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

# PROGRAM & ABSTRACTS

## 35th Annual Meeting

Avenue Congress Center, Airport City

11th-12th March, 2015

# תכנית ותקצירים

## הכינוס השנתי ה-35

## מרכז הכנסים Avenue, קרית שדה התעופה

## 11-12 במרץ, 2015

**עריכת התוכנית:**

**פרופ' אבי סלומון, דבורה מרקס-אוחנה**

**מזכירות הכנס:**

**עיצוב והבאה לדפוס:** יעקב אלבז, דבורה מרקס אוחנה

**ISRAELI SOCIETY FOR VISION AND EYE RESEARCH**
**The 35th Annual Meeting, March 11-12, 2015**
**Program at a glance**

## Wednesday, March 11th , 2015

| Session | Location | Time | Page |
|---|---|---|---|
| Coffee & Exhibition | Exhibition Hall | 08:00 – 08:30 | 14 |
| Opening Remarks | Lecture Hall | 08:30 – 08:35 | 14 |
| Retina 1: Retinal Cell Biology | Lecture Hall | 08:35 – 10:15 | 14 – 19 |
| Coffee & Exhibition | Exhibition Hall | 10:15 – 10:45 | 19 |
| Oncology | Lecture Hall | 10:45 – 11:30 | 20 – 21 |
| Guest lecture 1: Simon Benita | Lecture Hall | 11:30 – 12:00 | 22 |
| Guest lecture 2: Yoram Ben Shaul | Lecture Hall | 12:00 – 12:30 | 22 |
| Lunch break | Dining Room | 12:30 – 13:30 | 22 |
| Cornea | Lecture Hall | 13:30 – 15:15 | 23 – 27 |
| Coffee & Exhibition | Exhibition Hall | 15:15 – 15:45 | 27 |
| Retina 2: Clinical Studies, Imaging & Function | Lecture Hall | 15:45 – 17:00 | 28 - 30 |

## Thursday, March 12th , 2015

| Session | Location | Time | |
|---|---|---|---|
| Coffee & Exhibition | Exhibition Hall | 08:00 – 08:30 | 31 |
| Retina 3: Retinal Degenerations | Lecture Hall | 08:30 – 10:00 | 31 – 35 |
| Coffee & Exhibition | Exhibition Hall | 10:00 – 10:30 | 35 |
| Retina 4: AMD | Lecture Hall | 10:30 – 11:10 | 36 – 37 |
| Guest lecture 3: Rony Paz | Lecture Hall | 11:10 – 11:40 | 37 |
| Awards & ISVER update | Lecture Hall | 11:40 – 12:00 | 37 |
| Guest lecture 4: Gideon Amichay | Lecture Hall | 12:00 – 12:30 | 37 |
| Lunch break | Dining Room | 12:30 – 13:30 | 37 |
| Glaucoma | Lecture Hall | 13:30 – 14:10 | 38 – 39 |
| Cataract & Refractive Surgery | Lecture Hall | 14:10 - 15:00 | 39 – 40 |
| Coffee & Exhibition | Exhibition Hall | 15:00 – 15:30 | 40 |
| Visual Perception | Lecture Hall | 15:30 – 17:00 | 41 – 43 |

## יושבי-ראש של האגודה הישראלית לחקר העין והראייה

**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 ז"ל** |
| **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** |
| **Prof Avi Solomon** | **2012** | **פרופ' אבי סלומון** |

ARVO CHAPTER AFFILIATE

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

## BOARD MEMBERS OF THE ISRAEL SOCIETY FOR VISION AND EYE RESEARCH

| | |
|---|---|
| **Prof. Avi Solomon – Chairman** | **פרופ' אבי סלומון - יו"ר** |
| **Prof. Jacob Pe'er – Treasurer** | **פרופ' יעקב פאר - מזכיר-גזבר** |
| **Prof. Ehud Assia** | **פרופ' אהוד אסיה** |
| **Prof. Ruth Ashery-Padan** | **פרופ' רות אשרי-פדן** |
| **Prof. Tamar Ben-Yosef** | **פרופ' תמי בן יוסף** |
| **Prof. Goldenberg- Cohen** | **פרופ' ניצה גולדברג - כהן** |
| **Prof. Itay Chowers** | **פרופ' איתי חוברס** |
| **Dr. Hani Levkovitch-Berbin** | **ד"ר חני לבקוביץ – ורבין** |
| **Prof. David Zadok** | **פרופ' דוד צדוק** |
| **Prof. Igor Kaizerman** | **פרופ' איגור קייזרמן** |

ARVO CHAPTER AFFILIATE

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

## מרצים המקבלים השנה פרס על עבודות שהוצגו בכנס השנה שעברה (הכנס ה-34, 26-27 במרץ 2014)

## Award Recipients for the Best Papers Presented at the Previous Annual Meeting (the 34th Meeting, March 26th-27th 2014)

מלגות נסיעה ל- ARVO ניתנות בעזרת מענקים שנתרמו באדיבות עמותת "לראות" (מלגות 1-2); ובאדיבות משפחת מרין לזכרו של פרופ' שאול מרין ז"ל (מילגות 3-4).

1. **Raaya Ezra-Elia**: Cone function in normal and day blind sheep. A large animal model fro CNGA3 achromatopsia patients.
   *Koret School of Veterinary Medicine, Hebrew Univeristy, Rehovot, Israel.*
2. **Dan Heller**: Digoxin derivatives with selectivity for the α2 isoform of Na,K-ATPase efficiently reduce intra-ocular pressure.
   *Department of Ophthalmology, Asaf Harofeh Medical center, Zerifin.*
3. **Orly Gal-Or**: Efficacy of subconjuctival Aflibercept Versus Bevacizumab for corneal neovascularization in a rat model.
   *Department of Ophthalmology, Rabin Medical Center, Petah-Tikva.*
4. **Samer Khateb**: A nonsense mutation in CEP250, a mammalian-specific homolog of Rootletin, causes a new type of Usher syndrome.
   *Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem.*

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

ARVO CHAPTER AFFILIATE

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

# תודה לעמותת "לראות"

לראות

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

## תודה לחברות שתרמו לכינוס
## Thanks to the sponsoring companies

LAPIDOT MEDICAL

TRADIS GAT
רואים את האיכות בעיניים

Johnson & Johnson
Vision Care

KIEMA
איכות בבריאות

NOVARTIS
PHARMACEUTICALS

tzamal
צמל 2B טכנולוגיות רפואיות בע"מ

BAYER
Bayer

# אודות עמותת "לראות"

## מטרות עמותת "לראות"

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

## בין יזמות עמותת "לראות" בשנת 2014

**"אל תעצמו עיניים, היבדקו למניעת עיוורון" -** חודש מודעות לבריאות העין השישי שכלל בדיקות ראיה ללא עלות בכל רחבי הארץ, יעוץ רפואי טלפוני, הפצת מוסף בריאות העין שהתמקד בנושא AMD והופץ בתפוצה ארצית עם ישראל היום לצד קמפיין בתקשורת.

