce the Intra Ocular Pressure (IOP) by enhancing the drainage of the Aqueous Humour. The technique is based on the unique characteristics of the CO2 laser (wavelength - 10.60 μm), which is highly absorbed by water and effectively ablates dry tissues. Collateral thermal damage to adjacent un-ablated intact tissue may include tissue scarring, which jeopardize the procedure efficacy.

Purpose: To test the feasibility of utilizing an isotopic 13C16O2 laser (wavelength - 11.15 μm) for the CLASS procedure. The working hypothesis was that isotopic laser will decrease the depth of the residually coagulated layer, due to this laser higher absorption coefficient in water, 50% higher than standard 12C16O2 laser.

Methods: Standard and isotopic CO2 lasers were used to comparatively ablate scleral tissue of ex-vivo pig and human cadaver eyes. In each eye, 5 and 10 laser applications of each laser were performed on one area using the IOTiMateTM Beam Manipulating System (BMS). Specimens were stained with Hematoxylin & Eosin for histological evaluation and the thickness of the coagulated tissue was measured and compared.

Results: The coagulation depth was significantly lower using the isotopic CO2 laser, as compared to the standard CO2 laser, both for pig and human eyes models undergoing 5 or 10 laser applications. Mean overall difference was 14.1±4.4% (range 10.2-20.2%; $p<0.05$).

Conclusions: Using the isotopic CO2 laser, tissue coagulation is significantly lower than using standard CO2 laser, without a significant difference in the ablation depth. This may help reduce residual tissue damage and provide an added value to increasing safety of the procedure

PHOSPHOPROTEOMICS OF AXONAL SIGNALING IN GLAUCOMA

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Purpose: To identify retrograde axonal signaling mechanisms activated in glaucoma using phosphoproteomics.

Methods: Experimental glaucoma was induced unilaterally in 120 Wistar rats using the translimbal photocoagulation laser model. Optic nerves and retinas were removed separately from control and IOP-elevated eyes for phosphoproteomic characterization 5 days after the induction of glaucoma. Protein samples were reduced, alkylated and digested by trypsin. To quantify differences in the phosphorylation levels between the samples peptides were labeled with ITRAQ and enriched for phosphopeptides.. Labeled phosphopeptides were fractionated by strong cation exchange chromatography and analyzed by mass spectrometry. Transpath database (implemented in ExPlain) was used to construct signaling networks supported by the differentially phosphorylated protein in retina and optic nerve.

Results: We have identified 38 and 60 differentially phosphorylated proteins in glaucomatous retinas and optic nerves, respectively. Glaucoma induced increase in the phosphorylation levels of more than 2/3 of differentially phosphorylated proteins (30 in retina, 49 in optic nerve), eight of them were identified both in retinas and in optic nerves (STAT3, Erk1, Erk2, Hsp27, Nestin, Palladin, Protein DEK and Protein Ag2).
Bioinformatics analysis identified 4 molecules (Stat3, Erk1, Erk2 and PKCdelta) that are involved in common signaling pathways. In glaucoma the increase in the phosphorylation levels in the retinas and optic nerves were 2.6 and 2.2 fold for Erk1, 2.32 and 2.03fold for Erk2, 3.34 and 2.49 fold for STAT3 respectively, as compared to control samples.
GO annotation analysis (DAVID bioinformatics) revealed that most of the differentially phosphorylated proteins are involved in regulation of cytoskeleton (microtubule, actin, and neurofilament cytoskeleton), cellular transport and phosphorylation.

Conclusions: Using quantitative phosphoproteomic approach we were able to identify almost 100 differentially phosphorylated proteins in glaucomatous retinas and optic nerves. Bioinformatics analysis suggests that phosphorylated STAT3, Erk1, Erk2 and PKCdelta are important molecules involved in common signaling pathways affected by glaucoma.

GENETIC VARIATIONS IN DIABETIC PATIENTS WITH PROLIFERATIVE AND NON-PROLIFERATIVE RETINOPATHY

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Introduction and Purpose: Type 2 diabetes mellitus is thought to develop from an interaction between environmental and genetic factors. A recent study suggested that single-nucleotide polymorphisms (SNPs) in 16 genes are associated with the risk of developing type 2 diabetes or impaired beta-cell function. We examined whether these genetic factors could also predict progression to proliferative retinopathy in diabetic patients.

Patients / Methods: In this study we enrolled 197 subjects with documented medical history, clinical and fundus exam. Of them, 51 were healthy adults, 130 were diabetic patients with normal to mild non-proliferative diabetic retinopathy (NPDR) and 16 were diagnosed with proliferative diabetic retinopathy (PDR). DNA was extracted from blood samples, and genetic analysis was performed using a chip-based matrix-assisted laser desorption-time-of-flight (MALDI-TOF) mass spectrometer. We genotyped 16 single-SNPs in the following genes: TCF7L2, PPARG, FTO, KCNJ11, NOTCH2, WFS1, CDKAL1, IGF2BP2, SLC30A8, JAZF1, HHEX, CDKN2, TSPAN8, ADAMTS9, CDC123, THADA.

Results: Variants in 2 genes (NOTCH2 and WFS1) were significantly associated with PDR when compared to controls. A variant in the FTO gene was significantly associated with NPDR when compared to controls. No significant differences in variants could be detected between diabetic patients with or without retinopathy (PDR and NPDR).

Conclusions: SNPs in NOTCH2, WFS1 and FTO genes may play a role in prediction of progression to PDR and NPDR respectively. However, results in the other genes analyzed were not in line with previous observations, as variations in the other genes only had a slight effect on the ability to predict the development of type 2 diabetes. Further investigation and clinical correlation are needed to confirm our results.

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MUTATIONS IN A TRANSIENT RECEPTOR POTENTIAL CHANNEL GENE (TRPM1) ARE A MAJOR CAUSE OF CSNB IN THE ISRAELI POPULATION

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Introduction and Purpose: As part of our on-going effort to characterize the genetic causes of inherited retinal diseases in the Israeli population, we have recruited patients affected with congenital stationary night blindness (CSNB). The aim of this study was to identify genes causing autosomal recessive (AR) CSNB using homozygosity..

Patients / Methods: Clinical analysis included family history, ocular examination, full-field electroretinography (ERG), and funduscopy. Molecular analysis included homozygosity mapping using whole genome Single Nucleotide Polymorphism (SNP) arrays. Direct Sanger sequencing was used to screen TRPM1 for mutations and to characterize deletion boundaries.

Results: We recruited for the study patients with CSNB from 46 families, in 23 of whom (46%) the inheritance pattern was autosomal recessive. Using the homozygosity mapping approach in nine of the families, we were able to identify a shared locus on chromosome 15. This locus harbored the TRPM1 gene, reported recently to cause CSNB and coat spotting patterns in Appaloosa horses. Mutation screening of this gene in patients with CSNB revealed two founder mutations in 18 out of 35 (51%) families with either recessive inheritance or isolates cases. A large genomic deletion (of over 36Kbp) covering 7 coding exons was found in seven Ashkenazi Jewish (AJ) families and a nonsense mutation was found in 11 Muslim families residing in East Jerusalem. Most patients were clinically diagnosed at a relatively young age, had high myopia, and low visual acuities. Only minimal funduscopic changes were evident.

Conclusions: TRP ion channel subunit genes were first defined in the Drosophila visual system. TRPM1 was reported to encode an ion channel that is located in the on bipolar cells of the neural retina and was initially associated with retinal disease in the Appaloosa horses. Recent studies on the European population indicated that TRPM1 mutations are a major cause of AR-CSNB. Our data provide another support this result and allow a relatively efficient genetic screening of the genetic cause of CSNB in the AJ and Muslim populations.

MUTATIONS IN CRB1 ARE A RELATIVELY COMMON CAUSE OF AUTOSOMAL RECESSIVE EARLY-ONSET RETINAL DEGENERATION IN THE ISRAELI AND PALESTINIAN POPULATIONS

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Introduction: The rate of consanguineous marriages in the Israeli and Palestinian populations is relatively high, leading to homozygosity in autosomal recessive (AR) disease-causing genes. This fact gives us the opportunity to use the homozygosity mapping approach as the main screening tool in our populations. The CRB1 (crumbs homolog 1) gene is expressed in the inner segment of mammalian photoreceptors and is responsible for various AR retinal phenotypes, mainly retinitis pigmentosa (RP), Leber congenital amaurosis (LCA). The purpose of this study was to evaluate the role of CRB1 in AR retinal diseases in the Israeli and Palestinian populations using mainly the homozygosity mapping approach.

Patients / Methods: Clinical analysis included family history, ocular examination, full-field electroretinography (ERG), and funduscopy. Molecular analysis included homozygosity mapping using whole genome Single Nucleotide Polymorphism (SNP) array and mutation analysis of the CRB1 open-reading-frame and flanking intronic sequences.

Results: Our lab recruited so far over 400 families with AR non syndromic retinal degenerations. Whole genome SNP array analysis was performed on 175 index cases, and in ten of these cases a large homozygous region containing CRB1 was identified. A subsequent CRB1 mutation analysis of these 10 families, followed by screening of candidate founder mutations in the whole cohort of patients, revealed a total of 13 mutations, 6 of which are novel, in 15 families. Nine of the mutations were family-specific and four were founder mutations identified in patients of Arab-Muslim origin and Jews originated from Iraq and Kurdistan. Interestingly, a null mutation on one of the two mutated CRB1 alleles is sufficient for a LCA diagnosis, whereas patients carrying missense mutations were diagnosed with either RP or LCA. The average age in which CRB1 patients were referred to ERG testing was relatively young (11 years, ranging from 6 months to 53 years). In 5 of the 28 CRB1 patients identifi ed in the study, 5 developed Coats like exudative vasculopathy.

Conclusions: Our data show that mutations in CRB1 are a relatively frequent cause of AR early-onset retinal degeneration in the Israeli and Palestinian populations (10% of LCA families), and usually cause severe retinal degeneration at an early age.

THE PAX6 GENE NETWORK REGULATING LENS DEVELOPMENT IN MAMMALS

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Introduction: Aim: The ocular lens provides an excellent model for investigating the transition from progenitor to differentiated cells. The transcription factor Pax6 plays an important role in eye development as it is essential for eye formation and is capable of inducing eye structures following misexpression in vertebrate and invertebrate species. Pax6 is essential for initiation of lens formation during the lens induction stage. During secondary lens fiber differentiation, Pax6 is required for cell-cycle exit and differentiation of lens progenitors.
We have recently conducted microarray analysis revealing genes with altered expression following somatic inactivation of Pax6 in the lens. The aim of this study is to decipher the gene network that mediates Pax6 activity during the transition of lens progenitors to differentiated lens fibers. The Notch signaling pathway was recently demonstrated to play key role in maintaining the lens epithelium and regulating the differentiation of lens fiber, therefore, specific emphasis will be given to Notch pathway components.

Patients / Methods: Suspected Pax6 downstream targets were validated using in situ hybridization and immuno-labeling on control and lens-specific Pax6 mutants (Pax6loxP/loxP;Mrl10-Cre). Direct regulation of the putative target genes by Pax6 was evaluated using reporter assays in Electromobility Shift Assay (EMSA) and chromatin immunoprecipitation (ChIP).

Results: Analysis of the Microarray study revealed enrichment of genes that are part of the Notch signaling pathway. Validation demonstrated reduced expression of Jagged1 and Hes5 in the Pax6 deficient lens. ChIP analysis conducted using Pax6 antibodies on embryonic mouse eye (E13.5) revealed that Pax6 associates with the promoter of Jagged1. Recognition sites for Pax6 were identified in silico in the Jagged1 promoter and in-vitro binding assays confirm that Pax6 is associated with Jagged1 regulatory sequences.

Conclusions: This study reveals that Pax6 regulates the Notch signaling in the lens through direct regulation of ligand Jagged1. This finding contributes to our understanding of the Pax6 dependent gene network that regulates the lens fiber differentiation program in mammals.

CHARACTERIZATION OF CERAMIDE KINASE-LIKE (CERKL) IN THE MAMMALIAN RETINA

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Introduction and Purpose: CERKL mutations are associated with severe retinal degeneration. CERKL encodes for a novel ceramide kinase (CERK)-like protein. Both CERK and CERKL harbor a kinase domain related to the diacylglycerol kinases, a Pleckstrin Homology domain, and a CERK-specific region, bearing a putative calmodulin binding motif. Several studies have been conducted to prove a biochemical similarity between CERK and CERKL enzymatic activities. However, so far there has been no evidence that CERKL phosphorylates ceramide or any other lipid substrate in vitro or in vivo. CERKL's function in the retina is unknown. The purpose of this work is to characterize CERKL's retinal expression pattern and function.

Patients / Methods: A specific anti-CERKL antibody was used to study the localization of the endogenous CERKL protein in the mouse retina. A calcium-overlay assay was used to determine whether CERKL directly binds calcium. Co-immunoprecipitation will be used to investigate a possible interaction between CERKL and calmodulin. In order to investigate CERKL behavior under stress conditions, we grew 661W cells (a retina derived cell-line) in serum free medium for different time phases. These cells underwent immune-staining and western blot analysis with anti-cerkl antibody.

Results: In the mouse retina CERKL is located in the cytoplasm of the ganglion cell layer, in amacrine cells of the inner nuclear layer, and in cone photoreceptors, whereas in retina derived cell lines (ARPE19 and 661W) its subcellular localization was variable and was distributed in the cytoplasm, perinuclear region and in the nucleus. Based on a calcium-overlay assay, CERKL does not appear to bind calcium directly. Serum deprivation led to CERKL up-regulation, as indicated by western blot analysis and immune-staining.

Conclusions: The severe retinal phenotype associated with human CERKL mutations indicates that this gene plays a crucial role in retinal activity. The high expression level of CERKL in cones correlates with the CERKL-associated phenotype in humans, which involves severe cone degeneration. CERKL up-regulation under stress conditions may imply a role for CERKL in cell survival.

DEVELOPMENT OF OCULAR VASCULATURE IN ZEBRAFISH

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Introduction and Purpose: Ocular vascularization defects play a role in several human diseases that lead to impaired vision. Hence, understanding the molecular mechanisms that govern normal and abnormal ocular blood vessel development is important for understanding the mechanisms underlying these diseases. In this work we characterize the development of ocular vasculature in zebrafish and investigate the effects of perturbing the activity of various signaling pathways on the development of these blood vessels.

Patients / Methods: We use transgenic zebrafish in which endothelial cells are highlighted by the expression of fluorescent proteins to visualize ocular blood vessel development in vivo. Manipulation of various signaling pathways is achieved using mutants, transgenic lines and treatment of embryos with small molecules.

Results: By fate-mapping experiments we show that the hyaloid and choroidal systems arise from different origins. The choroidal system forms in a highly stereotypic spatiotemporal manner and originates from the primordial midbrain channel (PMBC) by VEGF- and FGF-dependent angiogenesis. Blocking or over-activating several signaling pathways leads to abnormal patterning of choroidal vasculature. Current efforts focus on identifying signaling molecules expressed by eye tissues, which provide cues for the correct growth of choroidal blood vessels.

Conclusions: The simple and highly stereotypic pattern of zebrafish embryonic eye vasculature provides a useful model for identifying genes that influence ocular blood vessel growth and patterning.

FLEXIBLE CARBON NANOTUBE BASED MICRO-ELECTRODE ARRAY FOR RETINAL IMPLANTS APPLICATION

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Introduction and Purpose: To create an artificial device that can take over the physiological function of retinal structures such as retinal pigment epithelium and photoreceptors as a way to save sight in diseases and conditions that destroy them.Such implants consist of a micro-electrode array (MEA) and are implanted in the sub retinal or epi retinal space.The electroded are intended to inject low electrical currents that activate the remaining healthy retinal neural cells, the ganglion cells (RGC).

Methods: For the goal of the presented project we developed flexible implant architecture, made of a medical tape as a substrate,and carbon nanotube (CNT) film which serve as high-capacitance electrodes and low-resistancetraces to the power source.Silicone membrane (polydimethylsiloxane,PDMS) was used for passivation.

Results: In-vitro tests were performed with embryonic chick retina under physiological conditions.Activation thresholds similar tothose obtained with standard commercial MEA were achieved.Preliminary epiretinal implants in rar and rabbit presented no inflammation and no damage to the retina and other structures of theeye during a two months period of follow up.The process flow, electrochemical measurments, in-vitro electrophysiological results and preliminary in-vivo data will be presented.

Conclusions: The described micro-electrodes present up to now promising results to be a new type of retinal prosthesis.

HIGH RESOLUTION OPTICAL COHERENCE TOMOGRAPHY RETINAL AND CHOROIDAL FINDINGS IN OCULAR TOXOPLASMOSIS

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Introduction and Purpose: To demonstrate the different retinal and choroidal morphological characteristics on Spectral Domain Optical Coherence Tomography (SD-OCT) in ocular toxoplasmosis.

Methods: Case series of patients presented with ocular toxoplasmosis from August 2009 were included in the study. All patients underwent a detailed ophthalmic examination, fundus color photography and Spectralis SD-OCT imaging at presentation and during follow-up. OCT scans were directed to the pathological retinal and choroidal areas that were demonstrated in the clinical examination.

Results: Sixteen eyes (13 patients) were included. Eleven active lesions were demonstrated in 9 eyes (8 patients) and 25 chorioretinal scars were demonstrated in 12 eyes (10 patients). The active lesion demonstrated retinal thickening, disruption and hyper-reflectivity of the retinal layers. During follow-up the retina became thinner and a scar formation was noted. Hyper-reflective deposits were noted on the posterior hyaloid, within the vitreo-retinal interface and in the inner retina layres. Those deposits fade with time. Vitritis could be demonstrated as multiple hyper-reflective dots in the vitreous cavity during the active phase, which resolved during follow-up. Choroidal findings included significant thickening returning to normal thickness when scars were formed.
OCT findings of the chorioretinal scars demonstrated sharply demarcated borders, thinning of neurosensory retina, ELM & IS/OS junction interruption, disorganization of the retinal layers and RPE changes. The choriocapillaries demonstrated a specific pattern with a significant hypereflectivity. In addition, the posterior hyaloid was thickened and partially detached over the toxoplasma scar. The OCT retinal and choroidal features remained unchanged during the follow up.

Conclusions: SD-OCT is a useful tool in the diagnosis and follow-up of patients with ocular toxoplasmosis and provides a better understanding of the pathogenesis of the disease.

IN VIVO FUNDUSCOPY AND TARGETED HOLOGRAPHIC RETINAL STIMULATION

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Introduction and Purpose: Degenerative diseases of the outer retina lead to photoreceptor loss and eventually cause blindness. However, the retinal ganglion cells (RGCs) are relatively preserved. Artificial photo-stimulation of these functional cells could be the key to developing retinal neuroprosthetic devices, which will restore patients' vision.
Previous work done in our lab demonstrated patterned photo-stimulation of RGCs in-vitro, exploiting different stimulation mechanisms. The research presented here constitutes the first step in advancing towards in-vivo retinal stimulation.
A successful retinal prosthesis should induce cortical activity which will enable downstream circuits to correctly interpret the artificially generated activity as the intended image. Thus it is necessary to record responses to the artificial stimuli in the visual cortex. This may be achieved by utilizing two-photon microscopy in combination with a calcium indicator to functionally image neuronal populations in the living brain.

Patients / Methods: We have constructed a system which integrates precise spatiotemporal holographic photo-stimulation with high resolution fundus imaging. This system allows one to target the projected pattern at specific locations in order to excite desired RGCs.

Results: The system was utilized to acquire both brightfield and fluorescence fundus images of mice and rats in-vivo. In addition, holographic patterns were projected onto the rodents' retinas and imaged.
The optical parameters of the holographic photo-stimulation system have been characterized. The system's imaging resolution allows one to identify single RGCs for stimulation. The stimulation spot diameter is sufficient for cellular targeting using patterned photo-stimulation in vivo.

Conclusions: Our system enables single-cell resolved patterned holographic photo-stimulation of RGCs.
It will allow the integration of two-photon calcium imaging of V1 neuronal activity as part of the further development of a novel optical retinal prosthesis.

LIGHT INTENSITY DRIVEN RETINAL TYROSINE HYDROXYLASE EXPRESSION, AND REFRACTIVE DEVELOPMENT OF THE CHICK'S EYES

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Introduction and Purpose: Recently we associated the light-intensity-dependent refractive development of the chick's eyes with its retinal dopamine (DA) release rate. In the present study we further examined the effect of ambient light intensity on dopamine system including: dopamine release rates, dopamine synthesis enzyme, dopaminergic amacrine cells activity, and evaluate their interrelations with refractive development.

Patients / Methods: Newly hatched chicks were divided into 3 ambient illumination groups: light intensity of 50 (n=8, low), 500 (n=8; medium), and 10000 lux (n=8; high) under light-dark cycles of fluorescent light. On week 14 post-hatching refractive measurements were performed and included: retinoscopy, keratometry, and A-scan ultrasound. Dopamine system evaluation comprised measurements of the dopamine release indices, vitreal DA and DOPAC concentration, using high performance liquid chromatography (HPLC); retinal tyrosine hydroxylase (TH) quantification by western blot; and immunohistochemistry staining (IHC) of the dopaminergic amacrine cells. Refractive measurements were correlated with that of the dopamine system.

Results: High-intensity group had hyperopic refraction, steep cornea, and shorter eyes relative to the low-intensity. High-intensity of light induces 2.95 folds increase in retinal dopamine release (DOPAC concentration 30.6 ng/ml vs. 13.5 ng/ml), 3.1 folds increase in TH expression (optical density: 11263 vs. 33274), and higher signal in IHC staining of the dopaminergic cells, compared to the low-intensity of light The associations between TH expression and refraction, keratometry, and axial length were 0.81: $P<0.0001$, 0.7: $P<0.0001$, -0.53: $P=0.02$, respectively.

Conclusions: In chicks, ambient light intensity regulates the activity of dopaminergic amacrine cells to produce TH and meet the release rate of dopamine. The refractive development is associated both with dopamine release rate and with dopamine synthesis TH enzyme level.

MONOCYTE-DERIVED MACROPHAGE DIVERSITY IN EAU

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Introduction and Purpose: We recently showed that monocyte-derived macrophages take part in protecting retinal ganglion cells (RGCs) after glutamate-induced retinal insult, by locally exerting an immunoregulatory phenotype. In experimental autoimmune uveitis (EAU), macrophages are commonly associated with induction and progression of the disease. In light of the functional diversity of monocyte-derived macrophages, we set out to discover whether the subsets of monocyte-derived macrophages that were found to bring benefit following glutamate intoxication are also involved in protection against immune-mediated damage associated with EAU.

Methods: EAU was induced in C57BL/6J mice by injection of human interphotoreceptor retinoid binding protein (IRBP)-derived peptide 1-20. The infiltration of monocyte-derived macrophages to the eye along disease course was monitored in CX3CR1-GFP bone marrow chimeric mice. The effect of monocyte-derived macrophages on EAU induction and resolution was evaluated by conducting monocyte depletion experiments.

Results: A distinct myeloid population was found to appear in the retina following EAU induction. Monocyte-derived macrophages infiltrated diseased retinas, and were absent from retinas of control mice. Inhibiting this infiltration at the induction phase prevented EAU onset, whereas monocyte depletion at the resolution phase of EAU resulted in a decrease in FoxP3+ regulatory T cells, and affected the local cytokine milieu.

Conclusions: Monocyte-derived macrophages are prominent cells in EAU. These macrophages are present in the eye throughout disease course, where they affect the milieu in terms of cytokines and T cell accumulation, and may play a role in disease resolution that is apparently distinct from their involvement in disease induction.

RETINAL BLOOD VESSELS DIAMETER IN A HEALTHY COHORT AS MEASURED BY THE SPECTRAL DOMAIN OCT (SD OCT).

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Introduction and Purpose: To describe a method of measuring large retinal blood vessels diameter using spectral-domain optical coherence tomography (SD-OCT).

Patients / Methods: A prospective study. 29 healthy subjects (58 eyes) with a mean age of 41.45±15.53 years, without any prior ocular history underwent SD-OCT exam. Two cube scans composed of seven horizontal scans each, were placed at the superior and inferior borders of the disc (one cube scan superiorly and one cube scan inferiorly) to include the large retinal vessels originating from the disc The diameter of the temporal retinal arteries and veins was measured and an artery to vein ratio (a-v ratio) was calculated at 10 measurement points (480-1440 µm from the optic disc border superiorly and inferiorly).

Results: Average retinal artery and vein diameter (µm) was 135.73 µm +/-15.64 and 151.32 µm +/-15.22 at the nearest measurement point at 480 µm with gradual decrease to 123.01 +/- 13.43 and 137.69 +/-13.84 at 1440 µm, respectively. No statistical difference was found in mean arterial diameter between the superior and inferior arteries and between the right and left eyes at all measurement points. No statistical difference was found in mean venous diameter between the superior and inferior veins. Statistical significance between veins diameter in the right and left eyes was found only at 960 and 1200 µm measurements points. The artery-vein ratio (a-v ratio) was ~ 0.9 at all measurement points.

Conclusions: This is a novel non invasive method for retinal blood vessels diameter measurement using the SD OCT imaging modality. This method coupled with the infrared image may be useful for accurate evaluation of retinal vascular caliber in retinal as well as systemic vascular diseases. It may serve in the future for diagnosis and follow up of various primary and secondary ocular vascular abnormalities.

HIGH ORDER ABERRATIONS & TOPOGRAPHY IN NORMAL, KERATOCONUS-SUSPECT & KERATOCONIC EYES

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Introduction and Purpose: This study was designed to compare higher-order aberrations of the cornea and of the eye with inferior-superior (I-S) corneal topographic values in keratoconic eyes.

Methods: We studied 92 eyes from 78 subjects: 21eyes of 14 subjects with suspected keratoconus, 23 eyes of 16 subjects with manifest keratoconus and 48 eyes of 48 subjects without keratoconus using the L80 wave+, an instrument which can measure corneal topography and aberrations simultaneously with a large dynamic range making it possible to evaluate higher-order aberrations to the 7th order of the Zernike polynomial function series.

Results: All ocular and corneal higher-order aberrations were found to be significantly higher for keratoconic than normal eyes, but for suspected keratoconus the results were mixed. Corneal aberrations were higher than ocular aberrations, due to compensation from the internal aberrations. For manifest keratoconus, the corneal and ocular vertical coma displayed the largest difference being 38.6 and 78.5 times higher, respectively than normal eyes, while the largest differences for suspected keratoconus were only 5.25 and 4.6 times higher, respectively. On the other hand, inferior-superior dioptric asymmetry (I-S) was 9.3 and 37 times higher, for suspected keratoconus and keratoconic eyes, respectively than normal eyes. The separation of normality curves between suspected keratoconus and normal eyes was 28.6% for I-S and 14.3% for both corneal vertical coma and corneal total coma.

Conclusions: Although corneal vertical coma and, to a lesser extent, ocular vertical coma were found to be good indicators for the detection of keratoconic eyes, the traditional corneal topographic value such as the inferior-superior dioptric asymmetry remains an important predictor for identifying suspected keratoconus. However, ocular vertical coma and ocular higher-order total RMS also represent a good means of identifying suspected keratoconus.

IL-17 AND VEGF IN OCULAR SURFACE EPITHELIAL DISORDERS

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Introduction and Purpose: The expression of IL-17, a cytokine which was recently associated with various inflammatory processes, and its correlation to VEGF were examined in several ocular surface lesions which are associated with inflammation, including pterygium and Juvenile Conjunctival Nevus(JCN) representative of inflammatory disorders.

Methods: Pterygia and JCN specimens were collected from surgical samples after surgeries at the Department of Ophthalmology, Hadassah Medical Center. Normal conjunctival samples were collected from residual tissue which was removed during strabismus surgery. Formalin-fixed and paraffin-embedded blocks were cut into 5μm sections and processed for immunohistochemical analysis using a monoclonal antibody for IL-17 or VEGF. Analysis was performed to evaluate its distribution, localization and correlation to VEGF .

Results: Positive IL-17 immunohistochemical staining was observed in samples of 42 of 50 patients with pterygia. IL-17 was expressed in the perivascular tissues, vascular endothelial cells and in the basal layer of epithelial cells in the pterygia sections .
Positive VEGF staining was observed in 46 of 50 patients. VEGF was expressed in the surface epithelial layers of the pterygium, and in the vascular endothelium. Positive VEGF and IL-17 staining were found in 9 sections of 9 patients with JCN. IL-17 was expressed mainly in inflammatory cells, particularly esoinphils.In normal conjunctival epithelia IL-17 was barely detected, and was positive in one of 9 samples. VEGF were expressed in the perivascular spaces in 6 of 9 normal conjunctival sections.

Conclusions: The present study is the first to describe the expression of IL-17 in ptergyium and in JCN. These findings provide new insights to pterygium pathogenesis, in which IL-17 blockade may have a potential role in managing of pterygium or preventing its recurrence. The expression of IL-17 and VEGF in JCN is the first evidence for the activity of these inflammatory cytokines in the pathogenesis of this disorder.

PPM1A REGULATES ANGIOGENESIS IN MOUSE CORNEA THROUGH P38

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Introduction and Purpose: One of the major causes of blindness is corneal angiogenesis. Neovascularization (NV) may be a consequence of infection, inflammation, trauma and toxic or degenerative disorders. It is also an important risk factor for immunological rejection or failure of corneal grafts. Under physiological conditions, the corneal a-vascularity requires low levels of angiogenic factors and high levels of anti-angiogenic factors. During wound healing, when this balance is interrupted, it is tilted towards proangiogenic molecules such as VEGF.
The main regulator of wound healing is the TGF-beta signaling pathway. Protein phosphatase magnesium dependent 1A (PPM1A) was recently reported to be a negative regulator of Smads in the TGF-beta response. Our aim is to delineate the role of PPM1A in wound healing

Methods: To uncover the role of PPM1A in wound healing we have used PPM1A knockout mice generated in our laboratory that underwent corneal alkali burn, a well-known model for inflammation and angiogenesis.

Results: Studying wound healing following corneal alkaline burn we found elevated PPM1A expression in the corneal epithelial, keratocytes and endothelial cells. PPM1A KO mice displayed high levels of inflammation, developed angiogenesis and failed to repair the damaged tissues. Histological analysis, immunohistochemistry and gene expression data revealed that the lack of PPM1A led to continuous activation of the inflammatory response in the stroma, elevated expression of TGF-beta related genes including VEGF, TGF-beta, Collagen1 and MMP-9, dis-regulated VEGF secretion and the generation of new blood vessels.
In vitro studies, using TGF-beta treated primary corneal keratocytes demonstrates that PPM1A downregulats TGF-beta signaling by de-phosphorylating p38. In the absence of PPM1A the dis-regulated TGF-beta signaling increased expression of pro-angiogenic factors, enhances keratocytes activation and subsequently leads to increased collagen contraction. Exposure of the TGF-beta treated cells to p38 inhibitor abolished all these processes demonstrating that these effects are mediated through p38 activation. Finally, we have shown that phospho-p38 is the immediate PPM1A substrate as recombinant PPM1A dephosphorylats phospho-p38 in vitro.

Conclusions: We report hereby for the first that PPM1A is a prominent negative regulator of neovascularization that terminates TGF-beta activation through the dephosphorylation of p38.

CLINICAL AND BIOCHEMICAL BENEFICIAL EFFECTS OF PROLONGED TREATMENT WITH THE MMP INHIBITOR, DOXYCYCLINE, FOLLOWING OCULAR CHEMICAL INJURY IN RABBITS

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Purpose: The sulfur mustard (SM) ocular injury is characterized by acute lesions, followed by a delayed pathology, clinically characterized by epithelial defects and neovascularization (NV). Steroidal short term treatment has been shown to attenuate the ocular injuries but was insufficient to prevent the delayed pathology. We have previously shown the involvement of the extracellular matrix remodeling enzymes MMP-2 and MMP-9 during the acute phase, and in vascularized tissue of corneas displaying delayed pathology. This study aimed to evaluate the beneficial effect of treatment with the MMP inhibitor, doxycycline, in this unique chemical injury.

Methods: Rabbit eyes were exposed to SM vapor. A clinical follow-up was carried out up to 2 months. Tear fluid and corneal samples were collected at different time points for measurements of MMPs activity by zymography. Efficacy of post exposure topical doxycycline (2mg/ml in PBS, x4/day) beginning at 1 hr post exposure or following the appearance of NV was evaluated. The efficacy of post exposure short term (1w) topical doxycycline was compared to that of topical steroidal treatment (dexamethasone 1mg/ml).

Results: Topical doxycycline treatment during the acute phase (1w) was less efficient than dexamethasone in reducing the ocular injury and in postponing the appearance of NV. However, prolonged topical doxycycline treatment (8w) beginning before the appearance of delayed pathology, reduced NV extent and incidence. In addition, doxycycline treatment reduced MMP-9 activity in tear fluid. Similar beneficial effects were seen with prolonged oral doxycycline treatment (30mg/kg/day).

Conclusions: Prolonged topical or oral doxycycline treatment was beneficial during the acute phase and reduced the development of delayed NV, and should be considered as a medical countermeasure in ocular SM injuries. The decreased MMP-9 activity in tear fluid during treatment, strengthen the clinical findings, and points towards the use of tear fluid as a non-invasive tool for monitoring this ocular surface pathology. Finally, a combined therapy of short term dexamethasone followed by prolonged doxycycline treatment should be evaluated for SM induced ocular injuries.

THE EXPRESSION OF TOLL-LIKE RECEPTORS ON HUMAN CORNEAL EPITHELIAL CELLS AND CONJUNCTIVAL FIBROBLASTS

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Introduction and Purpose: The Toll-like receptors (TLRs) family of pathogen recognition molecules is a fundamental component of the innate immune system. TLRs are being increasingly recognized as important contributors to the initiation and modulation of the inflammatory response in the eye. This study evaluated the expression of TLRs in normal and activated cells.

Methods: The mRNA expression of TLR 2,3,4,7 and 9 in human corneal epithelium (HCE) and conjunctival fibroblasts was determined using real-time PCR analysis. We used flow cytometry to measure cell surface expression of these proteins and to compare the staining of cells incubated in medium to cells incubated with lipopolysaccharide (LPS) or polyinosinic:polycytidylic acid (poly I:C). The protein contents and mRNA expression levels of interleukin (IL)-6, IL-8, IL-1β and tumor necrosis factor-α (TNF-α) were measured using cytometric bead array (CBA) and real-time PCR, after incubation with LPS alone, LPS complex and poly I:C. We used human peripheral blood monocytes as positive control for flow cytometry and CBA, and neuron-committed teratocarcinoma 2 cell line as negative control for flow cytometry.

Results: mRNA expression of TLR 2-4, 7 and 9 was detected in HCE and human conjunctival fibroblasts. TLR3 and TLR4 were expressed on the surface of both corneal and conjunctival cells. Following incubation with LPS, the percentage of HCE cells staining positive for TLR4 decreased from 10.18% to 0.62% ($P<0.0001$). Incubation with poly I:C lowered the percentage of HCE cells staining positive for TLR3 from 10.44% to 2.84% ($P<0.0001$). Using CBA, HCE cells incubation with LPS alone elicited up to 2.8-fold higher levels of IL-6 ($P<0.05$), 1.5-fold IL-8 ($P>0.05$), 2.35-fold IL-1β ($P>0.05$) and 5.8-fold TNFα ($P<0.05$) compared to cells incubated in medium alone. The cytokine secretion profile was similar in real-time PCR.

Conclusions: For the first time, we report the results of a systematic characterization of TLRs expression in human conjunctival fibroblasts. We provide evidence for gene and surface expression of various TLRs on HCE cells and conjunctival fibroblasts, and demonstrate their functionality using cytokine profile secretion measurements. Interestingly, we have found that stimulation of HCE cells with LPS or poly I:C led to decreased levels of TLR-cell surface expression.

A NOVEL CORNEAL ANATOMY OBSERVED IN THE FLORIDA MANATEE

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Introduction and Purpose: The cornea is a transparent convex anterior portion of the outer fibrous coat of the eyeball that is continuous with the sclera. The normal, healthy cornea in all mammals is smooth. In this work the authors report a novel corneal structure observed in the Florida Manatee.

Methods: Biomicroscopical examination of 10 Florida Manatees (20 eyes) and histological evaluation of six manatees' corneas (which died from reasons unrelated to this study) were performed.

Results: Ophthalmological examination of the manatees' corneas consistently revealed ridged corneal surface. The histological evaluation showed that the outermost layers of the corneal anterior epithelium were intermittently elevated and that these elevations mostly likely formed the ridges seen ophthalmoscopically.

Conclusions: The corneal anatomy of the Florida Manatee is unique and differs from all other mammalians reported to date. The unique structure of the cornea, which includes ridges and normal vascularization of its anterior-most portion (including the anterior epithelium and its ridges), may have resulted evolutionarily from adaptations that allow this species to exist in both fresh water and marine environs. Associations with its prominent tear film and naturally hypotensive IOP will be discussed.

THE INHIBITORY EFFECTS OF ALPHA-LINOLEIC ACID ON NITRIC OXIDE SECRETION BY HUMAN OCULAR SURFACE CELLS

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Introduction and Purpose: To study the anti-inflammatory effects of alpha linoleic acid (ALA) on human ocular surface cells, compared to the effects on activated peripheral blood mononuclear cells (PBMC).

Methods: Human conjunctival fibroblasts (HCF) and corneal epithelial cells were grown in culture and treated with different combinations of inducers of inflammation, including IL-6,LPS,TNF-a,INFy and IL-1β. Nitric Oxide (NO) levels were measured at 24, 48 and 72 hours after treatment by assaying the culture medium for nitrite using the Griess reaction test. In cytokine treated HCF, expression of nitric oxide synthase 2 (NOS-2) was evaluated by real time PCR. NO and NOS-2 levels were examined again after applying ALA to cytokine treated HCF. PBMC cells were isolated from human peripheral blood and cultured with LPS to induced an inflammatory response. NO levels were measured with and without ALA.

Results: An in-vitro model that mimics ocular surface inflammation was established using the NO system. All cytokine combinations had an inducible effect on NO secretion in HCF. Treatment with a combination of IL-6,LPS,TNF-a,INFy and IL-1β induced the highest NO secretion, eliciting 2.84 fold ($P<0.01$) higher levels of NO after 72 hours, compared to cells incubated in medium alone, while treatment with a combination of LPS, TNF-a, and IL-6 had the least effect on NO secretion, eliciting only 1.68 fold higher levels of NO ($P>0.05$), compared to cells incubated in medium alone. In HCF, treatment with ALA decreased NOS-2 expression by 2.06 ($P<0. 01$) fold after 72 hours as evaluated by real time PCR. NO secretion was reduced by 39.4 percent ($P<0.05$) in response to treatment with ALA. This is in comparison with 4.1 fold higher levels of NO in LPS treated PBMC compared to PBMC incubated in medium alone and a 50 percent reduction in NO secretion after applying ALA.

Conclusions: In cultured HCF, NO secretion was up-regulated the most by treatment with a combination of IL-6,LPS,TNF-a,INFy, and IL-1β. NO levels were significantly higher LPS treated PBMC, compared to the cytokine treated HCF, indicating that peripheral immune cells are mostly responsible for the rise in NO levels in ocular surface inflammation. ALA was shown to have an anti-inflammatory effect both on HCF and on PBMC by decreasing NO and NOS-2 levels, raising the possibility of using topical ALA treatment in ocular surface inflammatory diseases.

ASSOCIATION OF DRUSEN MORPHOLOGY WITH MAJOR RISK SINGLE NUCLEOTIDE POLYMORPHISMS FOR AGE RELATED MACULAR DEGENERATION

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Introduction and Purpose: Drusen subtypes were recently described in Age Related Macular Degeneration (AMD) patients according to SD-OCT findings. It is unclear if formation of these drusen subtypes share similar pathways. We aim to evaluate if drusen subtypes are related to the major risk Single Nucleotide Polymorphism (SNP) in the CFH, HTRA1, and C3 genes.

Methods: Genotyping for the rs1061170 SNP in CFH gene, the rs11200638 SNP in HTRA1 gene and the rs2230199 SNP in C3 genes was performed in 51 patients (66 eyes) with neovascular AMD. Three SD-OCT images were evaluated from each eye. One of the sections was through the fovea center while the two other were 200 micron below and above the fovea center, respectively. Drusen were classified and counted as subretinal, cuticular, or typical AMD according to an accepted nomenclature. The observer was masked with respect to patient genotype. Statistical analysis was performed to evaluate for association between genotype and drusen subtypes.