**"פרויקט הניידת לבדיקות עיניים של קשישים נזקקים"** – קרוב ל 4000 קשישים נבדקו במרכזי יום, בתי אבות מתנ"סים במסגרת ימי בריאות במרפאות קופות החולים. ניתן לסכם שקרוב ל13% מהנבדקים, ניצלו מסכנת עיוורון עקב האבחון הרפואי על ידי רופא עיניים מפרויקט הניידת לבדיקות עיניים של קשישים , בקרב אוכלוסייה שלא מגיע בכוחות עצמה לטיפול רפואי. רבים הופנו להמשך טיפול רפואי בקופות החולים.

**מחקר מיפוי גנטי של חולים במחלות ניווניות ברשתית** –קונסורציום של 11 מרכזים באוניברסיטאות ובתי חולים בארץ, הכוללים 6 מרכזים גנטים, 4 מרכזים לאלקטרופיסיולוגיה קלינית של הראיה ומרכז לביואינפורמטיקה המשתפים פעולה בפרויקט ייחודי בעולם למיפוי תפקודי וגנטי של מרבית החולים בארץ במחלות תורשתיות של ניוון פוטורצפטורים ומטרתו לקדם רפואה אישית המותאמת לחולה.

# תכנית לשנת הפעילות 2015

## <u>פעילות שוטפת</u>

1. תכנית למימון מחקרים במוסדות מחקר רפואיים בישראל ובארה״ב
2. מתן יעוץ רפואי ב-5 פורומים של רופאים מומחים ומנהלי מחלקות עיניים
3. ארגון חודש המודעות ה- 7 לבריאות העין
4. ניידת בדיקות עיניים לקשישים נזקקים
5. גיוס חולים למחקר מיפוי גנטי של מחלות רשתית

## <u>פרויקטים מתוכננים</u>

1. קידום פעילות סקר ראיה לילדים עם הפוטו סקרינר
2. המשך גיוס משאבים למחקר רפואי בארץ ובחו״ל
3. הקמת אתר חדש לחולי RP ומשפחותיהם כולל פורום יעוץ רפואי.
4. קידום כנסים של במיזמים אופתלמולוגים בישראל ובחו״ל.

## <u>המועצה המדעית של עמותת ״לראות״</u>

מורכבת מרופאים וחוקרי עיניים מהשורה הראשונה בישראל וגורמים 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 מחקר בינלאומית.


## המחקרים הממומנים בעזרת עמותת "לראות" ב-2014

השנה כ-12 מחקרים קבלו מימון כתוצאה מפעילות עמותת "לראות". בין החוקרים המקבלים מענקי מחקר של המדען הראשי במשרד הבריאות:

**ד"ר שחר פרנקל, פרופ' דרור שרון, ד"ר חטיב סאמר, פרופ' איתי חוברס, ד"ר חיים כהן, פרופ' אברהם קציר, ד"ר עדי ענבל, פרופ' תמר בן-יוסף, פרופ' איתן גלון, פרופ' אדו פרלמן, ד"ר ערן פרס, ד"ר מנדל יוסף.**

**<u>הועד המנהל של עמותת "לראות"</u>**

אוהד להב, יו"ר

פרופ' אדו פרלמן, יו"ר המועצה המדעית

חברי הועד המנהל: פרופ' ארי ברזילי, פרופ' דב ויינברגר, פרופ' אלי חזום, פרופ' ענת לבנשטיין, פרופ' חנא גרזוזי, פרופ' יעקב פאר, פרופ' אהוד אסיה, פרופ' אדו פרלמן, פרופ' דרור שרון, פרופ' יאיר מורד, פרופ' אבי סלומון, ד"ר חני לבקוביץ'-ורבין, ד"ר רונית לוינגר, ד"ר יפית שטרק, גב' איריס שפיגל, מר מרק עמוס, ד"ר ניר ארדינסט, מר יאיר שפר, מר אשר גרינבאום.

**<u>צוות עמותת "לראות"</u>**

מנכ"ל: נדין הולנדר

מנהל פרויקטים: דורון זרצקי

מנהל פרויקט הניידת: צדקיהו ברוך

www.eyes.org.il

www.lirot.org

# הרצאות אורח בכנס ה- 35

## Keynote Speakers at ISVER 2015

**Wednesday, March 11 th 2015, 11:30 – 12:00**

**Prof. Simon Benita**

The Institute for Drug Research, School of Pharmacy, Faculty of Medicine, The Hebrew University of Jerusalem

### Novel Nano Delivery anti-VEGF Strategies for AMD.

Today, anti-VEGF agents are the standard treatment for Age-related Macular Degeneration (AMD) and Diabetes Retinopathy. Blocking VEGF leads to regression of the abnormal blood vessels, and thus, effectively reverses the process that leads to blindness. These anti-VEGF agents include mainly monoclonal antibodies and share the same drawback. Their clearance is not slow enough to allow prolonged activity, thus requiring frequent monthly injections to the vitreous and consequently increasing the risk of severe damage to the eye. The development of sustained release delivery systems for anti-VEGF agents is needed to decrease the frequency of injections. Nanoparticulate drug delivery systems offer two main advantages which can be exploited in an ocular drug delivery system, increase in drug stability and sustained drug release. Poly-Lactic-co-Glycolic-Acid (PLGA) is a biocompatible and biodegradable polymer, already approved for various therapeutic applications, and most often used for NPs preparation, including targeted nano-delivery systems in our laboratory. Oleic Cysteine Amide (OCA) is a novel cross-linking molecule synthesized in our laboratory. OCA exhibits amphiphilic properties enabling interfacial anchoring and thiol surface functionalization of PLGA NPs, facilitating bio-conjugation to activated-MAbs by thio-ether bonds. In this research, Bevacizumab (Avastin®) was selected as the first MAb to be conjugated to NPs, for its relative availability and worldwide use, although off-label. Over time, it is anticipated that the polymeric NPs will progressively degrade, releasing slowly the free active molecule which still binds with high affinity to VEGF molecules, until elimination. Conjugating 2mg of Bevacizumab on the interface of the NPs in 1ml of the dispersion containing 30mg of PLGA elicited a conjugation rate efficiency of 57%. Attempts to improve and optimize the binding efficiency are being performed. In addition, other more potent MAbs, eliciting a pharmacological activity at lower doses than Bevacizumab, are being conjugated to NPs. Other approaches of MAb incorporation into NPs, are being investigated and preliminary tested in mice models.

## Wednesday, March 11th 2015, 12:00-12:30

**Dr. Yoram Ben Shaul**

Department of Medical Neurobiology, Hebrew University Medical School, the Hebrew University of Jerusalem

## Obtaining Social Information from Pheromone Cues: Not As Simple As You Might Think.

Unlike humans, where vision plays a key role in guiding interactions with the external environment, for many animals the dominant sense is chemosensation. In fact, most mammals have two major chemosensory systems: the main olfactory system, and the lesser known vomeronasal system. In my lab, we study the vomeronasal system, which is considered to be dedicated for social information processing. In my talk I will introduce this system and describe some of the problems it must solve to extract social information. I will argue against the commonly held notion that social information processing via so called pheromones is trivial. Rather, it involves challenges similar to those relevant for vision.

## Thursday, March 12th, 2015, 11:10 – 11:40

**Prof. Rony Paz**

Department of Neurobiology,

Weizmann Institute of Science

### Value Modulation of Early Sensory Perception: From Neural Mechanisms to Psychopathology.

Negative experiences result in learning to avoid the stimulus that produced them. Importantly, we learn to avoid not only the original stimulus, but also stimuli that resemble and are similar to it - a "better safe than sorry" generalization approach. I will describe results that suggest that this generalization is not only an active choice-behavior strategy, but also stems from changes in early sensory perception. The evidence comes from psychophysics, electrophysiology and imaging in humans and non-human primates that investigate the mechanisms and circuitry underlying the learning and the plasticity it induces in specific brain regions. These changes in sensory perception underlie normal everyday behavior but can also lead in extreme cases to pathological maladaptive learning, as in the case of anxiety disorders and post-trauma.

## Thursday, March 12th, 2015, 12:00 – 12:30

### Gideon Amichay

Former Chief Creative Officer & Joint Managing Partner of Shalmor-Avnon-Amichay

No,No,No,No,No,Yes®

### Every "NO" is a great opportunity to search for the next "YES"

**No.** It is a word that every CEO, entrepreneur and creative professional has confronted. It is a word that both novices and seasoned professionals dread. It is a word that can easily seem like death to a dream.

And yet it is also a word that can point in the right direction. It is a word that motivates us to do something differently, try someone else, get better, innovate and keep going. "No" is a word that looms over every business person's innovator's and artist's life. And yet the word is universally met with trepidation and fear because the value of being told "No" is so little understood. Based on his **TEDx talk** Amichay will walk you through his life journey and show you how important are the NO's we collect along the way. Motivation is a key - inspire your people to deal with a NO.

# Wednesday, March 11th 2015

**Coffee and Exhibition** 8:30 – 8:35

**Opening remarks** 8:30 – 8:35

Prof. Avi Solomon

## Retina 1: Retinal Cell Biology 8:35 – 10:15

**Moderators:**

Prof. Adi Barak

Dr. Tami Livnat

**1** 8:35 **Correlation between coagulation and inflammatory systems in a rabbit model LPS-induced Uveitis.** p. 44

Atamney M1, Barliya T2, Ehrlich R1, 2, 3 , Weinberger D1, 2, 3 and Livnat T1, 2, 4

*1. Division of Ophthalmology, Rabin Medical Center- Beilinson campus, Petah Tikva, Israel. 2 Laboratory of Eye research Felsenstein Medical Research Center (FMRC). 3. Sackler School of Medicine, Tel-Aviv University, Israel. 4. The Israeli National Hemophilia Center, Sheba Medical Center, Tel Hashomer, Israel*

**2** 8:40 **Early vascular changes in eyes treated with bevacizumab compared with eyes treated with laser for type-1 retinopathy of prematurity** p. 45

Yuval Cohen [a,f], Domenico Lepore [e], Gui-shuang Ying [b], Clare M. Wilson [c,d] Jiayan Huang [b], Karen A. Karp [a], Agnieshka Baumritter [a], Akosua Nti [a], Giovanni H. Greaves [a], Graham E. Quinn [a,b]

*[a]Division of Ophthalmology, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania; [b]Scheie Eye Institute, University of Pennsylvania, Philadelphia; [c]Visual Science, UCL Institute of Ophthalmology, London, United Kingdom; [d] Department of Ophthalmology, Great Ormond Street Hospital, London, United Kingdom, [e]Catholic University of the Sacred Hearts, Rome, Italy, [f] Hillel Yaffe Medical Center, Hadera, Israel.*

**3** 8:45 **Pax6 role in the regulation of retinal pigmented epithelium maturation** p. 46

Yamit Cohen-Tayar[1], Ruth Ashery-Padan[1]

*[1] Department of Human Molecular Genetics and Biochemistry, Sackler School of Medicine, Tel-Aviv University, Israel*

**4** 8:50 **A *SEMA3E* mutant resistant to cleavage by furins (*UNCL-SEMA3E*) inhibits laser induced choroidal neovascularization** p. 47

Allon Gilad [1], Toledano Shira [2], Kigel Boaz [2], Kessler Ofra [2], Hagbi-Levi Shira [3], Tiosano Liran [3], Schaal Shlomit[4], Neufeld Gera [2], Barak Yoreh[1]

*1.Ophthalmology Department, Rambam Health Care Center, Haifa, Israel. 2.Cancer Research and vascular Biology Center, The Bruce Rappaport Faculty of Medicine, , Technion, Israel Institute of Technology, , Haifa, Israel. 3.Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel. 4. Department of Ophthalmology and Visual Sciences, University of Louisville, Louisville, KY, United States.*

**5** 8:55 **Penetration of Intravitreal Injected Tissue Plasminogen Activator to the Retina - Rats Model Study** p. 48

Tal, Kfir1, 2; Dotan, Assaf1, 2; Nisgav, Yael3, 2; Mor Dachbash3; Ehrlich, Rita1, 2; Weinberger, Dov1, 2; Livnat, Tami3, 2

*1. Department of Ophthalmology, Rabin Medical Center ,Beilinson Campus Petach Tikva 49101, Israel, Petach Tikva ,Israel. 2. Sackler School of Medicine, Tel Aviv University, Tel Aviv , Israel. 3. Laboratory of Eye Research, Felsenstein Medical Research Center, Petah Tikva, Israel*