Results: Subretinal, typical AMD, and cuticular drusen were observed in 47%, 71%, and 31% of patients, respectively. Each of the drusen subtypes was present in individuals carrying each of the three risk genotypes. Mean (±SEM) number of AMD drusen and cuticular drusen was higher in patients lacking the CFH risk SNP (13.8±2.9 vs. 7.8±1.1; p=0.05), but showed a trend towards higher number of drusen in patients carrying the HTRA1 risk SNP (12.6±1.8 vs. 8.2±1.3; p=0.058). Subretinal drusen were not associated with

Conclusions: These data suggest that subretinal, cuticular, and typical AMD drusen formation is not exclusively related to the main risk SNPs for AMD. Yet, while drusen subtype formation may share overlapping mechanisms, pathways related to specific SNPs may modulate drusen subtype quantity differentially.

INTRAVITREAL BEVACIZUMAB TREATMENT FOR EXUDATIVE AGE-RELATED MACULAR DEGENERATION WITH GOOD VISUAL ACUITY

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Introduction and Purpose: Exudative age-related macular degeneration (EAMD) is the leading cause of visual loss in the elderly population in western countries, and its impact on visual acuity (VA) in older age is expected to rise. According to the MARINA and ANCHOR studies, treatment with the anti-vascular endothelial growth factor (VEGF) agent ranibizumab led to preservation of the initial VA in 94.5%3 and 90% of patients with EAMD, and an improvement in VA in 36% to 41%. Consequently, prompt diagnosis and treatment of EAMD are of paramount importance.
However, in these and in other pivotal studies of EAMD, such as the PRONTO and EXCITE, the inclusion criteria allowed patients with a VA of 20/40 to 20/320, because they were designed to test the efficacy of ranibizumab specifically in terms of preserving and improving VA. Little attention was addressed to patients with a good initial VA (≥20/40) in whom the benefit of treatment is more difficult to determine given the small range of possible improvement.
The purpose or our stuey is to investigate the effect of intravitreal bevacizumab (IVB) on the visual and anatomic outcome of patients with exudative age-related macular degeneration (EAMD) presenting with good VA.

Methods: A file review was performed for all consecutive patients with newly diagnosed EAMD and initial VA of ≥20/40 treated in 2005-2010 and followed for at least 6 months. Treatment consisted of 3 loading doses of IVB every 6 weeks and was repeated when fluid or hemorrhage was present.

Results: The cohort included 130 patients (150 eyes). Mean follow-up was 20.2±13.2 months, and mean number of injections was 11.3±6.2. At the last examination, VA was stable or improved in 106 eyes (70.7%); 11 eyes (7.3%) lost ≥3 lines. Mean logMAR VA measured 0.22±0.1 (0-0.3) at presentation and 0.22±0.2 (0-1.3) at the last visit. Corresponding values for central macular thickness were 267±75 μM (137-562) and 226±75 μM (75-568) (P=0.14). The most frequent complication (18 eyes, 12%) was corneal epithelial defects.

Conclusions: Prompt IVB treatment for newly diagnosed EAMD in patients with good initial best corrected VA is associated with sustained or improved vision and a good safety profile. Attempts should be made to expedite the access of these patients to treatment, regardless of initial VA.

MODULATION OF LASER-INDUCED CHOROIDAL NEOVASCULARIZATION BY DIFFERENTIATED MACROPHAGES FROM PATIENTS WITH AGE RELATED MACULAR DEGENERATION

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Introduction and Purpose: Monocyte/macrophages were implicated in the pathogenesis of age-related macular degeneration (AMD), and it was speculated that macrophages can modulate the formation of choroidal neovascularization (CNV). We aimed to clarify if macrophages have pro- or anti-angiogenic capabilities in the context of AMD.

Methods: Macrophages were isolated from peripheral blood of neovascular AMD (NVAMD) patients (n=7), cultured and matured to MO phenotype and then polarized to either M1 or M2 phenotypes. Generation of polarized macrophages was validated by Q-PCR for CCL22 and CCL17. Polarized macrophages were fluorescently labeled and injected into the vitreous of rats following induction of CNV by laser photocoagulation. Angiogenic effect was assessed by measurements of CNV size using fluorescein angiography (FA) and isolectin staining of RPE-choroid flat mounts, respectively.

Results: Q-PCR of differentiated macrophages documented appropriate macrophage polarization based on CCL22 (M1:M2= 3.7:22.2; RQ) and CCL17 (M1:M2= 0.37:11.2 RQ) levels, respectively. Intravitreal delivery of polarized human macrophages did not cause inflammation, and injected cells survived up to 7 days following the injection. Injected macrophages were detected throughout the retinal layers while a minority of cells migrated to the vicinity of CNV lesions. Masked quantification of CNV in FA images showed that M1/M2 macrophages delivery was associated with increased leakage ($p<0.05$). According to isolectin staining of RPE-choroid flat mounts M1 macrophages delivery was associated with increased CNV as compared to PBS ($P=0.0003$, T-test), M2 ($P=0.03$), and M0 ($P=0.0007$) injected eyes, respectively.

Conclusions: Intravitreal delivery of macrophages from NVAMD patients was associated with pro-angiogenic effect in the rat model of laser-induced CNV. These data support the putative pathogenic role of macrophages in NVAMD and suggest that macrophages may serve as therapeutic target for NVAMD.

MONOCYTE CHEMOATTRACTANT PROTEIN-1 IN THE AQUEOUS HUMOR OF PATIENTS WITH AGE-RELATED MACULAR DEGENERATION

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

Methods: Samples of aqueous humor were collected from 34 patients with AMD and 16 age-matched control subjects undergoing cataract surgery. AMD stage (AREDS) was determined clinically, before surgery. Levels of cytokines were measured using Luminex X-MAP technology, and positive results were verified by Western blot.

Results: AMD was moderate in 18 patients and advanced in 16. The advanced-AMD group was further divided into patients with active choroidal neovascularization (CNV) (n=7), disciform scar (n=7), or central geographic atrophy (n=2). Higher-than-normal levels of monocyte chemoattractant protein-1 (MCP-1) in the aqueous humor were associated with advanced AMD (200±140 pg/ml vs 100±61 pg/ml; p=0.03), especially active CNV (255±155 pg/ml; p=0.02), Western blot analysis verified the MCP-1 findings. Patients with disciform scar showed a trend of abnormally high levels of IL-12 (p70) (1.7±2.4 pg/ml vs 0.2±1 pg/ml; p=0.07), tumor necrosis factor (TNF)-α (1.8±2.4 pg/ml vs 0.3±1 pg/ml; p=0.06), and IL-8 (4.7±6.4 pg/ml vs 1.2±2.1 pg/ml; p=0.08).

Conclusions: Elevated levels of inflammation-related cytokines in the aqueous humor in various stages of AMD may suggest a pathogenic role of inflammation. MCP-1 may be indicative of the angiogenic phase. Further corroborative studies are required.

MONOCYTE-DERIVED MACROPHAGES ARE HEALING CELLS ESSENTIAL FOR NEUROPROTECTION AND PROGENITOR CELL RENEWAL IN THE INJURED MAMMALIAN RETINA

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Introduction and Purpose: Retinal ganglion cell (RGC) death is a hallmark of many ocular pathologies. Neuroprotection and cell renewal are therefore vital for the integrity of the visual system following insult, yet are limited in the adult mammalian retina. As healing in other tissues is highly dependent on monocyte-derived macrophages, we tested whether these cells are also required following an insult to the visual system.

Methods: Adult mice were subjected to retinal insult in models of glutamate intoxication and increased intraocular pressure. Renewal of retinal progenitor cells (RPCs), RGC survival, the recruitment of distinct myeloid populations and their contribution to the local retinal milieu were analyzed by immunohistochemistry, retrograde tracing, flow-cytometry and quantitative Real Time PCR. Bone-marrow chimeras were used to characterize these myeloid populations and specifically to follow the infiltration of monocyte-derived macrophages to the injured eye. Effects of monocyte depletion or augmentation were tested using the anti-CCR2 antibody, MC-21, or adoptive transfer of monocytes, respectively.

Results: Following glutamate intoxication, monocyte-derived macrophages infiltrated the retina and localized mainly to the ganglion cell layer. Enhancement of the monocytic population augmented the numbers of proliferating RPCs and increased the survival of RGCs, whereas depletion of monocytes in the blood resulted in diminished RGC survival and RPC renewal. The monocyte-derived macrophages contributed to the immunoregulatory and neuroprotective milieu of the injured retina. They down-regulated the accumulation of other immune cells and restored immune homeostasis. The neuroprotective effect of these macrophages was dependent on their potential to produce the anti-inflammatory cytokine, interleukin-10.

Conclusions: Retinal insult evokes recruitment of monocyte-derived macrophages to the damaged retina. These cells enhance RGC survival and progenitor cell renewal by orchestrating an anti-inflammatory neurotrophic environment. We thus attribute to monocyte-derived macrophages a novel role in resolution of local retinal inflammation, with far-reaching implications to retinal neuropathies and other neurodegenerative disorders.

THE RELATIONSHIP BETWEEN LIGHT PERCEPTION AND PAIN PERCEPTION IN SIMULTANEOUS STIMULUS

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Introduction and Purpose: To test the ability of patients who are undergoing laser photocoagulation to locate the light and the pain in simultaneous stimuli

Design: Prospective, interventional, patient-masked study.

Participants: Fifty- five patients who needed pan retinal photocoagulation (PRP) at their first or second session of treatment.

Methods: Laser beam was projected on the four quadrants of the periphery of the retina of patient that needed pan retinal photocoagulation (PRP) for different conditions. This was applied with aiming beam, double frequency YAG laser and diode laser. Patients were asked to locate simultaneously the site of the light and the site of the pain.

Results: 26 males and 29 women were included in this study. Age ranged between 40 and 81 years old. 50 patients were treated with double frequency YAG laser that causes simultaneous light and pain, and 5 patients were treated with diode laser which has infra-red light and causes only pain perception. Aiming beam that causes light perception but no pain was applied to all patients. All patients located correctly the site of the aiming beam. 4 out of 5 patients (80%) who were treated with diode laser located correctly the site of the pain. Only 9 out of 50 patients who were treated with double frequency YAG laser (18%) located correctly both light and pain perceptions $X2=4.09$, $df=1$, $p=0.05$. All 11 patients who located correctly the pain site but incorrectly the light site located the light mistakenly at the pain site. In contrast, 22 patients located correctly the light site but incorrectly the pain site. 11 of them (50%) located the pain at the light site and 11 (50%) located the pain in other places. The difference of the dependence between these two perceptions were statistically significant ($X2=8.25$, $df=-$, $p<0.01$).

Conclusions: Simultaneous light and pain stimuli to the retina usually confuses the location of one of them. When the pain perception dominates, the pain tends to “pull” the light perception towards it. But when the light perception dominates, it “pulls” the pain toward it only in part of the cases.

RETINAL BREAKS IN SMALL GAUGE VITRECTOMY

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Introduction and Purpose: To determine the frequency of peripheral iatrogenic retinal breaks in eyes undergoing small gauge pars plana vitrectomy.

Methods: Prospective, single center, non-comparative interventional case series of patients that undergone 23 or 25-gauge vitrectomy between July 2010 and end of October 2010 were included in the study. We excluded patients with retinal detachment, dislocated crystalline lens from complicated cataract surgery, endophthalmitis, and previous history of eye trauma or vitrectomy. We recorded prospectively the frequency of all retinal breaks noted during surgery of patients undergoing 23 or 25-gauge vitrectomy. The indications for vitreo-retinal surgery were recorded, as were the location of retinal breaks, the presence or absence of an intact posterior hyaloid, status of lens, method of retinopexy, and use of a tamponade, together with the onset of a rhegmatogenous retinal detachment during the 3 month follow up interval. Main outcome was rate of entry site breaks in small gauge vitrectomy.

Results: We included 184 patients in this study. The mean age was 65.6 years (SD 13.2) and 46% were males. Retinal breaks occurred in 29 (15.7%) patients but only 6 (3.2%) were deemed to be related to the sclerotomies. Entry site breaks were not linked to the gauge of the instruments but retinal breaks were more common in 23 gauge surgeries although this was not statistically significant. One rhegmatogenous retinal detachment occurred in the post operative period.

Conclusions: Entry site retinal breaks are not common in small gauge vitrectomy.

TOPICAL TACROLIMUS TREATMENT FOR EXPERIMENTAL ALLERGIC CONJUNCTIVITIS

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Introduction: Purpose To evaluate the efficacy of tacrolimus ointment, tacrolimus eye drops, and dexamethasone eye drops on allergic conjunctivitis in a mouse model.

Patients / Methods: Twenty four Balb/c mice were actively sensitized by intraperitoneal injection of ovalbumin (OVA) mixed with aluminium hydroxide on day 1 and 8, and challenged with OVA eye drops twice daily for 7 consecutive days (from day 15 to 21). The mice were divided into four groups (6 in each group) and received topical treatment twice daily from day 17 to 21. Group 1- tacrolimus 0.03% drops, group 2-Tacrolimus 0.03% ointment, group 3- dexamethasone 0.1% drops and group 4 (control) - PBS. All mice underwent clinical examination on day 22 and were sacrificed. Blood samples were taken for serum OVA specific IgE to support the induction of the allergic reaction. The conjunctivas were subjected to histopathological evaluation for eosinophilic infiltration.

Results: Increased serum anti - OVA IgE antibodies titers were found in all mice. Clinical signs of allergic conjunctivitis were found only in the control group, treated with PBS. A statistically significant lower counts of eosinophils were found in the tacrolimus eye drops group as well as the dexamethasone group as compared to the control group (PBS) ($p<0015$). The eosinophil count in the tacrolimus eye drops group where similar to the counts in the dexamethasone eye group ($p=1$).

Conclusions: Our experimental mouse model of allergic conjunctivitis showed a significant effect of tacrolimus eye drops, similar to the gold standard treatment of dexamethasone. These results may have an important clinical implication, offering a viable steroid-sparing alternative treatment for allergic conjunctivitis.

INFLAMMATORY EFFECTS OF CONTACT LENS MULTIPURPOSE SOLUTIONS ON HUMAN CORNEAL EPITHELIAL CELLS

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Introduction and Purpose: Clinical data show that contact lens multipurpose solutions (MPS) may cause damage to the ocular surface.This study examined the inflammatory effects of contact lens MPSs and characterized the molecular events affected by this process on cultured human corneal epithelial (HCE) cells.

Methods: HCE cells were exposed to eight different commercially available MPS products (MPS A to H) at concentrations of 30% v/v and 50% v/v for 12 hours. Cytotoxic effects were examined with FITC-Annexin V/ PI and MTT assay. After exposure to MPSs, cells and supernatants were collected and tested for the expression of pro-inflammatory cytokines. The protein contents and mRNA expression levels of Interleukin (IL)-6, IL-8, IL-1β, Tumor necrosis factor-α (TNF-α) were tested with multiplex fluorescent bead immunoassay and real time-PCR, respectively. The expression of inhibitory factor-κBα (I-κBα) was measured with real time PCR. Lipopolysaccharide (LPS) complex, polyinosinic: polycytidylic acid (Poly I:C) and non-neutralized hydrogen peroxide lens disinfection system served as positive controls. Phosphate-buffered saline (PBS) was added as a negative control.

Results: Incubation of the various MPS with HCE cells showed that all the MPS examined induced significant increases of the levels of the pro-inflammatory cytokines compared to the negative control (PBS). Specifically, five of the MPS (A, B, E, F and H) stimulated the highest levels of pro-inflammatory cytokines. In addition, MPS H and B increased the mRNA levels of inhibitory factor-κBα (I-κBα) by 16.5±1.13 and 5.18±1.6 fold, respectively, compared to the negative control ($p<0.05$). In contrast, no significant differences were noted between the hydrogen peroxide lens disinfection system and the negative control.

Conclusions: Hydrogen peroxide lens disinfection system is preferable as a disinfecting and sterilizing system for contact lenses. The inflammatory responses in HCE that result from exposure to MPS are mediated through NF-κB signal transduction.

REPEATABILITY AND INTRA-SESSION REPRODUCIBILITY OBTAINED BY THE SIRIUS ANTERIOR SEGMENT ANALYSIS SYSTEM

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Introduction and Purpose: To analyze repeatability and intra-session reproducibility of anterior segment measurements using the newly developed Sirius Scheimpflug system (CSO, Florence, Italy)

Methods: Three consecutive measurements on 100 eyes of 50 healthy subjects were performed on the same session by the same technician using the Sirius device at Assuta Optic laser center, Tel-Aviv, Israel. For each eye, the following parameters were measured: anterior chamber angle (ACA), volume (ACV) and depth (ACD), thinnest corneal location, keratometry (anterior and posterior), cylinder and axis. Repeatability was assessed using the coefficient of variation (CoV). Intra-session reproducibility was assessed using intraclass correlation coefficient (ICC).

Results: Coefficient of variation (CoV) of 2% and less were observed for anterior chamber angle, depth (ACD), thinnest corneal location, and anterior keratometry. Intraclass correlation coefficients (ICC) were high for ACA, ACD, anterior keratometry measurements and moderate for anterior Cylinder and axis.
Higher CoV with relatively low ICC values were noticed with ACV, the posterior keratometry measurements, posterior cylinder and axis. The Last two have the highest CoV and lowest ICC; 48.79% (range: 37.64%-59.95%), and 0.38, respectively.

Conclusions: The Sirius scheimpflug system has a very high repeatability and intrasessional reproducibility when measuring the ACD, ACA, anterior curvature parameters, and the thinnest corneal location. Thus, it can be used with confidence in clinical practice.

THE EFFECT OF ERYTHROPOIETIN ON THE HEALING PROCESS OF CORNEAL EPITHELIAL EROSIONS IN RABBIT EYES

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Introduction and Purpose: To examine the effect of Erythropoietin on the healing process of corneal epithelial erosions in rabbit eyes.

Methods: Uniform corneal epithelial erosions were performed on the right eye of 15 new-zealand albino rabbits using application of 35% alcohol for 50 Sec., followed by mechanical removal of the epithelium with a surgical blade.
Rabbits were randomized into 3 groups: Group 1 eyes were treated locally with cellulose gel containing erythropoietin 4 times daily after epithelial erosions induction. Group 2 eyes were treated with the cellulose based gel, without erythropoietin, 4 times daily (control). Group 3 eyes were not treated (control). All rabbits were photographed with cobalt blue filter at time zero and three times daily then on, until complete re-epithelialization was achieved.
The digital images of the fluorescein stained corneas at each time point were evaluated morphometrically by computerized digital image analyzer (Image J, NIH). At re-epithelialization corneas were removed for histologic processing.
One-Way ANOVA and Mann-Whitney tests were used for statistical analysis

Results: Mean time (±SD) to complete re-epithalization was 55 ±2.19 hours in group 1, 66.5 ±14.25 Hours in group 2 and 62.2 ±9.09 Hours in group 3 ($p=0.16$). No significant difference was found between the groups regarding the duration to complete re-epithelialization and regarding the rate of epithelial healing. Histologic evaluation of the rabbit corneas revealed stromal vascularization in 2 of the 6 erythropoietin treated rabbits and in none of the control groups.

Conclusions: Erythropoietin has no beneficial effect on the rate of the healing process of corneal epithelial erosions in rabbit eyes.

OUR RESULTS WITH THE Z-FLEX 690TA A HYDROPHILIC ACRYLIC TORIC IOL

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Introduction and Purpose: To evaluate the outcomes of cataract surgery with hydrophilic acrylic toric intraocular lens (IOL) implantation.

Methods: This prospective study enrolled consecutive patients who had 1.75 diopters (D) or more of preexisting corneal astigmatism. Patients had cataract extraction surgery with implantation of a Z-flex 690TA toric IOL (Medicontur, Hungary). Uncorrected (UDVA) and corrected (CDVA) distance visual acuities (Decimal), keratometry, residual refractive cylinder, surgically induced astigmatism (SIA) were evaluated. The Alpins vectorial method was used to analys the target (TIA) and surgically induced astigmatism, difference vector and magnitude of error. Retroillumination images were used to evaluate IOL alignment.

Results:
Eighteen eyes of 13 patients were evaluated. The mean follow-up time was 4.47 ± 2.25 month. The mean preoperative keratometric astigmatism was 3.11 ± 0.71 D. The mean UDVA was 0.67 ± 0.12 Decimal, and the mean CDVA was 0.81 ± 0.2. The mean deviation from the anticipated spherical equivalent was +0.195 ± 0.37 D (range -0.45 to +0.93 D), with 100% of eyes achieving a spherical equivalent within ±1.00 D of the target refraction. The mean deviation from the anticipated refractive cylinder was -0.49 ±0.44 D (range -1.67 to +0.41 D). The post operatives mean refractive cylinder was -0.75 ± 0.45. The mean correction ratio was 0.93 ± 0.25, and the mean IOL misalignment was 5.88 ± 6.58 degrees. One patient undergone reoperation with IOL rotation into the proper axis and one patient refused to have a reoperation to rotate the IOL.