**6** 9:00 **TNFα- induced TGFβ activation in RPE cells** p. 49

Orit Adir[1], Zeev Dvashi[1] and Ayala Pollack[1]

*Kaplan Medical Center affiliated to the Hebrew University of Jerusalem, Israel*

9:05 **Discussion**

**7** 9:10 **Retinal toxicity of intravitreal clindamycin in albino rabbits** p. 50

Orit Mazza[1], Zohar Habot-Wilner[2], Jonathan Shahar[2], Amir Massarweh[1], Irit Mann[1], Anat Loewenstein[2], Ido Perlman[1]

*Department of Physiology and Biophysics, the Ruth and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology and the Rappaport Institute, Haifa, Israel.[1], Division of Ophthalmology, Tel-Aviv Medical Center, Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel.[2]*

**8** 9:15 **Presence of Bevacizumab in the iridocorneal angle following intravitreal injection in a rat model** p. 51

Orly Gal-Or[1], Assaf Dotan[1], Mor Dachbash[3], Yael Nisgav[3], Dov Weinberger[1,2,3] Rita Ehrlich[1,2] ,Tami Livnat[1,2,3]

*[1] Department of ophthalmology, Rabin Medical Center, Petach-Tikva,[2] Sackler School of Medicine, Tel-Aviv University, Tel Aviv, [3] Laboratory of Eye Research, Felsentatein Medical Research Center, Rabin Medical Center, Petach –Tikva*

**9** 9:20 **Differentiation and paracrine activity of adipose tissue derived mesenchymal stem cells when exposed to normoxic and hypoxic RPE** p. 52

Aya Barzelay[a], Ran Levy[a], Emmanulle Kohn[a], Meirav Sella[b], Nir Shani[b], Benjamin Meilik[b], Eyal Gur[b], Anat Loewenstein[a], Adiel Barak[a]

*[a]Ophthalmology Laboratory, Department of Ophthalmology Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel, [b]Department of Plastics and Reconstructive Surgery Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel, [a,b]Affiliated with Sackler Faculty of Medicine Tel Aviv University, Ramat Aviv, Israel*

**10** **The Effects of the ApoE4 Genotype on the** p. 53
9:25 **Developing Murine Retina**

Idit Maharshak[1,2], Shiran Salomon-Zimri[1], Ran Antes[1],Tami Livnat[3], Arieh S. Solomon[4], Dov Weinberger[5,2], Carol A. Colton[6], Daniel M. Michaelson[1]

*1Department of Neurobiology, George S. Wise Faculty of Life Sciences, Tel Aviv University, Tel Aviv, Israel; 2Department of Ophthalmology, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel; 3Laboratory of Eye Research, Felsenstein Medical Research Center, Rabin Medical Center, Petach Tikva, Israel; 4Goldschleger Eye Institute, Tel-Aviv University, Tel-Hashomer, Israel; 5Department of Ophthalmology, Rabin Medical Center, Petach Tikva, Israel; 6Division of Neurology, Duke University Medical Center, Department of Medicine, Durham, NC*

**11** **The interplay between the coagulation and** p. 54
9:30 **inflammatory systems in retinal pathologies**

Alon Zahavi, [1,2,3] Tami Livnat, [2,3,4] Ruth Axer-Siegel, [1,2] Ayelet Dreznik, [1,2,3] Elinor Megiddo, [1,2] Mor Dachbash, [3] Dov Weinberger, [1,2,3] Rita Ehrlich, [1,2,3]

*[1]Department of Ophthalmology, Rabin Medical Center, Petah Tiqwa, Israel; [2]Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel; [3]Felsenstein Medical Research Center, Rabin Medical Center, Petah Tiqwa, Israel; [4]The Israeli National Hemophilia Center, Sheba Medical Center, Tel Hashomer, Israel*

**12** **Light-induced retinal damage in dark-reared** p. 55
9:35 **albino rats, its reversibility and the link to acetylcholinesterase**

Amir Massarweh, Ronit Heinrich, Olga Medvedev, Ido Perlman

*Department of Physiology and Biophysics, Ruth & Bruce Rappaport, Faculty of Medicine, Rappaport Institute, Technion—Israel Institute of Technology*

9:40 **Discussion**

**13** 9:45 **Evaluation of anti VEGF single injection on diabetic retinopathy of non-obese diabetic (NOD) mice** p. 56

Moshe Ben-Hamou[1,2], Orit Barinfeld[1,2], Tamar Azrad-Leibovich[1,2], Nitza Goldenberg-Cohen[1,2,3].

*1Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv; Israel, 2The Krieger Eye Research Laboratory, FMRC, Rabin Campus, Tel Aviv University; 3Pediatric Ophthalmology Unit, Schneider Children's Medical Center of Israel, Petach Tikva*

**14** 9:50 **Changes in retinal function and cellular remodeling following experimental retinal detachment** p. 57

Barliya T*[1,2] , Ofri R[*3], Sandalon S[3], Livnat T,[1,2,4], and Weinberger D[1,2,5]

*1.Division of Ophthalmology , Rabin Medical Center- Beilinson campus, Petah Tikva, Israel., 2 Laboratory of Eye research Felsenstein Medical Research Center (FMRC), Rabin Medical Center, Petah Tikva, 3. Koret School of Veterinary Medicine, The R.H. Smith Faculty of Agriculture, Food and Environment, The Hebrew University of Jerusalem, Rehovot, Israel, 4. The Israeli National Hemophilia Center, Sheba Medical Center, Tel Hashomer, Israel, 5. Sackler School of Medicine, Tel-Aviv University, Israel*

**15** 9:55 **Evaluation of experimental carotid stenosis created in laboratory rat** p. 58

Solomon AS[1], Rudoler N[1], Rotenstreich Y[1],Levi N[1],Tzameret A[1], Sher I[1],Pointkevitz Y[2],Zilberstein Y[3], Ziv H[1], Pri Chen Sara[1]

*[1]The Goldschleger Eye Research Institute, Faculty of Medicine, Tel-Aviv University, Sheba Medical Center, Tel Hashomer, Israel;[2] Strauss Center for Computational Neuroimaging, TAU;[3]Sackler Cellular and Molecular Imaging Center, TAU*

**16** 10:00 **TNF-alpha receptors 1 and 2 play a role in mouse model of optic nerve crush** p. 59

Moran Fridman,[1,2] Myles Brookman,[2] Orit Barinfeld,[1,2] Nitza Goldenberg-Cohen.[1,2,3]