Conclusions: The Z-flex 690TA hydrophilic acrylic toric IOL implantation was safe, effective, predictable, and stable in correcting corneal astigmatism during cataract surgery. Implantation of hydrophilic acrylic toric IOL during cataract surgery resulted in There was no compromising of patient's safety as compared to regular cataract surgery.

COMPARISON OF DIFFERENT CONTACT LENSES AND SURFACES AS CARRIERS FOR HUMAN CORNEAL LIMBAL EPITHELIAL CELLS

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Introduction and Purpose: To delineate the best technique for culturing and carrying human corneal limbal epithelial cells on therapeutic contact lenses, for the purpose of cell transplantation for limbal stem cell deficiency.

Methods: Limbal explants from corneoscleral rims, remaining from cornea donor tissue used in corneal transplantation, were placed on 5 types of contact lenses of variable chemical composition, and cultured in media. Comparison between the growth patterns on different contact lenses was made with regard to epithelial proliferation rate, and epithelial cell morphology, by using light and electron microscopy. The 5 types of contact lenses were placed in medium free wells for 24 hours to allow better attachment to the well and then covered with gelatin for 2 hours and washed with Phosphate-buffered saline (PBS) prior to placing the limbal explants on them. A comparison between the two types of application was made with regard to the same criteria mentioned above.

Results: There were marked differences in growth patterns between the different contact lenses. The explants placed on siloxane–hydrogel contact lens - Focus Night & Day (lotrafilcon A, CIBA Vision, Duluth, GA, USA) showed the fastest proliferative and migratory rate. Explants seeded on to lotrafilcon A were tightly attached to it, growth was detected first on day 4 and confluence was reached by day 12. Cells examined under light microscopy were morphologically alike and looked similar to corneal epithelium grown on plastic. Electron microscopy revealed cell-to cell links and multiple cell layers. Microvilli and cell projections were also evident and most probably served as anchorage points on the contact lens surface.

Conclusions: Focus Night & Day contact lenses were advantageous over the four other types of lenses for culturing and carrying human ocular surface epithelial cells. These contact lenses may be used as possible carriers for cultured human ocular surface epithelial cell sheets as a part of a cell therapy strategy in limbal stem cell deficiency.

PHASE I GENE THERAPY TRIAL IN ISRAELI PATIENTS WITH LEBER CONGENITAL AMAUROSIS CAUSED BY A FOUNDER RPE65 MUTATION: AN UPDATE WITH UP TO TWO YEARS OF FOLLOW-UP

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Introduction: Gene therapy of human patients with Leber congenital amaurosis (LCA) due to mutations in the RPE65 gene became a reality following demonstration of safety and efficacy in RPE65-mutant dog and mouse models. Our phase I clinical gene therapy trial in Israeli patients, launched in February 2010, was the fourth of its kind worldwide (NCT00821340). The purpose of this report is to describe the results in the first three patients treated, with up to two years of follow-up.

Methods: Gene therapy was performed in three LCA patients (ages 21-29 years) who harbor a homozygous splicing mutation (c.95-2A>T; IVS2-2A>T) in the RPE65 gene. Subretinal injection of an AAV2-hRPE65 viral vector carrying the normal human RPE65 gene was carried out after vitrectomy in one or two sites, avoiding the foveal area. Ocular and systemic safety parameters were monitored closely, including resolution of the subretinal blebs, possible viral spread and immune response to the vector. Visual function and structure were evaluated repeatedly as per protocol using clinical eye exams, computerized light- and dark-adapted perimetry, Goldmann perimetry and non-invasive color, infrared, OCT and autofluorescence imaging.

Results: Two years of follow-up data are available for the first treated patient, one year for the second, and 9 months for the third. No toxicity or complications were observed to date in any of the patients. Post-operative data indicates stable visual acuity and increased sensitivity to light in the treated regions in all patients, to varying degrees. In the first patient, up to 100-fold increases persisted through the two year exam, and interestingly, he began to use these extra-foveal areas as his preferred locus for fixation. The third patient also reports and objectively shows significant functional improvement. The treatment effect in the second patient was slow to occur and is less pronounced.

Conclusions: Magnitude of the treatment effect varies between patients, but previous studies by others as well as the present study attest to the safety and efficacy of gene therapy for treatment of RPE65 LCA.

VEGF INDUCES NEUROGLIAL DIFFERENTIATION IN BONE MARROW-DERIVED STEM CELLS AND PROMOTES MICROGLIA CONVERSION FOLLOWING MOBILIZATION WITH GM-CSF

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Introduction and Purpose: This study sought to assess the impact of vascular endothelial growth factor (VEGF) on the differentiation and incorporation of bone-marrow-derived stem cells in a murine model of anterior ischemic optic neuropathy (AION).

Patients / Methods: One day after AION induction, a small-sized subset of bone marrow cells isolated by elutriation and depleted of hematopoietic lineage markers was administered by inoculation into the vitreous body (2.5x105) or intravenous injection (0.2 ml), alone or with intravitreal g). Cell engraftment and phenotype were examinedμinjection of VEGF (5 by histologic and microscopic analysis and real-time quantitative polymerase chain reaction after 30 and 180 days. In a second experiment, granulocyte-macrophage colony-stimulating factor (GM-CSF) or stem cell factor was administered intravitreally before cell implantation and VEGF injection to determine the impact of bone marrow mobilization.

Results: VEGF did not affect quantitative cell engraftment. However, it induced early neural differentiation of the donor cells incorporated in the retinal ganglion cell layer and increased the absolute numbers of astrocytes, endothelial cells, and immune cells in the retinal vasculature. These changes were signaled through VEGF-R1/flt-1, predominantly in cells inoculated directly into the vitreous body. VEGF-induced neuroglial differentiation was considerably slowed by cell mobilization with GM-CSF relative to intravenous stem cell infusion or mobilization with stem cell factor. Although VEGF synergized with GM-CSF, cell differentiation in the ischemic retina was narrowed to the microglia.

Conclusions: VEGF signaling through Flt-1 is a significant mediator of neural and astrocytic differentiation of adult bone-marrow-derived stem cells during stabilization of the ischemic retinal architecture.

THE ROLE OF THE FELLOW EYE IN VISUAL PERCEPTION: AN OPTIC NEURITIS STUDY

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Introduction and Purpose: Optic neuritis (ON), a demyelinative disease of the optic nerve, is usually presented monocularly, and manifested by prolonged Visual Evoked Potentials (VEP) latencies of the affected eye (AE). Yet, prolonged VEP latencies are also commonly found in the clinically unaffected fellow eye (FE). These are interpreted as evidence for sub-clinical demyelination in the fellow nerve. This work studies the possibility that delayed VEP latencies of AE and FE stem from different pathophysiological processes.

Methods: 16 patients 1-2 years following an ON attack & 16 aged-matched controls were studied. All subjects underwent VEP, high resolution MRI, Diffusion Tensor Imaging Diffusion (DTI) and fiber tractography. DTI and tractography were used to track the post-chiasmal visual pathways in all subjects. In addition, novel motion perception and dynamic stereopsis tests were applied. Latencies of the start, peak and end of VEP wave (corresponding to N75 P100 & N135) were measured.

Results: P100 was significantly prolonged in both AEs (127ms ±6) and FEs (118ms ±9). FEs exhibited normal visual functions (versus sustained motion perception deficits in AEs). Furthermore, their VEP latencies could not be explained by demyelinative lesions along the visual pathways as evident by T2 or FLAIR hyper-intense lesions. Inspection of the FEs' VEP wave revealed a delayed peak, but an intact start (75ms ±8 and 87ms ±10 in the FEs and AEs respectively). Thus FEs exhibit a widened VEP wave, approximating its peak with that of the AE. Significant correlation was found between the proximity of VEP peaks among the eyes and 3D perception, for stimuli presented during a limited time interval ($r=-0.67$, $p=0.01$). Across patients, those having smaller differences in VEP latencies among the eyes had better 3D perception.

Conclusions: While prolonged VEP latencies in the AEs result from peripheral demyelination, prolongation of the FEs may reflect adaptation mechanisms at the cortical level. These adaptive processes may have a role in adjoining the projection times of both eyes, contributing to accomplish binocular integration processes, such as dynamic 3D perception.

COMPARISON OF CHANGES IN ANTERIOR SEGMENT PARAMETERS BETWEEN EX-PRESS MINIATURE GLAUCOMA IMPLANT SURGERY AND TRABECULECTOMY

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Introduction and Purpose: To evaluate the effect of Ex-PRESS Miniature Glaucoma Implant surgery on anterior segment parameters obtained with the Pentacam rotating Scheimpflug camera (Oculus inc.), and to compare it to trabeculectomy.

Methods: In this prospective study, a group of 20 eyes who underwent Ex-PRESS implantation, and a group of 16 eyes who underwent trabeculectomy were evaluated preoperatively, on the first postoperative day and 3 months postoperatively with the Pentacam camera. We compared measurements of anterior and posterior corneal curvature, anterior and posterior corneal astigmatism, anterior chamber depth (ACD), anterior chamber volume (ACV) and anterior chamber angle (ACA) before and after surgery and between groups.

Results: IOP decreased significantly in both groups. On the first post operative day the change in IOP was -26.6±12.3 mmHg in the ExPress group and -14.3±16.5 mmHg in the trabeculectomy group (p=0.01). At 3 months following surgery the change in IOP was -14.6±12.3 mmHg in the ExPress group and -13.1±12.7 mmHg in the Trabeculectomy group (p=0.72). In the ExPress group, on the first post operative day, there was a statistically significant change in the posterior corneal astigmatism (p=0.008), anterior chamber depth (ACD) (p=0.0075) and anterior chamber volume (ACV) (p=0.0037). These changes in anterior segment parameters were not statistically significant at 3 months after surgery. In the trabeculectomy group, on the first post operative day, there was a statistically significant change in the anterior corneal astigmatism (p=0.01) and the posterior corneal astigmatism (p=0.01). Both changes in anterior segment parameters were not statistically significant at 3 months following surgery. When comparing the two groups, ACD and ACV were significantly higher in the trabeculectomy group at three months following surgery (p=0.02 and p=0.004 respectively).

Conclusions: Ex-PRESS Miniature Glaucoma Implant surgery and trabeculectomy both significantly decreased IOP, and have a transient effect on anterior segment parameters. Corneal curvatures, ACD, ACV, and ACA were not affected at 3 months follow up in both groups.

A NEW IN VIVO MODEL FOR TESTING TREATMENTS FOR LIVER METASTASES OF UVEAL MELANOMA: MODEL CONSTRUCTION AND USE FOR TESTING NFKB INHIBITION

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Introduction and Purpose: To describe a new animal model for in vivo testing of treatments for liver metastases of uveal melanoma, and its use for testing an NFkB inhibitor.

Methods: A metastatic uveal melanoma cell line (C918) was transfected with the luciferase gene in a stable transfection. The new C918-Luc cell line was trypsinized, washed in 1xPBS and injected directly into the livers of C57Bl mice (for the model construction) or SCID mice (for testing the NFkB inhibitor) through a small (1cm) abdominal wall incision via a 0.5cc insulin syringe (29 gauge needle) in a non-reflux technique. Cells were allowed to settle for 1 week before administration of the BMS-345541 NFkB inhibitor. Intra-hepatic cells were visualized with an IVIS bioluminescence camera (Caliper Life Sciences, Hopkinton, MA USA) 10 minutes after injecting the mice with luciferin (IP 300mg/0.3cc). BMS-345541 (5mg/kg) was administered by oral gavage 3 times a week for 3 weeks, followed by euthanasia and harvesting of the livers for histopathologic evaluation. Bioluminescence was measured twice a week. The research reported here was conducted in compliance with the ARVO Statement for th e Use of Animals in Ophthalmic and Vision Research.

Results: Bioluminescence was detectable in the liver immediately post op, increased over a period of one week in C57Bl mice and then decreased and disappeared over another week. In SCID mice, bioluminescence started decreasing after administration of the inhibitor. Experiments are not finished yet. Final results of the in vivo effect of NFkB inhibition will be presented at the meeting.

Conclusions: Combining the direct injection model with bioluminescence provides a way to follow the effect of anti-metastatic treatments in vivo. Inhibition of NFkB shows potential as a new treatment for metastatic uveal melanoma.

ADHESION PROPERTIES OF HUMAN UVEAL MELANOMA

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Introduction and Purpose: It is well known that proliferation and survival of malignant tumor cells depend on the presence of different extracellular matrix and various integrins. The purpose of this work was to examine the influence of different substrates on the adhesion properties of human uveal melanoma cell.

Patients / Methods: Two cell lines of primary uveal melanoma (OCM1 and C918) and one line of metastatic tumor cells (HMUM1) were examined. Expression of integrins subunits-VLA1-VLA5, at mRNA level and protein, was determined using PCR and FACS. Adhesion capabilities of the cell lines to laminin, fibronectin and collagen were examined. Control wells were lined by BSA.

Results: All 3 cell lines displayed various integrins expression. Accordingly, cells displayed better adherence to laminin, fibronectin and collagen compared with BSA. The OCM1 and C918 cells were 1.7 times more adherent to laminin, fibronectin and collagen, than to BSA. HMUM1 cells displayed an adhesion strength that was ten times more to these matrixes compared with BSA.

Conclusions: Uveal melanoma cells displayed better adherence properties to laminin, fibronectin and collagen compared with BSA. This feature was greater in the metastatic tumor line than the primary uveal melanoma line. Further investigation on tumor cell adhesion and its inhibition may yield useful knowledge regarding possible treatment modalities.

GENE EXPRESSION SIGNATURE IN THE MONOCYTE POPULATION OF PATIENTS WITH NEOVASCULAR AGE-RELATED MACULAR DEGENERATION

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Introduction and Purpose: Further evidence in recent years has linked monocytes/macrophages and their respective populations with the pathogenesis of age-related macular degeneration (AMD). We speculate that monocyte involvement in AMD is reflected in the peripheral blood circulation. To evaluate this hypothesis we have characterized the gene expression profile in patients with neovascular-AMD (NV-AMD).

Methods: Peripheral blood was taken from treatment-naïve NV-AMD patients (n=15), and age-matched controls (n=15). PBMC (peripheral blood mononuclear cells) were separated using a Histopaque gradient, and total blood monocytes, including the CD14+CD16+ subgroup of monocytes, were isolated using magnetic beads. Total mRNA was extracted using Tri-Reagent, and purity/quality was ascertained using a Nanodrop spectrophotometer and Agilent Bioanalyzer. Affymetrix Human Gene 1.0 ST microarrays were performed with quality mRNA. Microarray analysis was performed using the open sourceware programs R, DAVID, Expander, TANGO, and other genomics tools. Age, ethnicity, response to treatment, and severity of disease were taken into account for analysis.

Results: Using ANOVA for normalization, 1,522 genes were associated with NV-AMD ($P=<0.05$). Analysis with alternative algorithms (Expander program and RMA normalization) validated the existence of a differential expression pattern between NV-AMD patients and controls. DAVID functional analysis of the 1,522 genes generated 6 main annotation clusters of genes that were highly upregulated (FDR-corrected $P=< 0.05$). Analysis with an alternative algorithm (TANGO analysis on RMA-normalized data) detected 27 differentially expressed clusters (FDR-corrected $P=< 0.05$). Both algorithms identified “immune system process” as the highest ranked cluster. Other clusters involved cytokine/chemokine activity, defense mechanisms, activation of cellular response, and apoptotic response.

Conclusions: Microarray analysis revealed a variety of genes that are differentially expressed between NV-AMD patients and controls in peripheral blood monocytes. The data supports the activation of the systemic immune response in NV-AMD patients. Further research is needed to examine the potential of these gene expression signatures as biomarkers and therapeutic targets for the disease.

PREVALENCE OF MAJOR RISK POLYMORPHISMS FOR NEOVASCULAR AGE-RELATED MACULAR DEGENERATION IN ETHNIC SUBGROUPS COMPRISING THE ISRAELI POPULATION

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Introduction and Purpose: Single nucleotide polymorphisms (SNPs) in the CFH, HTRA1 and C3 genes are associated with age-related macular degeneration (AMD) in the Israeli population. Our aim was to compare the prevalence of these SNPs in the main ethnic subgroups comprising the Israeli population.

Methods: Genotyping for the rs1061170 SNP in CFH gene, the rs11200638 SNP in HTRA1 and the rs2230199 SNP in C3 gene was performed in 372 neovascular AMD (NVAMD) patients and 192 unaffected controls of Ashkenazi (n=332) and Sephardi (n=181) Jewish origin, and of Arab (n=48) origin. Clinical information and demographics were collected. Statistical analysis was performed to compare the prevalence of SNPs across the ethnic subgroups (using Chi-square test).

Results: Each of the three SNPs was associated with AMD in the Israeli population. The prevalence of HTRA1 and C3 risk SNPs was similar among patients from the three ethnic groups, as well as among unaffected individuals from the three groups. However, the prevalence of CFH risk SNP carriers was higher in Arabic AMD patients compared with Jewish patients (OR= 4.8; CI 1.1-20.7, P=0.02). Similarly, CFH risk SNP carriers were more common among unaffected Arabs compared with unaffected Jewish population (OR=3.0; CI 1.05-8.7, P=0.035). The prevalence of CFH risk SNP carriers was similar between patients and between controls from Ashkenazi and Sephardi background. Yet, Arab AMD patients had higher prevalence of CFH risk SNP carriers compared with Ashkenazi (OR=3.2; CI 1.1-9.3, P=0.05) and Sephardi (OR=4.9; CI 1.1-21.9, P=0.02) AMD patients. Unaffected Arab individuals had higher prevalence of CFH risk SNP carriers compared with Ashkenazi (OR= 4.7; CI 1.1-20.7, P=0.03) and showed a trend towards higher prevalence compared with Sephardi (OR=2.8; CI 0.9-8.7, P=0.07) individuals.

Conclusions: The prevalence of rs1061170 SNP in the CFH gene is higher among the Arabic population as compared with Ashkenazi and Sephardi Jewish populations, while risk SNPs in HTRA1 and C3 show similar prevalence among these populations. NVAMD was reported to be less common in Arabs compared with the Jewish population. Taken together, these data suggest the existence of factors yet to be identified which differentially modify the prevalence of AMD in the Jewish and Arab populations.

FAM161A PRODUCES TWO PROTEIN ISOFORMS WITH A DIFFERENTIAL RETINAL EXPRESSION PATTERN

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Introduction and Purpose: We have previously reported that mutations in FAM161A are the major cause of autosomal recessive retinitis pigmentosa in the Israeli population. In addition, we reported that FAM161A produces two alternatively-spliced transcripts in the retina. The more common transcript (#1) does not contain exon 4 while the less common transcript (#2) contains all known exons. The purpose of the current study is to verify the expression of the two transcripts at the protein level, to determine the expression pattern of each isoform, and to characterize the effect of blocking the expression of these isoforms in the zebrafish retina.

Methods: Polyclonal antibodies (Ab) were raised against the C-terminal and the alternatively-spliced and highly conserved exon 4 of FAM161A, using the rabbit as a host. Immunohistochemistry was first performed on mouse and human retinal sections using a commercial antibody (HPA032119), followed by using the two costume-made antibodies on retinal section from different species. Morpholino oligonucleotides (MO) that were designed to block translation or splicing of FAM161A were injected into 1-4-cell zebrafish embryos.

Results: All antibodies yielded a similar expression pattern in the mouse retina, with a major signal in photoreceptor inner-segments as well as a weaker staining in the outer plexiform layer. In the human retina, a similar pattern of expression was obtained with antibodies that are designed to recognize both isoforms, while the antibody designed to recognize isoform #2 showed a cone-specific staining. Double staining with FAM161A Ab and either PNA or S-cone opsin supported the cone-specific expression of this isoform. In Addition, MO were designed to block the translation of all isoforms or a specific splicing-site. RT-PCR analysis of injected embryos indicated that the splicing morpholino inhibited the expression of FAM161A transcripts. The effect of the different morpholinos on retinal structure and function is currently being evaluated.

Conclusions: We report here a unique expression pattern in which the same gene produces two isoforms with a differential expression pattern in either rods or cones. This phenomenon might be produced by retinal splicing factors that are expressed exclusively in one photoreceptor type.

REVEALING DEGENERATIVE RETINAL DISEASE CARRIERS USING NEXT GENERATION SEQUENCING

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Introduction and Purpose: Retinal degeneration ranks high among the many genetic causes of blindness.
Mutations in the multiple genes are responsible for a wide variety of retinal dystrophy phenotypes, such as autosomal recessive Stargardt disease, cone-rod dystrophy and retinitis pigmentosa. Here, we report the development of a new test to find all possible disease-associated variants in the coding sequences of 25 recessive degenerative retinal diseases, based on target enrichment and next generation sequencing (NGS).

Patients / Methods: 372 exonic regions from 25 target genes were enriched by hybrid capture, sequenced by next-generation sequencing (NGS) to a depth of up to 0.36 gigabases, and assessed with stringent bioinformatic filters. DNA samples of control subjects were investigated as a proof of concept study.

Results: Two DNA samples of control subjects not known to suffer from retinal degeneration or any other known eye disease were investigated.
We got an average target coverage of 192x (ranging from 167-218x for the two samples), 53.5% (45-62%) of nucleotides had at least 7x coverage, and 46.5% (39-54%) had at least 20x coverage. The enrichment factor which is the ratio of the coverage of the targeted region versus the coverage of the genome outside the target region was found to be 2613 (2158-3068). On average, 191 (153-229) SNPS and 8 (5-11) insertions/deletions were found, 138 (136-141) with median coverage > 37x, 95.5% of these (151-230) have been previously reported in dbSNP (v.132).
21 (19-24) aberrations were found in coding regions, of them 10 (9-12) resulted in changes of the protein sequence.

Conclusions: Given the difficulties in clinical diagnosis of similar phenotype, this method proved efficient for the first time in revealing the specific genetic mutation underlying retinal diseases, potentially lowering the costs of testing, and enabling broad screening for carriers and affected patients. NGS, if made available to the general population, may be an economical and superior method of diagnosis, genetic consultation and treatment for patients.

SUB-RETINAL INJECTION OF HUMAN ADULT STEM CELLS PRESERVES ERG RESPONSE IN RCS RATS

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Introduction and Purpose: To investigate the effect of subretinal injection of allogeneic human-derived bone marrow mesenchymal stem cell population (hBM-MSCs) on retinal functions. measured electroretinographically, and retinal structure of Royal College of Surgeons (RCS) rats.

Methods: hBM-MSCs (CD73+; CD90+, CD105+, CD45-) from healthy human donors were expanded ex-vivo up to for four passages. 0.25 Million cells in 5µl were transplanted into the sub-retinal space of one eye each of 54 4 weeks old RCS rats. Ten RCS rats were injected subretinally with saline as control. The ERG responses of both eyes of all the animals was tested before the injections and afterwards for ten weeks. Animals were dark-adapted for minimum of six hours prior to the ERG measurements. Scotopic and photopic ERGs were recorded from both eyes simultaneously using corneal golden wire loops . The eyes were then enucleated and processed for histology.

Results: Four weeks after injection, the b-wave amplitude responses of the scotopic and photopic ERG showed 74% deterioration from baseline compared to 94% deterioration ($p<0.05$) in the control groups (not injected eyes and saline injected eyes). These significant differences ($p<0.05$) were found up to the tenth week.

Conclusions: In this study we have shown for the first time that transplanting hBM-MSCs as a thin homogenous sub-retinal layer slows significantly the retinal deterioration rate as measured by ERG in RCS rats up to ten weeks. Subretinal injection of autologous hBM-MSCs may possibly be a therapeutic modality in patients with retinal degeneration.

THE EFFECT OF INTRAOCULAR OR SYSTEMIC INJECTION OF REVATIO (SILDENAFIL) ON MOUSE OCULAR BLOOD VESSELS AND NEURONS

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Introduction and Purpose: Revatio (Sildenafil) relaxes muscles and increases the blood flow to particular areas of the body. The purpose of this study was to measure the effect of Revatio on mouse ocular blood vessels and neuronal tissue.

Patients / Methods: Transgenic Thy-1-CFP and C57Bl6 mice underwent Revatio injection intravitreally to the right eye (IVT, n=12) or intraperitoneally (IP, n=12). The left eye with or without saline injection served as controls. Evaluation included: 1. Retinal fluorescence angiography, 2. Flat mount retinae analysis 3. Molecular analysis for the expression of apoptosis and ischemic related genes: SOD, HO1, GFAP, MBP, Bcl-2 and BAX. In a second step, optic nerve crush (ONC) was performed to measure the neuroprotective effect of Revatio (IVT and IP). Optic nerves and retina were analyzed histologically.

Results: Venous dilatation and increased choroidal effusion were detected by FA and flat mount retinae immediately following IVT and 30 minutes after IP Revatio injection. Molecular analysis of the optic nerves 1 day following IVT injection showed the increase of all genes measured: SOD-1(8.9), HO-1(1.8), GFAP (2.6), MBP (2), BAX (3) and Bcl-2 (1.7). This increase was maintained on day 3 except for HO-1 and Bcl-2 that reverted to baseline. RGC count 21 days following ONC without Revatio (n=3) revealed by histological analysis a 52% loss of RGCs. In the mice with ONC induced 30 minutes post IP injection of Revatio (n=3) RGCs loss was 55-65%. Histological analysis of the optic nerves (ONs) in mice injected with Revatio but without induction of ONC, showed apoptosis in the optic nerves immediately ONC induction.

Conclusions: Revatio injection dilated the retina blood vessels and increased choroidal perfusion. Following IVT injection, 3 mice had optic nerve damage detected by the increased expression of ischemic and apoptosis related genes. This was confirmed histologically. Following ONC, Revatio did not demonstrate a neuroprotective effect.

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ENHANCED S-CONE FUNCTION WITH PRESERVED ROD FUNCTION: A NEW CLINICAL PHENOTYPE

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Introduction and Purpose: To describe the clinical findings and genetic analysis in two brothers suffering from a novel retinal disease characterized by an enhanced S-cone phenotype with normal rod function.

Methods: Both patients underwent complete ophthalmologic examinations, including fundus photography, electroretinography (ERG), fluorescein angiography and optical coherence tomography (OCT). Mutation analysis of the following candidate genes was performed: nuclear receptor subfamily 2 group E member 3 (NR2E3), neural retina leucine zipper (NRL), nuclear receptor subfamily 1 group D member 1 (NR1D1), and thyroid hormone receptor beta (THRB).

Results: Spectral photopic ERG responses demonstrated enhanced S-cone function in both patients. Their scotopic b-wave ERG amplitude responses, however, were within normal limits. Their scotopic a-wave amplitude responses were within the lower limit of normal. The a- and b-wave latencies were normal for one sibling and on the upper limit of normal for the other. Peripheral retinal findings were normal. OCT showed flattening of the macular curvature and thinning of the photoreceptor layer. Mutation analysis of NR2E3, NRL, NR1D1, and THRB genes was negative.

Conclusions: We describe what appears to be a previously unidentified familial retinal phenotype with enhanced S-cone function and well-preserved rod system function in contrast to the severely reduced rod function seen in the enhanced S-cone syndrome (ESCS). Genetic analysis of candidate genes did not reveal the cause of disease. We postulate that the disease might be caused by mutation of another, as yet unidentified gene, which encodes a protein that functions as a negative inhibitor of rod and S-cone development.

OPTICAL COHERENCE TOMOGRAPHY IN PREECLAMPTIC WOMEN

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Introduction and Purpose: Visual disturbances are possible among preeclamptic women including visual obscuration, photopsia, scotoma, visual loss and cortical blindness. There are sparse data on the prevalence of ocular involvement in preeclampsia especially among non symptomatic patients. The currently available information on the use of optical coherence tomography (OCT) in preeclampsia is based on case reports.The purpose of this study was to evaluate retinal and OCT findings in preeclamptic women

Methods: The 27 preeclamptic women recruited for this study underwent ophthalmic and retinal OCT examinations. The size and location of ocular findings, involvement of the retinal layers and retinal nerve fiber layer (RNFL) thickness as determined by OCT were assessed. Data pertaining to preeclampsia were recorded and evaluated.

Results: Four women (14.8%) had funduscopic findings related to preeclampsia: two had retinal hemorrhages and two had retinal edema. OCT revealed retinal pathology in 3 eyes (5.6%) of 2 patients (7.4%). There was a higher prevalence of ocular findings among women with severe preeclampsia accompanied by severe hypertension and/or neurological signs. OCT findings included: retinal edema, subretinal fluid, photoreceptors irregularities and lesions at the retinal pigment epithelium level (Elschnig spots). The choroid layer was normal. Peripapillary RNFL tended to be thicker in eyes with pathological findings on OCT.
The figure below shows an OCT section through the fovea of a preeclamptic patient with ocular involvement. Subretinal fluid and RPE lesion (Elschnig spot) are noted.

Conclusions: The prevalence of ocular findings in both fundus and OCT examinations is relatively low in asymptomatic preeclamptic women. OCT was not more sensitive than funduscopy for detecting pathological ocular findings in preeclampsia, but it provided accurate definition and delineation of the findings. The fact that peripapillary RNFL tended to be thicker in eyes with pathological findings might be related to subclinical involvement of CNS. Given the unique ability of OCT to specifically define ocular findings in preeclampsia, we recommend that preeclamptic women diagnosed as having ocular involvement be evaluated and monitored by OCT.

TIMING OF ACUTE MACULA-ON RHEGMATOGENOUS RETINAL DETACHMENT REPAIR

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Introduction and Purpose: Determine if same day or next available surgery changed the outcome of patients presenting with acute, macula-on rhegmatogenous retinal detachments.

Methods: A retrospective review of patients presenting with acute macula-on rhegmatogenous retinal detachments treated with small gauge vitrectomy was performed. Data collection included subjects' demographics, duration of symptoms, location and extent of the retinal detachment, as well as timing of surgery. The primary outcome was anatomical and functional success rate for patients having same day surgery compared to those where surgery was delayed.

Results: One hundred and fourteen patients were included in this study. Sixty two patients operated on day of presentation, 46 patients operated the day after presentation and in 6 patients surgery was delayed from 2-5 days. Time to surgery in hours ranged between 1-120 hours (mean 14.5±15.05 hours). Retinal re-attachment was achieved in 95.6% of patients, with 80% requiring only one procedure. Mean initial visual acuity was LogMAR 0.42 (SD 0.6) and mean final visual acuity was LogMAR 0.39 (SD 0.67) ($p=0.53$). Time to surgery was not found to effect final anatomical outcome ($p=0.56$). No statistically significant association was observed between change in visual acuity and time to surgery. ($p=0.99$).

Conclusions: Modest delay in timing of surgery for macula-on rhegmatogenous retinal detachment did not adversely impact on patients' outcome.

TRANSCRANIAL MAGNETIC STIMULATION IMPROVES RETINAL FUNCTION IN AN ANIMAL MODEL WITH RETINAL DYSTROPHY

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Introduction and Purpose: To evaluate the effect of transcranial magnetic stimulation (TMS) on Royal College of Surgeons (RCS) rats.

Methods: Four weeks old RCS rats underwent ERG before TMS treatment and followed weekly for 7 weeks. The rats received 12 sessions (week 1-4) of either real (active, n=8) or sham (placebo, n=8) TMS over the right eye.

Results: Three weeks after treatment the maximal b-wave amplitude responses showed significant increase of 145% of change in the right eye and 178% of change in the left eye under scotopic conditions relative to placebo in both eyes ($P<0.05$) up to the ninth week. The single flash photopic responses showed increase of 74% of change in the right eye and 75% of change in the left eye

Conclusions: Using a new application for TMS we showed for the first time that TMS treatment seems to induce deceleration of retinal degeneration.

HUMAN RETINAL PROGENITOR CELL REPLACEMENT THERAPY AS A TREATMENT FOR RETINAL DEGENERATIVE BLINDNESS

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Introduction and Purpose: Photoreceptor degenerative diseases such as Retinitis Pigmentosa and Age related Macular Degeneration are currently the leading cause of blindness in the western world. The purpose of this study was to evaluate the effect of human retinal progenitor cell replacement therapy on retinal function of a transgenic miniature pig model of retinitis pigmentosa (p23h).

Methods: Six 2 month-old mini pigs (p23h) were used. Human retinal progenitor cells were injected into the subretinal space of six eyes. Three eyes were injected with 500,000 cells and the other 3 were injected with 2,500,000 cells. The other 6 eyes served as a control: three of which were injected with the vehicle alone (NAC/HBSS), and three were not injected at all. Electroretinography (ERG) was performed at 8 weeks after the injection and was repeated one month later. An eye examination was performed right after the ERG recordings.

Results: Injected eyes (in all groups) were associated with ocular abnormalities including corneal edema, uveitis, anterior synechia, cataract and retinal tear. The non-injected control eyes were free of abnormalities. Only one eye injected with 500,000 cells demonstrated residual rod function in response to scotopic stimuli 3 months after the injection (b-wave amplitude = 21μv). All of the other eyes from all groups did not have recordable rod activity at any time point. All injected eyes demonstrated lower combined rod-cone function compare to the non-injected controls. Eyes injected with 500,000 cells demonstrated the lowest rod-cone function compare to the other groups.

Conclusions: No rod function was restored in the p23h pigs after subretinal injection of human retinal progenitor cells 12 weeks post treatment. Subretinal injections (of all groups) were associated with ocular abnormalities and overall decreased retinal function, 12 weeks post injection.

A HOMOZYGOUS NULL MUTATION IN THE USH1C GENE CAUSES NON-SYNDROMIC AUTOSOMAL-RECESSIVE RETINITIS PIGMENTOSA

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Introduction and Purpose: Retinitis Pigmentosa (RP) is the most common inherited retinal degeneration and can be caused by mutations in each of at least 45 genes. In the Israeli population, however, the causative gene for most RP patients is still unknown. A recent next-generation sequencing tool, named Whole Exome Sequencing (WES), target the subset of the human genome that harbors protein-coding sequences, therefore making it a powerful and cost-effective modality to characterize the genetic basis of heterogeneous diseases. The purpose of this study was to use WES aiming to identify the cause of RP in patients of Yemenite-Jewish ancestry and to shed a light on the disease mechanism.

Methods/ Patients: Blood samples were drawn, genomic DNA was extracted and analyzed using whole genome Single Nucleotide Polymorphism (SNP) microarrays (Affymetrix) and WES (Otogenetics Corporation).

Results: We recruited for the study 31 families with autosomal recessive RP of Yemenite-Jewish origin who were negative for the founder mutation in the CERKL gene. Homozygosity mapping in two of the families revealed a few homozygous regions, one of which located on chromosome 11. Sequence analysis of a few candidate genes in those regions was negative. WES analysis of the two index cases revealed a shared homozygous novel frameshift mutation (c.1218delC) in an alternative exon (#15) of the USH1C gene (previously described to cause Usher type 1 and nonsyndromic deafness). Screening of additional 29 Yemenite-Jewish patients with RP for the mutation revealed a total of 14 patients (who belong to six families) who were homozygous for the mutation. Screening of 113 Yemen control subjects revealed one carrier only. USH1C is known to produce two protein isoforms, variant “a” and variant “b3”, through alternative splicing, with only variant “a” containing exon 15. Analys is of USH1C expression at the RNA level revealed additional transcript which was not previously reported. Interestingly, only exon-15 containing variants could be detected in the human retina, while other human tissues express both types of variants.

Conclusions: This is the first report of an USH1C mutation as a cause of non-syndromic RP. Together with the CERKL mutation we have reported previously, 50% of Yemenite-Jewish RP patients can be genetically diagnosed. The expression of only exon 15 containing variants pattern we identified is in-line with the severe retinal damage due to the USH1C novel null mutation.

GUCY2F ZEBRAFISH KNOCKDOWN - A MODEL FOR GUCY2D-RELATED LEBER CONGENITAL AMAUROSIS

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Introduction and Purpose: Mutations in retinal-specific guanylate cyclase (Gucy2d) are associated with Leber congenital amaurosis-1 (LCA1). Zebrafish offer unique advantages relative to rodents including their excellent color vision, precocious retinal development, robust visual testing strategies, low cost, relatively easy transgenesis and shortened experimental times.In this study we will demonstrate the feasibility of using gene-targeting in the zebrafish as a model for the photoreceptor-specific guanylate cyclase (GUCY2D)-related LCA1, by reporting the visual phenotype and retinal histology resulting from Gucy2fknockdown.

Methods: Gucy2f zebrafish LCA-orthologous cDNA was identified and isolated by PCR amplification. Its expression pattern was determined by wholemount in-situ hybridization and its function was studied by gene knockdown using two different morpholino-modified oligos (MO), one that blocks translation of Gucy2f and one that blocks splicing of Gucy2f. Visual function was assessed with an optomotor assay on 6 days post-fertilization larvae, and by analyzing changes in retinal histology.

Results: Gucy2f knockdown resulted in significantly lower vision as measured by the optomotor response compared to uninjected zebrafish larvae and morpholino (MO)-controls. Histological changes in the Gucy2f-knockdown larvae included loss and shortening of cone and rod outer segments.

Conclusions: A zebrafish model of Gucy2f-related LCA1 displays early visual dysfunction and photoreceptor layer dystrophy. This study serves as proof of concept for the use of zebrafish as a simple, inexpensive model with excellent vision on which further study of LCA-related genes is possible.

PRCD IS A SECRETED PROTEIN WHICH INTERACTS WITH OTHER RETINAL DEGENERATION CAUSATIVE PROTEINS

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Introduction and Purpose: PRCD mutations are associated with retinitis pigmentosa (RP) in both dogs and humans. PRCD encodes for a small protein (54 amino acids) of unknown function. The purpose of this work is to characterize PRCD's retinal function.

Methods: Myc-tagged PRCD expression construct was made and transfected into cultured cells to test for protein secretion. The p.C2Y mutation was inserted by site-directed mutagenesis. To identify PRCD-binding proteins we used the Ras-Recruitment system. Identified interactions were confirmed by co-immunoprecipitation (co-IP).

Results: The first 20 amino acids of PRCD appear to encode for a signal peptide, suggesting that PRCD is a secreted protein. To test this hypothesis we expressed a myc-tagged PRCD in cultured cells and used western blot analysis to test for the presence of the protein in both cell extracts and conditioned media. PRCD was found in both. Moreover, the p.C2Y mutation, which was found in both dogs and a human patient with RP, eliminated the secretion of PRCD from cells. Using the Ras-Recruitment system we identified two putative PRCD-binding proteins, including one which is involved in retinal degeneration and is important for the function of the retinal pigmented epithelium (RPE).

Conclusions: Our data suggest that PRCD functions in the retina as a secreted protein, since a mutation which eliminates its secretion leads to severe retinal degeneration. The identified PRCD-binding partner indicates that both proteins may act in a common pathway associated with RPE correct function. These findings shed a new light on PRCD function and the etiology of RP.

PATTERN DYSTROPHIES ASSOCIATED WITH MUTATIONS IN THE PERIPHERIN/RDS GENE

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Introduction and Purpose: To determine the underlying molecular genetic basis of retinal dystrophies identified in a Moroccan Jewish and a Christian Arab family, and to examine their phenotypes.

Methods: Ophthalmic examination included dilated fundus examination, flourescein angiography, fundus autoflouresence imaging, and optical coherence tomography (OCT). Selected family members underwent electrophysiological testing. Blood samples were obtained from affected family members for DNA extraction and mutation screening of the peripherin/RDS gene.

Results: A truncating peripherin/RDS gene mutation (c.441delT) was identified in affected members of the Moroccan Jewish family, whereas a missense mutation (R142W) was found in the Christian Arab family. Both mutations result in progressive retinal dystrophies displaying macular abnormalities and occasional peripheral retinal flecks in the fifth decade of life with subsequent development of macular atrophy and visual acuity deterioration with time. Electrophysiology may show abnormal EOG testing.

Conclusions: To the best of our knowledge these are the first descriptions of Israeli families carrying peripherin/RDS gene mutations. The evolvement of macular atrophy in elderly patients carrying these mutations may be misdiagnosed with age related macular degeneration owing to the phenotypic similarities between these conditions in the advanced state.