*[1]The Krieger Eye Research Laboratory, Felsenstein Medical Research Center, Tel Aviv University [2]Sackler School of Medicine, Tel Aviv University, Tel Aviv; Israel, [3]Pediatric Ophthalmology, Schneider Children's Medical Center of Israel, Petach Tikva, Israel*

**17** 10:05 **Bioactive magnetic near Infra-Red fluorescent core-shell iron oxide/human serum albumin nanoparticles for controlled release of growth factors for augmentation of human mesenchymal stem cell growth and differentiation.** p. 60

Ifat Sher[1*], Itay Levy[2]*, Enav Corem-Salkmon[2], Ofra Ziv[2], Amilia Meir[3], Avraham J Treves[3], Arnon Nagler[4], Shlomo Margel[2], Ygal Rotenstreich[1]

*[1]Goldschleger Eye Research Institute, Sackler Faculty of Medicine, Tel Aviv University Sheba Medical Center, Tel-Hashomer , [2]Department of Chemistry, Bar-Ilan Institute of Nanotechnology and Advanced Materials, Ramat-Gan, [3]Center for Stem Cells and Regenerative Medicine, Cancer Research Center, Sheba Medical Center, Tel-Hashomer, [4]Hematology Division, Sheba Medical Center, Tel-Hashomer*

10:10 **Discussion**

## Coffee and exhibition 10:15 – 10:45

## Oncology

10:45 – 11:30

### Moderators:

Dr. Shahar Frenkel

Prof. Nitza Cohen-Goldenberg

**18** 10:45 **Novel methods for the detection of occult metastatic disease in the CSF of children with medulloblastoma** p. 61

Sivan Gershanov,[1,2] Shalom Michowiz, [3,4] Helen Toledano,[3,5] Dror Fixler,[7] Gilad Yahav,[7] Orit Barinfeld,[2,3] Mali Salmon-Divon,[1] Nitza Goldenberg-Cohen.[2,3,6]

*[1]Genomic Bioinformatics Laboratory, Molecular Biology, Ariel University, Ariel, Israel, [2]The Krieger Eye Research Laboratory, Felsenstein Medical Research Center, and [3]Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel, [4]Pediatric Neurosurgery, [5]Pediatric– Oncology ,and [6]Pediatric Ophthalmology, Schneider Children's Medical Center of Israel, Petach Tikva, Israel, [7]Faculty of Engineering and Institute of Nanotechnology and Advanced Materials, Bar Ilan University, Ramat-Gan, Israel.*

**19** 10:50 **EGFR overexpression as a prognostic factor in glioblastoma multiforme** p. 62

Orit Barinfeld,[1,2] David Hazon, [3] Shalom Michowiz, [3] Helen Toledano,[4,2] Susana Fichman-Horn, [6] Rinat Ankri,[7] Ariel Ashkenazy,[7] Dror Fixler,[7] Nitza Goldenberg-Cohen.[1,2,5]

*[1]The Krieger Eye Research Laboratory, Felsenstein Medical Research CenterTel Aviv University, Petah Tikva [2]Sackler School of Medicine, Tel Aviv University, Tel Aviv, [3]Pediatric Neurosurgery, [4]Pediatric– Oncology ,and [5]Pediatric Ophthalmology, Schneider Children's Medical Center of Israel, Petach Tikva,. [6]Pathology Department, Rabin Medical Center, Beilinson Campus, Petah Tikva [7]Faculty of Engineering and Institute of Nanotechnology and Advanced Materials, Bar Ilan University, Ramat Gan, Israel*

**20** 10:55 **Generation of *in vivo* model for eyelid basal cell carcinoma and characterization of the tumor's microenvironment** p. 63

Stein Ran, Dvashi Zeev, Milstein Asher and Pollack Ayala

*Ophthalmology department, Kaplan Medical Center, Rehovot, Israel., Affiliated with the Hebrew University, Jerusalem*

**21** 11:00 **Diagnosis of vitreoretinal lymphoma: the use of cytology, gene rearrangement, and IL-10/IL-6 ratio** p. 64

Jacob Pe'er [1], Inna Kalickman[2], Yoav Sherman[3], Bela Maly[3], Dina Ben Yehuda[4], Vivian Barak[2], Shahar Frenkel [1]

*Departments of [1]Ophthalmology, [2]Oncology, [3]Pathology, and [4]Hematology, Hadassah-Hebrew Univ Med Ctr, Mevaseret Zion, Israel*

**22** 11:05 **Novel combinatorial treatment option for metastatic uveal melanoma** p. 65

Shahar Frenkel [1]; Dudi Shneor [1, 2]; Alik Honigman [2]; Jacob Pe'er [1]

*1. Ophthalmology, Hadassah-Hebrew Univ Med Ctr, Mevaseret Zion, Israel. 2. Biochemistry and Molecular Biology, IMRIC, The Hebrew University-Hadassah Medical School, Jerusalem, Israel.*

**23** 11:10 **Stereotactic radiosurgery for uveal melanoma** p. 66

Shahar Frenkel [1]; Atara Cohen [1], Hadas Rosenne [2], Mark Vigoda [3], Ygal Shoshan [4], Jacob Pe'er [1]

*Departments of [1]Ophthalmology, [2]Social work, [3]Radiotherapy, [4]Neurosurgery, Hadassah-Hebrew University Medical Center, Jerusalem*

**23a** 11:15 **A Biological Tissue Adhesive and Dissolvent System for Intraocular Tumor Plaque Radiotherapy: an *In-vivo* Animal Model Experiment** p. 67

Ofira Zloto, MD[1]; Dror Alezra, MD[2]; Oded Sagiv, MD[1]; Vicktoria Vishnevskia Dai, MD[1]; Iris Moroz, MD[1]; Gahl Greenberg, MD[3]; Elad Ben-Artsi, MD[1]; Ido Didi Fabian, MD[1,4]

*[1]Goldschleger Eye Institute, [2]Department of Radiation Oncology and [3]Department of Diagnostic Imaging, Sheba Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel. [4]Dr. Pinchas Borenstein Talpiot Medical Leadership Program 2012*

11:20 **Discussion**

## Guest lecture 1

11:30 - 12:00

**Simon Benita**

*The Institute for Drug Research, School of Pharmacy, Faculty of Medicine, The Hebrew University of Jerusalem*

**Novel Nano Delivery anti-VEGF Strategies for AMD**

## Guest lecture 2

12:00 – 12:30

**Yoram Ben Shaul**

*Department of Medical Neurobiology, Hebrew University Medical School, The Hebrew University of Jerusalem*