GENE THERAPY IN THE SHEEP MODEL OF CNGA3 ACHROMATOPSIA: DEVELOPING CONE-TARGETED VIRAL VECTORS AND ESTABLISHING THE SURGICAL PROCEDURE

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Introduction: Congenital achromatopsia (ACHM) is a hereditary vision disorder caused by cone photoreceptor dysfunction, leading to severe impairment of visual acuity, absent color perception and photophobia. ACHM is an important potential target for gene therapy since cone photoreceptors degenerate to only a limited extent in most cases, making them amenable for treatment. In the Israeli population, mutations in CNGA3 gene are by far the most prevalent cause of disease, accounting for over 70% of cases. A large animal model for pre-clinical evaluation of gene therapy for CNGA3 ACHM has been lacking till recently, when our group identified such a model in a herd of sheep in northern Israel. The aim of the present study was to develop appropriate viral vectors carrying the CNGA3 gene and to establish an efficient and safe surgical procedure for subretinal delivery of the vectors into the sheep eye.

Methods: Adeno-associated virus (AAV) serotype 5 vectors carrying the CNGA3 gene were produced by the 2-plasmid co-transfection method with modifications. Anatomical features of the sheep eye essential for the surgical procedure were studied in enucleated eyes. Surgery was performed under general anesthesia using a Zeiss operating microscope and a Premiere vitrectomy system. The fundus was examined and photographed before and after the procedure. A 34 Gauge cannula was used for subretinal injection.

Results: Two CNGA3- AAV vectors were developed, one carrying the mouse CNGA3 under control of the red-green opsin promoter, and one carrying the human gene under control of the IRBP and GNAT2 promoters. Anatomically, we found that in the sheep eye there is virtually no distance between the ora serrata and the limbus on the nasal and temporal sides, thus no port may be created in these regions without endangering the retina. On the dorsoventral axis there is a 4-5 mm distance corresponding to the pars plana area that may be used to safely create entry ports. We performed subretinal injections of saline in a number of normal sheep eyes with and without vitrectomy, and found that performing a vitrectomy is not necessary. Thereafter, all further surgeries were performed using a 2-port technique without vitrectomy. Preliminary experiments showed that up to 600µl of solution can be safely delivered subretinally in the sheep eye, with resolution of the bleb and no retinal detachment.

Conclusions: Two types of cone-targeted CNGA3 -AAV vectors were developed. We found that up to 600µl of fluid could be safety delivered into the subretinal space of the sheep eye using a dorsoventral 2-port access approach. In contrast to human surgery, vitrectomy is not a necessary step for successful subretinal delivery of fluid in the sheep eye. The results pave the way towards examining the effects of gene therapy in the sheep model of achromatopsia, in preparation for future application in humans.

RECOVERY OF VISUAL FUNCTION FOLLOWING GENE THERAPY IN A LARGE ANIMAL MODEL OF ACHROMATOPSIA

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Introduction and Purpose: Recently, we reported on novel congenital dayblindness in sheep. A mutation in CNGA3 gene was identified as the cause (Reicher et al., Genomics 95: 101-14, 2010). Since mutations in the same gene cause achromatopsia in humans, and are the most common cause of the disease in Israeli patients, we decided to evaluate CNGA3 human gene therapy using the sheep as an animal model for this disease.

Methods: Details of the modified virus and surgical technique are presented at this meeting by Banin et al. Operated animals were electrophysiologically and behaviorally assessed pre-operatively, and 2 and 6 months post-operatively. Cone function was assessed electroretinographically after light adaptation (10 min., 30 cd/m2). Photopic responses and flicker frequency fusion (FFF, 10-80Hz) to 4 intensities (1-10 cd/sec/m2) were recorded. Behavioral assessment included scotopic and photopic maze testing under standardized conditions. Passage times and number of collisions were recorded. Age-matched normal and day-blind sheep were similarly assessed as controls.

Results: All cone function parameters were significantly depressed in affected sheep prior to surgery. Following surgery, there was significant improvement (compared to dayblind controls) in a-wave time, b-wave amplitude and FFF of both operated and non-operated eyes. There were no differences between FFF of operated and normal controls. Behaviorally, there were no differences between dayblind and normal controls in scotopic testing, but dayblind animals were unable to navigate a photopic maze. Following surgery, operated sheep were able to navigate the photopic maze without collisions, and with timing not significantly different from those of normal controls. The electrophysiological and behavioral improvement in operated sheep persisted 6 months post-op.

Conclusions: AAV mediate gene therapy seems to improve visual function in both operated and non-operated eyes of dayblind sheep. The long-term electrophysiological and behavioral improvement in this naturally-occurring large animal model may pave the way to similar studies in human achromatopsia patients.

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WHOLE EXOME SEQUENCING AS A TOOL FOR IDENTIFICATION OF GENES CAUSING RETINAL DISEASES

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Introduction and Purpose: Over 200 genes are known or suspected to cause inherited retinal diseases, and the number is likely to dramatically rise within the coming years. Various techniques were used so far to identify those genes, and mainly linkage analyses, homozygosity mapping, and the candidate gene approach. In these protocols, each gene is individually analyzed (and sometimes a few dozen genes need to be analyzed) and therefore the progress can be very slow. The application of the so-called next generation sequencing (NGS) technique revolutionized our abilities, and for the first time all known genes can be sequenced simultaneously in each studied genome (Whole Exome Sequencing- WES), and even the whole genome can be sequenced within a few weeks (Whole Genome Sequencing- WGS).

Methods: Patients with inherited retinal diseases who agreed to participate in the study were recruited at Hadassah. Clinical data included family history, ocular examination and imaging. Genomic DNA was extracted from blood samples and analyzed using Affymetrix whole genome Single Nucleotide Polymorphism (SNP) microarrays and/or WES (Otogenetics Corporation).

Results: We have analyzed so far 14 genomes of patients with inherited retinal degenerations using WES. In most cases, only one affected individual was tested in each family. We obtained on average of 50 million sequences per genome and assembled them to the reference human genome sequence. Each genome was filtered against mutations that others and we identified in Israeli and Palestinian patients with retinal disease. In five genomes we have identified novel mutations in genes that were previously implicated in a different retinal disease. This includes mutations in genes that are known to cause achromatopsia in patients with cone-rod degeneration, and mutations in USH1C and BBS2 in patients with non-syndromic RP. The analysis of the remaining genomes is currently being performed in search for mutations in novel retinal disease genes.

Conclusions: In-line with data from other laboratories, WES is an efficient tool in identifying the cause of retinal diseases. In many cases, however, the mutation is identified in genes that are already known to cause a retinal disease. Improving WES analysis and available filtering data on genomes of Israeli and Palestinian origin, will improve our ability to detect mutations in novel retinal disease genes.

ABNORMAL VASCULATURE INTERFERES WITH OPTIC FISSURE CLOSURE IN LMO2 MUTANT ZEBRAFISH EMBRYOS

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Introduction and Purpose: Ocular coloboma is caused by failure of optic fissure closure during embryogenesis, and can lead to vision defects including blindness. Several genes have been shown to function in optic fissure closure; yet, to date, little is known about the mechanisms involved in this process. The purpose of this work was to identify new genes and mechanisms leading to ocular coloboma with the goal of better understanding the etiology of this debilitating developmental malformation.

Methods: A new mutation causing ocular coloboma was discovered by a forward genetic screen in zebrafish. The mutant gene was identified by positional cloning. The mechanism leading to coloboma in the mutants was revealed using live imaging of transgenic zebrafish lines, which allow visualization of vasculature, and by gene expression assays.

Results: A nonsense mutation in lmo2, a gene specifically required for hematopoiesis and vascular development, results in failure of optic fissure closure.
We have identified various malformations in ocular vasculature of mutant embryos, including delayed blood vessel growth, compromised blood vessel permeability (leakiness), and increased vessel size. The hyaloid vein that passes through the optic fissure is severely dilated in lmo2 mutants and remarkably, reducing its size leads to rescue of the coloboma. No changes have been found in the expression of genes known to be involved in optic fissure closure, suggesting that increased blood vessel size is the main mechanism leading to coloboma in lmo2 mutant embryos.

Conclusions: By showing that coloboma can be caused by an abnormally enlarged blood vessel that passes through the optic fissure, our results suggest that molecular or mechanical properties of ocular vasculature can affect eye morphogenesis.

PHOTONIC MEAN FOR REMOTE AND CONTINUOUS MONITORING OF INTRAOCULAR PRESSURE

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Purpose: To present the initial experimental testing of a new measurement principle for continuous, remote non-contact and monitoring of intra-ocular pressure (IOP).

Methods: A photonic device involving a fast camera and a laser was tested in rabbit's eyes for continuous remote monitoring of the IOP. The device is based on tracking the secondary speckle patterns trajectories produced by reflection of an illuminating laser beam from the iris, cornea or sclera. IOP fluctuations change the speckle distributions reflected from the rabbit's tissues that are acting as a transducer element of the sensing system. The distribution is continuously measured and analysed. The device is inexpensive since it requires only a laser, a camera and a computer. The anterior chambers of the eyes were canulated by an anterior chamber maintainer connected to a saline infusion bag. The IOP was varied by changing the elevation of the bag in respect to the position of the eye. The changes in the speckle pattern was continually monitored and analysed.

Results: Data from the photonic device were correlated with the IOP fluctuations resulting from raising and lowering the infusion bag. The measurements show a good correlation and sensitivity of the proposed device with IOP changes while providing a high precision measurement (5% estimated error) for the best experimental configuration. The results obtained via the photonic approach were also compared with a reference IOP measurement obtained with Goldmann tonometer.

Conclusions: The first experimental testing of a new photonic device has been performed with rabbits showing a promising new direction for remote and continuous monitoring of IOP. The system provides a high precision and non-invasive measurement method for IOP monitoring over prolonged periods.

CHARACTERIZATION OF PROSTAGLANDIN F2A RECEPTORS IN HAIR FOLLICLES OF EYELIDS

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Introduction and Purpose: To study the presence and distribution of prostaglandin F2α (PF) receptors in hair follicles of eyelids throughout the hair follicle cycle by immuno-histochemical methods, and to suggest a possible explanation for the clinical observation of elongation, thickening and crowding of eyelashes following topical use of prostaglandin analogs.

Methods: Specimens from patients undergoing resection of upper or lower eyelids were routinely processed for histologic preparations. Following the histopathological examination, the sections were evaluated for presence of hair follicles and 15 specimens were found suitable for inclusion in the study. Immunohistochemistry: The staining was carried out on Ventana Benchmark Automatic stainer, using polyclonal antibody directed against prostaglandin F2α receptor, diluted to 1:1000 (Cayman Chemical, USA, Catalog No. 101802). Evaluation of staining: Using a semi-quantitative 4-class scale (0-3), the intensity of staining in hair follicles and other epithelial elements in the specimens was assessed by 2 observers.

Results: Mean age of the 15 subjects was 77±14 and male/female ratio 2/1. The specimens were equally distributed between upper and lower lids. Matriceal cells were strongly stained (+3) and invariably present in bulbs and stems of hair follicles in the anagen phase. Inner root sheath of hair bulbs of anagen hair follicles were stained to a lesser extent. The staining was cytoplasmic, with membranous enhancement. Weak to no cytoplasmic staining (0-1) was seen in all epithelial cell, upper parts of hair follicles, catagen/telogen follicles, epidermis, conjunctival epithelium, sebaceous and sweat glands.

Conclusions: Elongation, thickening and crowding of eyelashes are commonly seen after topical use of prostaglandin analog eye drops. The observation that PF receptors are strongly expressed in the bulbs and stems of hair follicles during anagen phase provides a possible mechanism of action.

HUMAN AQUEOUS HUMOR PHOSPHATASE LEVELS, ACTIVITY AND REDOX STATE IN CATARACT AND GLAUCOMA

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Introduction and Purpose: To investigate the presence and activity of Protein Phosphatase-2A (PPase2A), Protein Phosphatase-2C (PPase2C) and protein tyrosine phosphatases (PTPs) in human aqueous humor (AH) from glaucoma and cataract patients, and to study the correlation between these phosphatases and the AH redox state.

Methods: AH samples were collected from 89 cataract and 29 glaucoma patients who were scheduled for cataract, glaucoma or combined surgery. PPase2A, PPase2C and PTPs levels in AH were measured by enzyme-linked immunosorbent assays, western blot analyses. These phosphatases activity was evaluated by spectral methods. Redox state was measured by spectral and fluorescent methods.

Results: The proportion of positive phosphatase was significantly higher in AH samples from the glaucoma group (PP2A $\chi 2(1)=11.754$, $p<0.01$; PP2C $\chi 2(1)=8.754$, $p<0.01$; PTP $\chi 2(1)=11.073$, $p<0.01$). Western blot analysis revealed higher PP2C levels in AH from glaucoma patients compared with PP2C levels in AH from cataract patients (ANOVA,$p=0.012$). Both oxidized/reduced glutathione ratio and superoxide dismutase levels in the AH were significantly higher in the glaucoma group compared with the cataract group (ANOVA, $p<0.05$).
Finally significant correlations were found between PP2A and PP2C; PP2A and PTP; and between total antioxidant activity and PTP levels.

Conclusions: There is a statistically significant difference in phosphatase levels and activity between the AH of glaucoma and that of cataract patients. The phosphatase content of the AH could be attributed to active cell signaling between surrounding ocular tissues or may represent surrounding tissue pathology.

PERSISTENT ELEVATION OF INTRAOCULAR PRESSURE FOLLOWING INTRAVITREAL INJECTION OF BEVACIZUMAB

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Introduction and Purpose: We describe persistent elevation of IOP following intravitreal injection of bevacizumab.

Methods: In our study we found 536 eyes of 432 consecutive patients, that received 1818 intravitreal injections of bevacizumab.
We reviewed consecutive cases of persistent IOP elevation after intravitreal bevacizumab injection. The study included 23 eyes (4.3%, 23/536) in 22 patients (5.1%, 22/432) with IOP elevated 30–70 mmHg, 3–30 days after injection.

Results: Mean IOP was 43.7 mmHg (range 30–70); IOP elevations occurred after an average of 7.5 (range 3–13) injections of bevacizumab. Injected eyes (23/536) had a significantly higher incidence of elevated IOP than uninjected eyes (fellow eyes) 1/328, $p<0.001$.

Conclusions: Intravitreal injection of bevacizumab for neovascular AMD may be associated with persistent IOP elevation. Providers should be aware that significant IOP elevation might occur after repeated treatments.

COMPARISON OF HUVITZ HT5000 ELECTRONIC APPLANATION TONOMETER AND HAAG-STREIT AT900 MECHANICAL APPLANATION TONOMETER

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Introduction and Purpose: To study the relationship between intraocular pressure (IOP) measurements by a recently introduced electronic applanation tonometer and the golden-standard mechanical applanation tonometer.

Methods: A prospective, cross-sectional study. Twenty-eight patients (53 eyes) randomly selected from patients scheduled for a routine examination in the glaucoma clinic at Soroka University Medical Center, Beer Sheva, Israel. Complete ocular examination was performed in each case. For each eye, the IOP was measured and recorded by two instruments; the Haag-Streit AT900 mechanical applanation tonometer (Haag Striet, Bern, Switzerland) and by the recently introduced Huvitz HT5000 electronic applanation tonometer (Huvitz, Gyeonggi-do, Korea). The order in which the two instruments were used in each eye was random. Pearson's correlation coefficient was used to determine correlation between paired IOP measurements. Bland-Altman plots were graphed for the analysis of differences between the instruments for the IOP values.

Results: The mean IOP for AT900 and HT5000 tonometers were 16.3±6.6 mmHg and 16.4±6.1 mmHg, respectively (p=0.47). A strong, significant correlation was found for paired measurements of IOP by the two instruments (ro=0.981; r2=0.962, P<0.0001). No systematic proportional bias was seen. The mean difference between paired measurements of IOP was 0.1 mmHg.

Conclusions: IOP measurements form HT5000 and AT900 tonometers are comparable and interchangeable. The difference in IOP measurements by the two instruments is clinically insignificant.

A NON-TOUCH SLIT-LAMP EXOPHTHALMOMTRY, A NOVEL TECHNIQUE

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Introduction and Purpose: To describe a novel exophthalmometry technique and to compare the measurements results with those of the Hertel exophthalmometer.

Methods: A millimeteric graph paper covered by transparency is attached to the slit-lamp table. The slit-lamp is first focused on the center of the cornea and the position of the microscope is marked on the transparency, then the slit lamp is focused on the lateral orbital rim and a second mark is drowned. The distance between the two lines as measured on the graph paper represents the exophthalmometry score. 60 patients with suspected orbital disease underwent both slit-lamp and Hertel exophthalmometry and the results were compared.

Results: Exophthalmometry mean results for the right eye were 19.8±3.3 mm with the Hertel and 19.5±3.4 with the slit-lamp. Mean meusurements for the left eye were 19.3±4 mm with the Hertel and 19.6±3.8 with the slit lamp. t test for paired samples did not show statistically significant difference in the measurements between the two methods.
In only 6 out of 120 measurements there was more than 2 mm of difference between the two techniques.

Conclusions: Slit lamp exophthalmometry is a reliable non-touch technique which does not require the use of an exophthalmometer.

DO HIGHER VISUAL AREAS HAVE A ROLE IN THE RECOVERY FROM OPTIC NEURITIS?

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Introduction and Purpose: Despite recovery of standard visual measures, patients after an acute optic neuritis (ON) attack continue to perceive difficulties in performing everyday visual tasks. We previously addressed the possibility that these may be related to deficit in dynamic visual functions. Improvement of vision (i.e. visual acuity) following ON was previously suggested to relate, at least partially, to central reorganization processes. In this longitudinal study we addressed the role of Neuro-plasticity at cortical visual areas in the recovery of both dynamic and static visual functions following ON.

Methods: 21 patients presenting with a first-ever episode of acute unilateral optic neuritis were followed over a year. A set of routine visual tests, visual evoked potentials; optical coherence tomography; and newly developed motion perceptual tasks were assessed repeatedly. Functional MRI (fMRI) examinations were performed to assess the cortical activation associated with static and dynamic visual functions by viewing luminance and motion defined objects respectively. We used different visual stimuli to activated regions along the cortical visual hierarchy; the primary visual cortex (V1), the object-related region (LOC) and the motion-related area (MT).

Results: Four months after the acute phase, a full recovery in cortical activation was found during static object processing. This was evident as opposed to sustained deficit in tasks that require motion perception. A sustained deficit in cortical activation during motion processing was evident even 12 months after the acute phase. These findings are in accordance with our behavioral results, showing a sustained deficit in motion perception throughout the 12 months period, despite recovery of visual acuity, contrast sensitivity and color perception.

Conclusions: Previous studies have suggested that plastic processes in higher cortical regions may contribute to the recovery of visual acuity following optic neuritis. Our results demonstrate that if higher cortical regions contribute to recovery; this may be limited to static visual functions. Alternatively, cortical activation, as shown by fMRI, reflects the visual percept (intact for visual acuity and impaired for motion perception) and do not indicate plastic processes.

NOVEL TECHNIQUE: A PUPILLOMETER-BASED OBJECTIVE CHROMATIC PERIMETRY

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Purpose: To evaluate the objective chromatic visual field of normal subjects, retinitis pigmentosa (RP) and glaucoma patients in comparison to the conventional subjective visual field examination.

Methods: The pupil light reflex (PLR) responses diameters were measured in 13 different points in the visual field. The PRL responses were measures for a short wavelength stimulus (peak 485 nm) and a long wavelength stimulus (peak 620nm), size V, at light intensity of 39.8 cd-s/m2 and duration of 1000 ms. In addition, the following data was collected from each patient: Best-corrected visual acuity (BCVA) with snellen projection charts, measurement of intraocular pressure (IOP), full ophthalmic slit-lamp biomicroscopy, iris architecture, visual field (Hamphry or Goldmann) and refraction.

Results: The RP patient group included 17 eyes of 11 patients and the normal subject group included 25 eyes of 14 subjects. The glaucoma patient group included 6 eyes of 5 patients and the normal subject group included 9 eyes of 6 subjects.The average of the PLR % of change in RP patients was found to be lower than in normals at all respective locations except in the center for the low light intensity short wavelength stimulus ($p<0.05$). The glaucoma group showed more reduced PLR % of change for the high light intensity short wavelength stimulus more profound in the nasal area ($p<0.05$).

Conclusions: The percentage of change of the pupillary light responses was found to be highly reduced in RP patients for the blue stimulus which corresponds with the loss of rods. A marked decrease in the percentage of change of the pupillary light responses to the higher light intensity blue stimulus in the glaucoma group can suggest that the damage in the ganglion cells can be better detected by this stimulus.