**Obtaining Social Information From Pheromone Cues: Not as Simple As You Might Think.**

## Lunch break

12:30 – 13:30

## Cornea

13:30 - 15:15

### Moderators:

Dr. Irina Barequet

Dr. Arie Markovich

**24** **p63 is essential for mouse eye development** p. 68

13:30 Waseem Nasser[1], Daniel Aberdam[2], Alea Mills[3], Caterina Missero[4], and Ruby Shalom-Feuerstein[1]

*[1]Department of Genetics and Developmental Biology, The Ruth and Bruce Rappaport Faculty of Medicine, Technion – Israel Institute of Technology, Haifa, Israel; [2]INSERM UMR-S976, Université Paris Diderot Hôpital Saint-Louis, PARIS; [3]Cold Spring Harbor Laboratory; Cold Spring Harbor, NY USA; [4]CEINGE Biotecnologie Avanzate, Napoli, Italy*

**25** **A comparison between bandage contact lenses, punctual plugs and standard measures in preventing corneal injuries related to exposure in patients admitted to the general intensive care unit.** p. 69

13:35

Irena Serov1 MD , Amir Sternfeld1 MD , Lewa Amar1 MD , Idit Dan1 MD , Yonatan Cohen1,2 PROF, Itay Ben Daviv1 MD ,Irit Bahar1,2 PROF, Iftach Yassur1,2 MD, Inbal Avisar1,2 MD

*1.Ophthalmology department, Rabin Medical Center, Petah Tikva, Israel*

*2.Sakler faculty of medicine, Tel aviv university, Tel Aviv, Israel*

**26** **Demographic factors, environmental, occupational and infectious exposures in Israeli patients suffering from dry eye syndrome and Sjogren's syndrome** p. 70

13:40

Ben-Eli Hadas[1,2], Solomon Abraham[1], Aframian Doron[3], Mevorach Dror[4], Ben-Chetrit Eldad[5] and Paltiel Ora[2,6]

*[1]Department of Ophthalmology, [2] Braun School of Public Health and Community Medicine, [3] Department of Oral Medicine, [4]Department of Internal Medicine, Unit of Rheumatology and [6]Department of Hematology, Hadassah-Hebrew University Medical Center, Jerusalem*

**27** **Pyerygium And Human Papilloma Virus In Israel** p. 71

13:45 Shirin Hamed-Azzam M.D.1, Natalia Edison Ph.D.2, Abed Mukari M.D.1 , Irit Elmalah M.D.2 , Daniel Briscoe M.D.1

*[1]Department of ophthalmology, Emek Medical Center, Afula, Israel. [2]The institute of tissue diagnostics and cancer reseach, Emek Medical Center, Afula, Israel.*

**28** **Synergism between anticholinergic and oxime** p. 72
13:50 **treatments against sarin induced ocular insult in rats**

Gore A[1]., Brandeis R[1]., Egoz I[1] ., Turetz J[1]., Nili U[1]. and Bloch-Shilderman E[1].

*Dept. of Pharmacology1, Israel Institute for Biological Research, Ness Ziona, 74100, Israel*

**29** **A Novel UBIAD1 Gene Mutation in an Ashkenazi** p. 73
13:55 **Jewish Family With Schnyder Corneal Dystrophy**

Adi Einan-Lifshitz, Isaac Avni, Nadav Shoshany, David Zadok, Eran Pras

*Ophthalmology department, Assaf Harofeh medical center, Zerifin, Israel*

**30** **Agreement and reliability in measuring central** p. 74
14:00 **corneal thickness between a new stationary Scheimpflug camera (VX120) and a rotating Scheimpflug camera (Sirius) in normal and keratoconic corneas**

Ariela Gordon-Shaag, David Markov , Tzadok Parnes and Einat Shneor

*Department of Optometry and Vision Science, Hadassah Academic College, Jerusalem, Israel*

**31** **Pterygium excision with superior conjunctival** p. 75
14:05 **flap: comparison of fibrin glue with vicryl suture. A randomized control study**

Greenbaum Eran[2], Zloto Ofira[1,2] and Ben Simon Guy[1,2]

*Ophthalmology Department, Sheba Medical Center[1], Tel Hashomer, Sackler School of Medicine[2]*

**32** 14:10 **Risk factors for keratoconus in Israel: a case control study** p. 76

Ariela Gordon-Shaag[1], Michel Millodot[2], Igor Kaiserman[3], Tzahi Sela[3], Guy Barnett Itzhaki[1], Yaffa Zerbib[1], Efrat Matityahuo[1], Shira Shkedi[1], Svetlana Miroshnichenko[1] and Einat Shneor[1]

*1Department of Optometry and Vision Science, Hadassah Academic College, Jerusalem, Israel; 2 School of Optometry, The Hong Kong polytechnic University, Hong Kong, China; 3 CARE Laser Medical Group, Tel Aviv, Israel*

14:15 **Discussion**

**33** 14:20 **A retrospective comparison of semi-scleral (ICD) and Hybrid (Ultra Health) Contact Lenses for Keratoconus** p. 77

Gantz L., Ehrlich E., Nostin L., Fine P.

*Dept. of Optometry and Vision Science, Hadassah Academic College, Jerusalem, Israel*

**34** 14:25 **Corneal Stiffening by WST-D / and NIR: Near infrared illumination of 1 and 30 minutes** p. 78

Alexandra Goz [1, 4], Jurriaan Brekelmans[5], Alexander Brandis[1], Ilan Samish[1], Daniel Wagner[3], Yoram Salomon[2], Arie Marcovich[1,4] , Avigdor Scherz[1]

*Departments of [1]Plant and Environmental Sciences, [2]Biological regulation, [3]Materials and Interfaces, The Weizmann Institute of Science, [4]Department of Ophthalmology, Kaplan Medical Center, Rehovot,Israel, [5]University Eye Clinic Maastricht, Maastricht, The Netherlands*

**35** 14:30 **Simultaneous topography-guided surface ablation with collagen cross-linking for keratoconus- case series** p. 79

Lily Karmona[1], MD; Tzahi sela[2]; Oz franco[2]; Avi shoshani[2]; Gur Mitzer[2]; Igor Kaiserman[2,3]

*1 Department of ophthalmology, Wolfson Medical center, Holon, Israel, 2 Care-Vision Laser center Institute, Tel-aviv, Israel, 3 Department of ophthalmology, Barzilai Medical center, Ashkelon, Israel*