”MY FIRST 100”: DSAEK’S LEARNING CURVE

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Introduction and Purpose: Many corneal surgeons are making the transition from penetrating keratoplasty to endothelial keratoplasty in the routine treatment of corneal endothelial failure. Donor dislocation is the commonest complication of these newer techniques. Our aim was to share our experience with the first 100 Descemet’s stripping automated endothelial keratoplasty (DSAEK) surgeries, perioperative complications and their management, highlighting the learning curve.

Methods: A retrospective, single-surgeon, comparative case series from a large teaching and referral center in Israel was conducted. One hundred consecutive cases of DSAEK (n = 100) performed between September 2008 and January 2011 were included. The number of eyes requiring surgical intervention to correct donor dislocation, and the number of eyes with donor endothelial failure within the follow-up period were evaluated. A comparison between the first and the last 50 cases was performed.

Results: The mean follow-up time was significantly shorter for the last 50 cases. Log MAR BCVA improved from 1.02 ± 0.36 to 0.48± 0.36 in the first 50 cases ($p<0.05$) and from 0.93 ± 0.48 to 0.35 ± 0.32 in the last 50 cases. ($p<0.05$) Although the second group included more complicated cases such as the presence of ACIOL, combination of cataract surgery or secondary scleral fixation of IOL, donor dislocation was more common in the first 50 cases (n=10, 20%) versus the last 50 cases (n=5, 10%) (P = 0.26) Primary and late graft failure was diagnosed only in the first 50 cases (n=6, 12%) (P = 0.03)

Conclusions: The learning curve of DSAEK correlate with primary failure and dislocation rate. The number of functional grafts increased with surgical experience, however, BC VA improved significantly regardless the experience gain.

CORNEAL GRAFT FAILURE FOLLOWING ND: YAG LASER DESCEMETOTOMY FOR INADVERTENT RETAINED DESCEMET MEMBRANE FOLLOWING PENETRATING KERATOPLASTY

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Introduction and Purpose: Retained Descemet's membrane (DM) following penetrating keratoplasty (PKP) is a rare finding, which may reduce visual acuity following opacification or endanger the graft endothelium. We report on the association between Nd: YAG laser Descemetotomy and corneal graft failure.

Methods: Five out of 1350 patients (0.37%) undergoing PKP for pseudophakic bullous keratopathy (PBK) or graft failure, between 1986 and 2008, presented with inadvertent retained DM located close to the graft endothelium. The membrane opacified within 3-4 months, reducing the patients' vision. Nd: YAG laser Descemetotomy was performed using low energy and a few pulses.

Results: Patients' visual acuity improved from 6/40 - 6/90 before treatment to 6/15(-) - 6/20 two weeks following Descemetotomy. However, the corneal graft decompensated within 6-8 weeks following this procedure, necessitating repeat PKP, with removal of the retained DM.

Conclusions: Nd: YAG laser Descemetotomy may lead to corneal graft failure due to shock wave damage created by the laser pulses, focused near the endothelial surface.

CORNEAL CROSSLINKING FOR PROGRESSIVE KERATOCONUS IN CHILDREN - OUR EXPERIENCE

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Introduction and Purpose: To assess the effect of corneal crosslinking on progressive keratoconus in children

Methods: In this retrospective study we enrolled 9 eyes of 9 consecutive children aged 11-17 years old who underwent corneal riboflavin-UVA induced crosslinking for progressive keratoconus at the department of ophthalmology at Assaf Harofeh medical center. They were followed for 6-24 months (average 16±8.1 months). Evaluated parameters were uncorrected visual acuity (UCVA), best spectacle corrected visual acuity (BSCVA), manifest refraction, pachymetry, slit lamp examination and corneal topography.

Results: Crosslinking resulted in stability of visual acuity in 7 of the 9 (77.8%) treated eyes. We found a non-significant improvement in UCVA and BSCVA with a small reduction of manifest cylinder. Furthermore, there was an improvement in spherical equivalent that was close to statistical significance ($p=0.07$). There was 0.86 D reduction of average Kmax value post-operatively ($p=0.36$). Most patients (7 of 9, 77.8%) showed a long-term stability or reduction in Kmax.

Conclusions: In this study we demonstrated the efficacy of corneal crosslinking in arresting the progression of keratoconus in children. We believe that larger scale studies in this age group should be performed to further establish the relevance of this technique in children

INTRACAMERAL RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR FOR REFRACTORY FIBRIN REACTION IN TASS

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Introduction: Toxic Anterior Syndrome (TASS) is a rare and devastating complication of intraocular surgery. It is an acute sterile anterior chamber inflammatory reaction that develops hours to days after surgery. The condition is usually responsive to topical steroids, however, resolution of the inflammatory process can be prolonged.

Purpose: This study investigated the effect of recombinant tissue plasminogen activator (r-tPA) in patients with refractory intracameral fibrin reaction after cataract surgery with posterior chamber intraocular lens implantation.

Metohods: In a prospective study, conducted between May 2010 till November 2011, 40 eyes of 40 patients with anterior chamber fibrin reaction after cataract surgery received intracameral injection of r-tPA (25µg /0.1ml). All patients failed to respond to conventional treatment with intensive topical and periocular steroid injection. They were evaluated for recurrence of fibrin reaction or complications by slitlamp biomicroscopy. Intraocular pressure was measured by Goldmann applanation tonometry. Visual acuity was tested using a standard Snellen chart. Corneal endothelial cell counts were evaluated before and after r-tPA injection.

Results: Patients were treated with intracameral injection of r-tPA 20.3 ± 9. 6 days after surgery. 80% of patients had complete clearance of fibrin reaction 1 day following r-tPA injection, and 94.7% had complete resolution 36 days following the injection. Partial clearance of fibrin appeared in 20% of patients.
Visual acuity improved from 0.61 ± 0.38 log MAR to 0.45 ± 0.37 log MAR 1 month following r-tPA injection. (P=0.06)
There were no statistically significant differences between early (10-15 days) (n=16) and late (16-49 days) (n=24) r-tPA injection with respect to visual acuity improvement and fibrinolysis rate.
No patient developed an increase in IOP or endophthalmitis following the procedure

Conclusions: Intracameral application of 25µg r-tPA was a safe and effective method for the treatment of refractory fibrin reaction after cataract surgery.

REMOTE MANIPULATION OF A POSTERIOR LAMELLAR CORNEAL GRAFT USING A MAGNETIC FIELD

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Introduction: Purpose - In DSAEK (Descemet's Stripping Automated Endothelial Keratoplasty) surgery an air bubble is used for attaching the posterior lamellar graft to the recipient's cornea. The disadvantages of using air bubble include direct damage to the graft, the creation of pupillary block, the need for the patient to remain supine for 24 hours as well as other technical difficulties. Early post operative dislocation of the graft is usually treated with reinjection of air bubble beneath the graft, after which the patient should again remain supine for 24 hours. In this study we have examined the feasibility of using a magnetic field for the manipulation of a posterior lamellar corneal graft as an alternative to air bubble.

Methods: Porcine and rabbit posterior lamellar corneal grafts were manually produced and immersed in a ferromagnetic solution containing nano-magnetic particles conjugated to streptavidin and in gadoteric acid, for 5 minutes and up to 24 hours. The grafts were then put in an artificial anterior chamber and were manipulated by a hand-held 20mm NdFeB disc magnet. The study also used biotinylated anti human VEGFR2-KDR/FLK1, and anti human VE-CADHERIN antibodies in an attempt to create a strong and specific bond between the magnetic particles and the target tissue.

Results: The grafts were successfully manipulated in all directions by the magnet, used from a distance of up to 7mm. The grafts remained ferromagnetic more than 24 hours after the immersion in the ferromagnetic solutions. Manipulation strength was affected by the graft shape, immersion time, time from immersion and immersion solution. Adding the above mentioned antibodies to the immersion solution did not have a consistent effect on the possibility of remote manipulation. Adding bovine serum albumin to the immersion solution had almost completely prevented the graft from becoming ferromagnetic.

Conclusions: Posterior lamellar corneal graft can be remotely manipulated by a magnetic field, after its immersion in ferromagnetic solution. This technique may be used in the future for attaching and repositioning grafts in posterior lamellar keratoplasty surgeries such as DSAEK and DMEK. Further research is needed to assess what effects ferromagnetic solutions have on corneal endothelial cells and on the clarity of the lamellar graft.

Financial Disclosure: US patent application relevant to this study was filed by the corresponding author

LATE ONSET TOXIC ANTERIOR SEGMENT SYNDROME: INVESTIGATING A QUIET OUTBREAK

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Introduction and Purpose: To report on 138 cases of late onset Toxic Anterior Segment Syndrome (TASS) after PHACO+PCIOL surgery.

Methods: Retrospective, case-control study. An inclusion criterion was TASS after cataract surgery. Study group (n=138), (125 patients) and Control group (n=149), (103 patients) were compared using clinical files and operational protocols. All surgeries were done at a single center between January 2009 and May 2011. Surgical staff included 13 surgeons and 6 nurses. Pre-operative, peri-operative and post-operative data was compared to a randomly selected control group. Known possible causes for TASS including Sterilization techniques, surgical equipment and topically used medication were thoroughly checked and compared with 13 fellow operating centers. Primary outcome was BCVA at last visit.

Results: Most TASS cases occurred in clusters (82, 59.4%). Incidence rate was 5.9% in 2010. 65 cases (47.1%) were identified during follow up. No TASS was seen in first 24h. 81 patients (58.7%) were asymptomatic. Clinically signs included fibrin without hypopyon. Preoperative evaluation did not revel age, systemic or ophthalmic differences (.681, .234, .704 respectively, $p<.05$). Difficult Surgical course, phacodonesis, pupil size and nucleus hardness were associated with TASS (.001, .021, .001, .000 respectively, $p<.05$). No correlation was found with surgical staff or IOL. BCVA was better in the control group (.000, $p<.05$). No major difference was found during sight- comparison.

Conclusions: Late onset TASS cases were site related, had an indolent appearance and resolved in a decreased BCVA. Although Patient related intra operative difficulties may be related to TASS formation, no single risk factor was found.
Moreover, no correlation was found with previously reported risk factors.

POST OPERATIVE ENDOPHTHALMITIS PREVENTION BY DIFFERENT MOXIFLOXACIN PROPHYLAXIS PROTOCOLS

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Introduction and Purpose: To investigate the ability to prevent post cataract surgery infectious endophthalmitis by different prophylaxis protocols in a rabbit model

Methods: Part A- Endophtahlmitis model: After lens aspiration and hydrophilic acrylic intraocular lens (IOL) implantation, different concentrations of Staph Coagulase Negative (SCN) were injected into the anterior chamber of 19 New Zealand White rabbit's eyes. 24 hours later the eyes were evaluated for endophthalmitis. The lowest concentration that induced endophthalmitis in all the tested eyes were validated in 6 more eyes. Part B: 28 rabbit's eyes were divided into 4 similar groups, after standard cataract surgery. Group A was implanted with a non-presoaked hydrophilic acrylic intraocular lens (IOL) and no intracameral antibiotic injection. Group B was implanted with a non-presoaked hydrophilic acrylic IOL and received an intracameral injection of 100mcg/0.1ml moxifloxacin at the end of the surgery. Group C was implanted with hydrophilic acrylic IOL that was presoaked in moxifloxacin 0.5mg/ml for 15 minutes and n antibiotic injection at the end of surgery. Group D receiv ed both intracameral moxifloxacin injection and presoaked IOL. At the end of all surgeries the lowest concentration of SCN that was found to induce endophthalmitis in part A was injected into the anterior chamber of all the eyes. All the eyes received topical treatment with moxifloxacin eye drops at the day of the surgery. 24 hours after surgery the eyes were evaluated for clinical signs of endophthalmitis.

Results: Part A: 0.1ml of 5X105 CFUs of SCN was found to be the minimum concentration that induced endophthalmitis in 100% of the eyes. Part B: The average infection ocular score was 18.6±1.7 in group A, 14.5±6.8 in group B, 10.6±4.5 in group C, and 12±3.9 in group D. Clinical endophthalmitis was found in 100% of the eyes in group A, 71% in group B, 57% in group C, and 29% in group D. Hypopion was noted in 87% of eyes in groups A, and in 29% of eyes in group B,C and D.

Conclusions: Prevention of post cataract endophthalmitis is possible. Combining intracameral moxifloxacin and short presoaking of hydrophilic acrylic IOL showed the best result.

THE EFFECT OF FIBRIN SEALANT ON CORNEAL ENDOTHELIAL LAYER EX-VIVO

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Background: One of the most promising methods for posterior lamellar keratoplasty, DMEK, has the advantages of good clinical results and low cost. The main difficulty in performing DMEK surgery is spreading the DMEK roll inside the anterior chamber. One method suggested recently is the creation of a DMEK flap with a supportive stromal ring (DMEK-S). The use of a fibrin sealant in the preparation of the DMEK donor graft would create a fibrin scaffold. Fibrin sealant was found to be safe when injected into the anterior chamber in rabbits, but has not been evaluated on dry donor corneas.

Methods: We harvested 66 corneas of 33 pigs, and then applied Evicel fibrin glue on the endothelial surfaces of one cornea of each pair. After removal of the glue, we evaluated the endothelial damage of half by Alizarin Red S 0.2% and Trypan Blue 0.25% staining, and half by specular microscopy examination performed daily for a week. The staining was evaluated by photography and the stained areas quantified using Image-Pro Plus Ver.6.1. Two corneas were evaluated by histological examination.

Results: 15.5% ± 9.3% of the total endothelial corneal surface in the Evicel group was stained compared to 2.7% ± 2.4% in the matched control corneas ($P<0.001$). There was no significant difference in the specular microscopy values between the two groups. Histologic examination suggested small attachment areas that caused endothelial edema.

Conclusions: Evicel attaches to the cornea in supposedly dry areas; its manual removal causes damage to the corneal endothelium. The use of fibrin sealant on corneal endothelium should be further examined In-Vivo.

SPLIT EYES, SPLIT BRAIN AND SPLIT ATTENTION IN THE COMMON CHAMELEON

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Introduction: Chameleons (Chamaeleo spp.; Chamaeleonidea, Reptilia) are arboreal lizards that forage visually for insect prey, using ”sitslow move and wait” tactics. Once prey is detected, their eyes converge, the tongue is loaded onto the hyoid (”initial protrusion”), distance is visually estimated and the tongue is shot at it. Chameleons’ eyes are highly mobile performing large amplitude, independent, saccadic movements while scanning. At any given time only one eye is accommodated, while the other is in a hyperopic, resting, refractive state. Attention switches between the eyes while they scan regions opposite one another. The optic nerves of chameleons are fully decussated and inter-tectal connections are not well developed. This may imply that the gathering of visual information and its processing is different from that of mammals. How, under such conditions, is a ”visual world” built? How do the eyes function when each needs to track a di fferent stimulus?

Aims: To determine (1) eye functioning under ”split target” conditions, (2) if eye use is lateralized.

Methods: Common chameleons (C. chameleon) were trained to respond to computerized prey model on an LCD screen. Subsequently, ’split target’ tests were performed: the chameleon’s attention was drawn to a single primary target at the centre of the screen and once it had achieved IP (implying that both eyes had received similar visual information), the target was split into two targets. These targets were identical or different in their parameters (size, contrast, velocity, etc.). The chameleon’s choice of target and its eye movements were analyzed to determine direction of attention and motor patterns.

Results: (1) The chameleons performed simultaneous tracking of two targets (similar or different in their parameters) - one target with each eye. (2) The left and the right eyes were not identical in their responses while tracking of ”split targets” that underwent a change in size.

Conclusions: (1) This is the first report of chameleons’ predatory responses to computerized ”prey”, (2) This is the first report of the capacity of chameleons to simultaneously track 2 targets and of lateralization under these conditions.
The research is supported by a grant from the Israel Science Foundation (ISF).

AMBIENT LIGHT INTENSITY OF FLUORESCENT VERSUS INCANDESCENT LIGHT AND THE EMMETROPIZATION PROCESS OF THE CHICK'S EYE.

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Introduction and Purpose: Chicks' emmetropization is dependent on the intensity of ambient incandescent (IC) illumination (Cohen et al., 2011). Myopia, emmetropia and hyperopia develop following 80 days of exposure to 50, 500, and 10 000 lux of light-dark cycle conditions (delineated throughout as low-, medium-, and high-light intensities, respectively). Fluorescent (FL) light, commonly used for indoor lighting, has a different characteristics from incandescent (IC), lighting, such as photon source, continuity of photon emission, and spectral light distribution. In this experiment, we evaluated the effect of ambient light intensity of FL light on chicks' emmetropization, and compared the developing refractions of chicks reared under IC or FL lighting.

Material and methods: Newly hatched white leghorn chicks were raised under FL light (low-, n=18; medium-, n=16; high-, n= 16, intensity of light, respectively). Streak retinoscopy, keratometry, and b-scan ocular ultrasound were sequentially performed from 10 until 90 days post-hatching. Refractive development data under FL light was compared to IC light data (low, n=13; medium, n=14; high, n= 13, intensity of light, respectively) previously reported (Cohen et al., 2011).

Results: The refractions correlated with log intensity of FL light (day 20 $r=0.75$, $p<0.0001$; day 90 $r=0.92$, $p<0.0001$). Under both FL and IC light, lower the ambient light intensity was associated with longer axial lengths, corneal flattening, lens thinning, and deepening of both anterior and vitreous chambers. After 90 days, all chicks exposed to low intensity of FL light developed myopia, with a mean refraction of -1.86±1.1 diopter (D), as compared to -2.4±1.2 D under low intensity IC light ($p=0.09$). High intensity FL light resulted in slower ocular growth and a mild hyperopic refraction. On day 90, the hyperopia developed under high intensity of FL light was 0.6 D greater than the hyperopia measured under high intensity of IC light ($p<0.0001$).

Conclusions: Chicks' emmetropization is influenced by the ambient intensity of both FL and IC light, with minor refractive differences under high intensity light. Like IC light, high and low intensities of FL light are associated with the development of hyperopia and myopia, respectively.

VISUO-MOTOR "STATION-KEEPING" AND LATERALIZED DETOUR BEHAVIOUR IN THE COMMON CHAMELEON

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Introduction: Chameleons (Reptilia) are slow moving arboreal lizards with large amplitude, highly independent eye movements, allowing rapid shifting between monocular and binocular vision., Their optic nerves, typical of reptiles, undergo full decussation with visual information from each eye is conveyed to, and processed by, the contra-lateral optic tectum, with minimal inter-tectal connections. When holding onto a vertical pole and facing a horizontally moving threat, chameleons smoothly change position so as to keep in a position ~180° to the threat., This visually guided concealment is performed from hatching and differs markedly from patterns while coping with obstacles during prey approach.
Aims: To analyze (i) Visuo-motor patterns in avoidance and their compliance with "station keeping", (ii) Eye use in detour behavior and it possible lateralization.

Methods: (i) Common chameleons (Chamaeleo chameleon, n=2, 2 month old) were subjected to a threat stimulus, while perched on a vertical pole. The threat was moved at an arc of 80° and at angular velocities 15°, 35° and 70°/sec. Video analysis of 3 response parameters was conducted; (1) α- head angle from threat to the sagittal axis on the chameleon's head, (2) β - head angle from threat to the sagittal axis on the chameleon's head - through the perching pole, (3) response latency (ii) Chameleon were tested on detouring an obstacle in a Y-maze, to reach food. Directions of detour eye use were analyzed.

Results: (i) in avoidance, the chameleons maintained angles α and β highly stable under all 3 angular velocities,(ii) Detour direction was lateralized at the individual level. Eye use was lateralized at the population level, with significantly longer durations of viewing the target with their right eye.

Conclusions: Chameleons' avoidance response conforms with "Station Keeping". This to our knowledge is the first description of its kind in a vertebrate. The capacity to "keep station" at high velocities may well exceed velocities that lead to visual blur. In detour, the chameleon preferred right eye use complies with known left hemisphere use in food related tasks. Different patterns of eye use in detour are discussed.

LATE PROPRANOLOL TREATMENT OF INFANTILE PERIOCULR CAPILLARY HEMANGIOMA BEYOND PROLIFERATIVE STAGE: FUNCTIONAL AND STRUCTURAL CHANGES

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Purpose: To evaluate the anatomical and refractive effects of oral propranolol therapy for infantile periocular capillary hemangioma (IPCH) beyond the proliferative phase.