**36** 14:35 **The Efficacy of Topical Aflibercept versus Topical Bevacizumab for the Prevention of Corneal Neovascularization in a Rat Model** p. 80

Ruti Sella[1,2], Orly Gal-Or[1], Eitan Livny[1], Mor Dachbash[3],Yael Nisgav[3], Dov Weinberger[1,2,3], Tami Livnat[1,2,3], Irit Bahar[1,2]

*[1]Department of Ophthalmology, Rabin Medical Center, Petah-Tikva, [2]Sackler School of Medicine, Tel-Aviv University, Tel Aviv, [3]Laboratory of Eye Research, Felsenstein Medical Research Center, Rabin Medical Center, Petah-Tikva*

**37** 14:40 **Impression cytology for monitoring ocular surface changes** p. 81

Tamar Kadar, Hila Gutman, Liat Cohen, Maayan Cohen, Vered Horwitz, Ariel Gore, Adina Amir and Shlomit Dachir

*Department of Pharmacology, Israel Institute for Biological Research, Ness Ziona*

**38** 14:45 **Lineage tracing of stem/progenitor cells of the murine corneal epithelium** p. 82

Aya Amitai-Lange[1], Anna Altshuler[1], Jeffrey Bubley[1], Noora Dbayat[2], Beatrice Tiosano[2], Ruby Shalom-Feuerstein[1]

*1Department of Genetics and Developmental Biology, The Ruth and Bruce Rappaport Faculty of Medicine, Technion – Israel Institute of Technology, Haifa, Israel; 2Department of ophthalmology – Hillel Yaffe Medical center, Hadera, Israel*

**39** 14:50 **Ocular surface reconstruction using limbal epithelial cells cultivated ex-vivo on contact lenses following limbal stem cell deficiency** p. 83

Gore A[1]., Horwitz V[1]., Cohen-Jacob O[1]., Gutman H[1]., Cohen M[1]., Cohen L[1].,Zadok D[2]., Turetz J[1]., Dachir S[1]. and Kadar T[1].

*1Dept. of Pharmacology, Israel Institute for Biological Research, Ness Ziona, 74100, Israel and 2Depart. of Ophthalmology, Assaf Harofeh Medical Center, Zerifin 73000, Israel*

**40** 14:55 **Specular microscopy analysis of post operative central and peripheral endothelial cells following Descemet membrane endothelial keratoplasty (DMEK)** p. 84

Eitan Livny1,2, Lisanne Ham1,3, Silke Ollerich1, Vasilis Liarakos1, Gerrit J Melles1'

*1. Netherlands institute for innovative ocular surgery, Rotterdam, The Netherlands, 2. Department of Ophthalmology, Rabin medical center, Petach Tiqva, Israel, 3. Amnitrans eye bank, Rotterdam, The Netherlands*

**41** 15:00 **Descemet's Memebrane Endothelial Keratoplasty- Early Experience** p. 85

Irit Bahar, MD[1], Eitan Livny,MD[1] , Ofer Daphna,MD, [1] David Rootman,MD [2]

*1Ophthalmology Department, Rabin Medical Center, Petach Tiqva, Israel, 2Ophthalmology Department, Toronto Western Hospital, Toronto,Canada*

**42** 15:05 **Bonding surgical incisions using a temperature-controlled laser system based on a single infrared fiber** p. 86

Ilan Gabay[1], Irit Barequet[2], David Varssano[3], Mordechai Rosner[2] and Abraham Katzir[1]

*1Tel Aviv University, School of Physics and Astronomy, Tel Aviv 69978, Israel. 2Tel Aviv University, Goldschleger Eye Institute, Sheba Medical Center, Sackler School of Medicine, Tel Aviv 52621, Israel. 3Tel Aviv University, Department of Ophthalmology, Tel Aviv Sourasky Medical Center, Sackler School of Medicine Tel Aviv 64239, Israel.*

15:10 **Discussion**

**Coffee and exhibition** 15:15 – 15:45

## Retina 2: Clinical Studies, Imaging & Function

15:45 – 17:00

**Moderators:**

Dr. Ygal Rotenstreich

Prof. Eyal Banin

**43** 15:45 **Pupillary responses of healthy subjects to chromatic light stimuli at incremental intensities at central and peripheral visual field locations** p. 87

Soad Haj Yahia[1], Ron Chibel[1], Daniel Ben Ner[1], Ifat Sher[1], Michael Belkin[1], Ygal Rotenstreich[1]

*[1]Goldschleger Eye Research Institute Sackler Faculty of Medicine Tel Aviv University Sheba Medical Center Tel-Hashomer, Israel*

**44** 15:50 **Chromatic multifocal pupillometer for objective perimetry in patients with macular degeneration** p. 88

Daniel Ben-Ner[1], Ron Chibel[1], Mohamad Mahajna[1], Ifat Sher[1], Michael Belkin[1], Ygal Rotenstreich[1]

*[1]Goldschleger Eye Research Institute, Sackler Faculty of Medicine, Tel Aviv University, Sheba Medical Center, Tel-Hashomer, Israel*

**45** 15:55 **Chromatic multifocal pupillometer for objective perimetry in healthy subjects and patients with retinal dystrophies** p. 89

Ron Chibel [1], Ifat Sher [1], Mohamad Mahajna [1] Michael Belkin[1] , Ygal Rotenstreich [1]

*1Goldschleger Eye Research Institute Sackler Faculty of Medicine Tel Aviv University Sheba Medical Center Tel-Hashomer, Israel*

**46** 16:00 **Prevalence and Risk Factors for Epiretinal membrane in patients with type-2 Diabetes Mellitus Screened with a Digital Non-Mydriatic Fundus Camera** p. 90

Perach Osaadon MD[1,2], Orit Schachter MD[1], Jaime Levy MD[1,2], Ygal Plakht RN, PhD [3], Yonathan Serlin MD[1], , Tova Lifshitz MD [1,2], Boris Knyazer MD [1,2]

*1Joyce and Irving Goldman Medical School, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel. 2Department of Ophthalmology, Soroka University Medical Center, Ben-Gurion University of the Negev, Beer-Sheva, Israel. 3 Nursing Research Unit, Soroka University Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel*

**47** 16:05 **Diameters of large retinal blood vessels in hypertensive patients as measured by spectral domain optical coherence tomography** p. 91

Amit Meshi MD[1], Jonathan Shahar MD[2], Yaron Arbel MD[3], Shlomo Berliner MD[3], Anat Loewenstein MD[2], Dafna Goldenberg MD[2]

*1. Department of Ophthalmology, Meir Medical Center, Kfar Saba, affiliated to the Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel. 2. Department of Ophthalmology, Tel Aviv Medical Center, Tel Aviv, affiliated to the Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel.3. Department of Internal Medicine "D" and "E", Tel Aviv Medical Center, Tel Aviv, affiliated to the Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel.*

16:10 **Discussion**

**48** 16:15 **Sub Retinal Fluid Optical Density in Rhegmatogenous Retinal Detachment** p. 92

Ari Leshno[1], Adiel Barak[1], Anat Loewenstein[1], Amit Weinberg [1] and Meira Neudorfer[1]

*[1]Department of Ophthalmology Sourasky Tel-Aviv medical center*

**49** 16:20 **Spectrally-resolved retinal imaging** p. 93

Oded Sagiv, GenadyKostenich, Gidi Arbel, Iris Moroz, Arie Orenstein, Michael Belkin

*The Chaim Sheba Medical Center*

**50** 16:25 **Define the surgical orbital apex using CT scans of the orbit** p. 94

Olga Zurinam, Dmitry Lumelsky, Ziv Neeman, Daniel Briscoe

*Technion Faculty of Medicine, Department of Ophthalmology, Department of Radiology, Emek Medical Center, Afula, Israel*

**51** 16:30 **Publication outcomes of abstracts submitted to the annual American Academy of Ophthalmology Meeting** p. 95

Michael Mimouni MD[1], Mark Krauthammer MD[2], Hamza Abualhasan MD[1], Hanan Badarni MD[1], Kamal Imtanis MD[1], Gilad Alon MD[1], Liron Berkovitz MD[1], Gil Amarilyo MD[3]

*[1]Department of Ophthalmology, Rambam Health Care Campus, Haifa, Israel,[2]Department of Ophthalmology, Sourasky Medical Center, Tel Aviv, Israel, [3]Schneider Children's Hospital, Tel Aviv, Israel*

**52** 16:35 **Giant Cell Arteritis associated with night sweats may be protective from vision loss** p. 96

Joshua Kruger[1], Joseph Rizzo[2]

*1) Department of Ophthalmology, Hadassah Medical Center, 2) Department of Ophthalmology, Harvard Medical School*

16:40 **Discussion**

# Thursday, March 12th 2015

## Coffee and Exhibition 8:00 -8:30

## Retina 3: Retinal Degenerations 8:30 – 10:00

### Moderators:

Prof. Dror Sharon

Prof. Tamar Ben Yosef

**53 Knobloch syndrome masquerading as albinism** p. 97

8:30 Libe Gradstein[1], Gerald F. Cox[2], Pablo Altschwager[3], Anne B. Fulton[3]

*1 Department of Ophthalmology, Soroka Medical Center and Clalit Health Services, Faculty of Health Sciences, Ben Gurion University, Beer Sheva, Israel, 2 Division of Genetics and Department of Pediatrics, Boston Children's Hospital and Harvard Medical School, Boston, Massachusetts, USA, and Clinical Development, Genzyme, a Sanofi company, Cambridge, Massachusetts, USA, 3 Department of Ophthalmology, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts, USA*

**54 Ophthalmic disease associated with natural and experimental infection with Tilapia Lake Virus in fish** p. 98

8:35

Asaf Berkowitz[1], Avi Eldar[1], Ron Ofri[2]

*[1] Department of Avian and Fish Diseases, Kimron Veterinary Institute, Ministry of Agriculture, Beit Dagan, Israel, [2]Koret School of Veterinary Medicine, The Hebrew University of Jerusalem, Rehovot, Israel*

**55 Time trends reveal a decrease of childhood blindness in Israel** p. 99

8:40

Eedy Mezer MD[1,2], Angela Chetrit MHA[3], Ofra Kalter-Leibovici MD[3,4], Michael Kinori MD[4,5], Itay Ben-Zion MD[4,5], Tamara Wygnanski-Jaffe MD[4,5]

*[1]Department of Ophthalmology, Rambam Health Care Campus, Haifa, Israe, I[2]Ruth and Bruce Rappaport Faculty of Medicine, Technion–Israel Institute of Technology, Haifa, Israe, I[3]Unit of Cardiovascular Epidemiology, Gertner Institute for Epidemiology & Health Policy Research, Tel Hashomer, Israel, [4] Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel, [5] The Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, Israel*

**56** **Generation and characterization of Fam161a** p. 100

8:45 **Conditional Knockout mice**

Avigail Beryozkin (1), Alexey Obolensky (1), Ayat Khalaileh (1), Carlo Rivolta (2), Yvan Arsenijevic (3), Eyal Banin (1), Dror Sharon (1)

*1.Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel, 2.Department of Medical Genetics, University of Lausanne, CH-1005 Lausanne, Switzerland,3.Department of Ophthalmology, University of Lausanne, Jules-Gonin Eye Hospital, FAA, Unit of Gene Therapy & Stem Cell Biology, Avenue de France 15, 1004 Lausanne, Switzerland*

**57** **The Genetics of Usher Syndrome in the Israeli** p. 101

8:50 **and Palestinian Populations**

Ayat Khalaileh (1), Tamar Ben-Yosef (2), Annick Raas-Rothschild (2), Itay Chowers (1), Eyal Banin (1), Dror Sharon (1), Samer Khateb (1)

*(1) Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel. (2) Genetics Department, Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel.*

**58** **Molecular, physiological and morphological** p. 102

8:55 **effects of DHDDS knockdown in photoreceptors of Drosophila**

Liliana Mizrahi-Meissonnier[1], Rachel Zaguri[2], Elisheva Rhodes[2], Vladimir Katanaev[3], Baruch Minke[2], Dror Sharon[1]

*1. Department of Ophthalmology, Hadassah Medical Center, Jerusalem, Israel. 2. Faculty of Medicine, Hebrew University, Jerusalem, Israel. 3. Faculty of Biology and Medicine, University of Lausanne, Lausanne, Switzerland.*

9:00 **Discussion**

**59** 9:05 **Immunological Properties and Interactions of Retinal Pigment Epithelium derived from Human Embryonic Stem Cells** p. 103

Ayala Ejzenberg(1), Ruslan Alper-Pinus (1), Alexey Obolensky(1), Maria Idelson(2), Benjamin Reubinoff(2), Eyal Banin(1).

*(1)Department of Ophthalmology, Hadassah-Hebrew University Medical Center. (2)The Hadassah Human Embryonic Stem Cell Research Center, The Goldyne Savad Institute of Gene Therapy & Department of Gynecology