Methods: A retrospective, comparative, interventional study of fourteen children (3 male, 11 female) aged ≥12 months diagnosed with IPCH was conducted from September 2009 to August 2011 at a tertiary pediatric medical center. They underwent evaluation by a pediatrician, pediatric-cardiologist, ophthalmologist, dermatologist, and orthoptists. Medical followup was performed regularly until the lesion disappeared. Changes in the anatomical extraocular extension, refractive sphere and cylindrical power, axis, and spherical equivalent in the involved eye and between the two eyes before and after treatment were evaluated.

Results: Mean age was 24.9±11.4 months at initiation of treatment and 37.9±12.7 months at the end. The lesions affected the right eye in 57.1% and were located preseptally in 78.6%. Six patients (42.4%) received steroids before propranolol. A fixed dosage of 2 mg/kg/day was started and continued in 12/14 patients (86%). Side effects occurred in 3 patients (21.4%), necessitating a dose reduction in one and discontinuation of treatment in one. The following findings were statistically significant: mean reduction in diseased extraocular area after treatment (p=0.03); difference in absolute mean spherical power in the involved eye from before to after treatment (p=0.03); difference in absolute mean spherical power in the involved eye from before to after treatment (p=0.03); difference in percentage of spherical power and in absolute power between the eyes from before to after treatment (p=0.05, p=0.03); difference in mean cylinder power and in absolute power between the eyes before treatment (p=0.034 for both) (but not after treatment); difference in percentage of cylinder power between the eyes from before to after treatment (p=0.05); difference in percentage of spherical equivalent between the eyes and in absolute difference in percentage from before to after treatment (p=0.051, p=0.021).

Conclusions: Treatment of IPCH with systemic oral propranolol after the proliferative phase induces a significant reduction in the diseased periocular area, spherical power, astigmatism, and spherical equivalent. It prevents amblyopia and ocular/facial deformation without rebound. Propranolol is recommended as the preferred therapy for IPCH, even in the late stage.

HIGH MYOPIA CAUSED BY A MUTATION IN LEPREL1, ENCODING PROLYL 3-HYDROXYLASE 2

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Purpose: To investigate clinical characteristics and molecular basis of high myopia in large consanguineous Bedouin kindred in south Israel.

Methods: Thirteen affected and 32 unaffected individuals of a consanguineous Bedouin tribe were subjected to a complete ophthalmologic examination followed by molecular genetic analysis.
Genome-wide linkage analysis was undertaken on DNA samples using microsatellite markers. Fine-mapping was carried out using polymorphic markers. Sequence analysis was performed on the coding regions and intron-exon boundaries of the 6 genes within the linked locus. Functional consequences of the found gene mutation were tested by analyzing the activity of wild-type and mutant human protein expressed in an insect cell.

Results: The pedigree indicated an autosomal recessive inheritance. All affected individuals presented with axial myopia since childhood (mean spherical equivalent -11.3 diopters; eye axial length 25.1- 30.5 mm). Eleven patients developed cataract which warranted surgery in the first or second decade of life. In three patients, subluxated lenses were detected. Peripheral vitreo-retinal degenerative changes were found in 9 patients. Four patients developed rheumatogenous retinal detachments leading to blindness in three of them (23% of affected individuals).
The disease-associated gene was mapped to ~1.7 Mb on chromosome 3q28 (maximum LOD score 11.5). Sequencing of the 6 genes within the defined locus identified a single mutation c.1523G>T in LEPREL1 in all affected individuals and not in 200 ethnically matched controls. LEPREL1 encodes prolyl 3-hydroxylase 2 (P3H2) involved in post-translational modification of collagen. The mutation results in a glycine-to-valine substitution at amino acid 508 (conserved) of P3H2. Functional assay revealed that the p.Gly508Val mutation led to complete inactivation of the recombinant P3H2 polypeptide expressed in insect cells.

Conclusions: In large consanguineous Bedouin kindred severe axial myopia was associated with variable expressivity of juvenile cataract and vitreoretinal degeneration leading to blindness in 23% of the patients. This is a first identification of a gene whose mutation is associated with monogenic recessive heredity of myopia.
Our findings demonstrate a significant role of LEPREL1 and collagen hydroxylation in the molecular pathways of ocular growth and development of myopia.

THE EFFICACY OF TINTED CONTACT LENSES IMPROVING PHOTOPHOBIA AND VISUAL FUNCTION IN PATIENTS SUFFERING FROM LOW VISION

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Introduction and Purpose: Our main aim was to determine objective improvement given by tinted contact lenses on visual acuity, contrast sensitivity, nystagmus and quality of life in patients with retinal diseases.

Methods: We herein describe ten patients, all with significant photophobia, poor visual acuity, whom tinted hydrogel contact lenses were successfully fitted. All patients were fitted with CD 60 Filcon ll 2, non-ionic, 60% water content contact lens (Soflex Ltd. Mishgav Industrial Park, Israel). Patients underwent a full eye examination with and without contact lenses, including visual acuity for near and distance, contrast sensitivity, EMR (Eye Movement Recording for nystagmus), refraction and fundus examination. The patients completed a quality of life questionnaire.

Results: All patients (aged 15 to 22) demonstrated improvement of binocular visual acuity as well as significant improvement in contrast sensitivity with the tinted contact lenses. Nine from ten patients improved monocular visual acuity with the contact lenses. Regarding EMR, one patient had significant improvement recordings using contact lenses, while the others did not show any improvement. Subjectively all the patients described a striking improvement in their photophobia both outdoors and indoors and a marked improvement in quality of life.

Conclusions: Tinted contact lenses have demonstrated a striking improvement in quality of vision and quality of life in patients suffering from retinal diseases causing low vision and glare. These lenses should be a part of the regular assessment in specific clinics treating patients with low vision, and considered an important visual aid that can dramatically improve visual function in visually impaired population.

HANG-BACK VERSUS CONVENTIONAL MEDIAL RECTUS RECESSION FOR THE CORRECTION OF INFANTILE ESOTROPIA

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Introduction and Purpose: To compare surgical outcome of Hang-Back and Conventional Bimedial Rectus Muscle Recession in Infantile Esotropia.

Methods: The charts of 67 consecutive patients with infantile esotrpia who underwent bilateral medial rectus muscle from 1990 through 2005 were retrospectively reviewed. Thirty patients were operated by hang-back technique (group 1) and 37 by conventional bimedial rectus recession (group 2). In each group the angle of esotropia (PD (prism diopers)) before and 6 months after surgery and the success rate (deviation of ≤ 10 PD) were documented.

Results: Esotropia improved an average of 39.7 ± 14.9 PD in group 1 (from a preoperative 42.7 ± 11.6 PD to 3.0 ± 8.5 PD postoperatively) and 45.5 ± 19.3 PD in group 2 (from a preoperative 54.3 ± 16.8 PD to 8.7 ± 12.1 PD postoperatively) (p=0.18, independent sample t-test). Success rate (defined as deviation of ≤ 10 PD at 6 months postoperative examination) was 83.3% in group 1 and 70.2% in group 2 (p=0.21, chi-square). Multivariate logistic regression suggests that surgical outcomes are not significantly influenced by age and preoperative angle of esotropia. No complications occurred in both groups.

Conclusions: Hang-back technique is as effective as the Conventional Bimedial Rectus Muscle Recession in correcting infantile esotropia.

IN VITRO CONTROL OF AN OPTOGENETIC NEURAL PROSTHETIC FOR A BLIND RETINA

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Introduction and Purpose: In cases of outer retinal degeneration diseases, optogenetic stimulation may be used as an alternative to electrical stimulation for temporally precise, minimally-intrusive control of retinal ganglion cells (RGCs). The technique is attractive in visual neuroprosthetics development since the optics of the eye may be utilized for optimal pattern delivery onto the damaged retina. We have previously presented a novel optical approach based on a digital holographic projection that is capable of eliciting thousands of spikes per second, with millisecond timing precision in light sensitive neurons. The objective of this study was to examine the optimal conditions for robust control of RGCs using photo-stimulation.

Methods: A spatial light modulator (SLM)-based system was used to optically drive neural activity of Channelrhodopsin-2 (ChR2) expressing RGCs in a mouse model of retinal degeneration. To gain a better understanding of RGCs' optogenetic control, blind artificially light-sensitive retinas were stimulated with a diversity of holographic light patterns and their responses were recorded using a Multi-Electrode Array (MEA).

Results: In this study we focused on extraction and examination of conditions for efficient and robust optical control of RGCs utilizing the holographic projection system. We show that the precision of ChR2-expressing RGCs activity is strongly dependent on the amount of light delivered to the cell's membrane. This can be adjusted by a modification of the spot size and the intensity of light delivered by the projected spot. Both can be easily tuned using our holographic projection system.

Conclusions: Our results, together with further investigation of optogenetic control properties, can advance the development of a non-contact retina neuroprosthetic device which allows activation of multiple RGCs with high spatial and temporal precision.

THE FUNCTIONAL ROLE OF CONTACTIN ASSOCIATED PROTEIN IN THE MOUSE RETINA

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Introduction and Purpose: Contactin associated protein (CASPR) is part of the axon-glial paranodal complex that defines the boundaries of the node of Ranvier (NOR). CASPR knockout (KO) mice show reduced concentration of sodium voltage gated channels (Na+v) in the NOR together with altered distribution pattern of Na+v subtypes. Recently, positive immunohistochemistry (IHC) staining for CASPR was found in the retina. Since the retina is unmyelinated and has no NORs, the functional role of CASPR in the retina is unclear. The purpose of this study was to evaluate the functional role of CASPR in the mouse retina and the effect of retinal CASPR on Na+v localization and subtype distribution in the retina.

Methods: CASPR KO and wildtype mice, 40 and 90 days old, were studied using dark and light adapted full field flash electroretinogram (FERG) and pattern ERG (PERG). IHC for CASPR, Na+v1.2 and Na+v1.6 was performed on cryo-sections. Retinal ganglion cell (RGC) counts were performed on fluorogold labeled flatmounts.

Results: Preliminary IHC results show reduced expression of Na+v1.6 in the nerve fiber layer (NFL) and retinal ganglion cell (RGC) layers, and elongation of Na+v1.2 positive neuronal extensions from the RGC to the inner plexiform layer. Preliminary RGC counts were similar between groups. Dark and light adapted FERG amplitudes and implicit times were similar between groups (t-test, $p>0.05$) except for a-wave amplitudes of dark adapted 90 days old KO mice, in response to highest flash intensity, where 20.9% attenuation ($p=0.02$) was shown. PERG P1 and N2 amplitudes of CASPR KO mice showed a significant attenuation of 41 and 49% respectively ($p<0.0003$). There were no significant differences between the groups in PERG implicit times ($p>0.19$).

Conclusions: Attenuation of mixed rod-cone a-wave amplitudes, in conjunction with normal photopic FERG responses, may reflect impaired recovery of rods in CASPR KO mice. Attenuated PERG responses, in conjunction with normal photopic FERG responses, in CASPR KO mice indicate possible RGC dysfunction or loss in these animals. Based on preliminary RGC counts, it seems that our ERG findings are explained by RGC dysfunction, rather than loss. As RGC and NFL are the main sites of Na+v activity, our results indicate possible changes in Na+v expression or distribution in these layers.

ROLES FOR PAX6 IN THE MELANOGENESIS OF THE RETINAL PIGMENTED EPITHELIUM IN MICE

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Introduction: The ocular pigmented epithelium (PE) of the optic cup differentiates to the retinal pigmented epithelium (RPE) and components of the iris and ciliary body. Defects in PE tissue types dramatically hamper ocular physiology and are associated with diseases leading to blindness in humans. Pax6 is dynamically expressed in the PE progenitors and detected in a subtype of PE cells in the adult eye. It was previously demonstrated that Pax6, together with Pax2, are required for an early step in the specification of PE cell types. However, Pax6's role after the specification was not resolved. To discover the roles of Pax6 in the differentiation of the prospective PE to RPE cells we performed conditional elimination of Pax6 using the DctCre transgene, in which Cre is expressed in the developing pigmented epithelium after the specification. This inactivation resulted in microphthalmia, lack of anterior ocular structure, and surprisingly a dramatic reduc tion in the pigmentation of the RPE without altered specification. Molecular analysis revealed a reduction in the expression of key genes that are involved in melanogenesis including Mitf D, the RPE specific Mitf isoform, Tyrosinase (Tyr) and Tyrosinase related protein 1 (Tyrp1). Analysis of Mitf D knock out mice suggests that reduced RPE pigmentation in Pax6 mutants cannot solely be attributed to lower Mitf D expression. In summary, this study reveals the role of Pax6 in ocular melanogenesis by the regulation of key melanogenic genes during early stages of RPE differentiation.

THE ROLES OF PAX6 DURING LATE STAGES OF MAMMALIAN RETINOGENESIS

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Introduction: Objective: The transcription factor Pax6 is the key regulator of eye development, as it is essential for eye formation in different organisms as well as sufficient to induce ectopic eyes in flies and frogs upon misexpression. Moreover, the correct dosage of Pax6 is crucial for normal eye development. Previous studies revealed dual role for Pax6 in retinal progenitor cells (RPCs): RPCs located in the peripheral optic cup require Pax6 for inhibition of the photoreceptor transcription factor Crx and for completion of neurogenesis, while RPCs located more centrally require Pax6 for their multipotency, but not for completion of neurogenesis. The goal of this study is to unravel the roles of Pax6 in the specification of late-born retinal cell types and to determine the molecular mechanisms underlying these activities.

Methods: The in vivo electroporation technique was employed to misexpress Pax6 variants in the neonatal retina (postnatal day 0, P0), in the late-born RPCs. The retinal phenotype was determined after completion of retinogenesis (P14) using immunohistochemistry for detection of specific retinal cell types.

Results: Elevation of Pax6 in the postnatal retina resulted in malformation of outer segments of photoreceptors and a change in the location of cell bodies within the photoreceptor layer. In the inner nuclear layer (INL), Pax6 elevation caused a change in cell-type specification towards generation of a subtype of amacrine interneurons at the expense of other late-born retinal cell types.

Conclusions: Our findings reveal roles for Pax6 during the differentiation of late-born retinal lineages including the photoreceptors and amacrine subtypes.

THROMBIN AND ACTIVATED PROTEIN C (APC) INDUCE OPPOSITE EFFECTS ON RPE PERMEABILITY

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Introduction: Thrombin and activated protein C (APC) are serine proteases that play central roles in coagulation. In addition to their opposite effects in the plasma (thrombin–procoagulant and APC-anticoagulant), both proteins were found to induce significant opposite effects on endothelial cells. Thrombin increased endothelial permeability, while APC was found to exert a protective effect on the endothelial barrier. Retinal pigment epithelium (RPE) forms the outer blood retina barrier (oBRB), and its integrity is essential for normal retinal function. BRB integrity is maintained by a series of tight junction proteins (TJ) that control the intercellular space and the transport from the choroid to the retina. Retinal pathological conditions such as diabetic retinopathy, inflammation, vascular occlusions and surgical complications have been observed to be accompanied by elevation in thrombin levels.

Purpose: To investigate whether thrombin and APC affect the pathogenesis of retino choroidal vascular disorders. To study the effects of thrombin and APC on the RPE function, permeability, and expression and distribution of TJ proteins. To study the involvement of permeability induced factors (VEGF, FGF, PEDF) in thrombin and APC activity.

Methods: ARPE-19 cells were grown for one month to obtain definite polarity properties. The expression of permeability and TJ genes was evaluated using real time PCR. Permeability was evaluated based on spectrophotometric assay. Intracellular localization of TJ proteins was studied using immunohistochemistry staining. Actin polymerization was visualized using Phalloidin staining. VEGF protein level was measured by ELISA.

Results: Thrombin and APC exerted opposite effects on RPE cells. Thrombin induced increased permeability, disrupted the actin structure, increased the levels of VEGF and FGF and decreased the level of PEDF. In contrast, APC induced a decrease in RPE permeability. In addition, APC induced translocation of ZO1 (TJ protein) to the membrane, decreased the level of VEGF and increased the level of PEDF.

Conclusions: The data indicate that exposure of RPE to thrombin or APC leads to either disruption or improvement, respectively, of the barrier functions. Thrombin elevation in retinal pathologies may partially contribute to BRB failure. APC seems to tighten the RPE barrier. Further investigation is required to clarify the potential benefit of APC as an optional treatment for RPE leakage.

A NEW TECHNIQUE FOR EXPERIMENTAL CREATION OF CHOROIDAL NEOVASCULARIZATION (CNV) IN PIGMENTED MICE USING INDIRECT DIODE LASER

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Purpose: CNV creation in animal models is an essential tool for investigation of various aspects of the pathophysiology and of the different treatment modalities of many chorioretinal diseases. These models should be efficient, reproducible and stable over-time. The most popular mice-model for CNV is currently based on disruption of the Bruch's membrane with the usage of a direct-laser beam. The use of this immobile laser is difficult to attain and is very much inconvenient for research proposes.
The work consisted of 2 purposes: the first was to create an easy to use laser-induced lab model of CNV in pigmented mice using an indirect-diode laser. The second was to determine the settings of the physical parameters of the treatment lens and laser beam that will ensure a consistent model of CNV creation.

Methods: Determinations of dioptric power of treating lens, treatment distance and energy density of the indirect diode laser (Oculight SLX ©, Iris medical) to induce CNV were made using standardized black photo paper (AGFA©,Agfa-Gevaert,N.V.,Belgium). Thirty eyes of 30 pigmented male mice (CD57BL/6J strand) were then treated at 6 spots around the optic disc, using laser power values between 200-800mW and durations of 100-200 msec. Eyes were enucleated after 2 weeks. Thin frozen sections were made and stained with Hematoxylin & Eosin to demonstrate CNV. CNV was also confirmed by fluorescein angiography.

Results: The 90D lens yielded the best linear correlation between the laser power, the duration of application and white spot number, and was chosen as the treatment lens. Suprathreshold energy levels were shown to induce tears of the Bruch's membrane and immediate bleeding, which ultimately resulted in scar formation. When subthreshold levels were applied, no lesion formation was observed. FA demonstrated the presence of CNV when laser was applied at the range of 200-400 mW for 100-200 msec. H&E staining confirmed CNV formation at the sites of laser applications.

Conclusions: Preliminary results show that indirect diode laser application is capable of CNV formation in pigmented mice. Thus, the indirect laser can be potentially used for animal models. Further work should be done in order to standardize the laser parameters.

PREVALENCE AND RISK FACTORS FOR CHOROIDAL NEVI USING OPTOS SCANNING LASER OPHTHALMOSCOPE

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Introduction and Purpose: Choroidal nevi (CN) are a common incidental finding in many fundus examinations and the clinical significance relates to their rare potential for malignant transformation. Reported nevus prevalence rates vary widely (0.2%-30%; e.g. Greenstein et al., 2011). However, most studies have been from autopsy series or clinic-based studies and have used fundus camera for imaging only 35-70° of the retina after pupil dilation.
This study aims to determine the prevalence and risk factors, associated with CN, using the Panoramic 200 Scanning Laser Ophthalmoscope (Optos plc, Dunfermline, UK), which can capture up to 200º view of the retina, without pupil dilation.

Methods: A large cohort of healthy students was recruited from the student body of Hadassah Academic College. Preliminary analysis was carried out on the first 151 subjects (47 men, 104 women, average ages 23.60±4.99).
Images from each eye were obtained using the Optos along with a visual assessment. Each Optomap image was examined independently by 3 experts to assess for CN. Subjects were asked to complete a self administered questionnaire covering socio-economic status, ethnicity, medical and eye health history. Hair, eye and skin pigmentation was assessed using previously reported methodology. Prevalence was calculated, and control and nevi cohorts were compared using chi-square analysis.

Results: 15 subjects (9.9%) had one or more CN. Nevus prevalence was lower in women than men (5.8% vs. 19.1%, $p<0.001$). 12 subjects had a nevus in only one eye and three had bilateral nevi. Multiple Nevi were observed in five subjects.
Nevus was found to be more prevalent in subjects with blond hair than in brown/black hair (18.2% vs. 7.8%, $p<0.01$) and in green/blue eyes than in brown/black eyes (10.2 vs. 9.1%, $p<0.01$).
There was no statistically significant difference in visual acuity between the two groups.

Conclusions: We found high prevalence of CN using the Optos. Nevus was found to be more prevalent in men and in subjects with light pigmentation. The presence of CN does not adversely affect visual acuity. Further analysis of the large cohort is required to assess for risk factors in terms of ethnicity, lifestyle and health.

Notes: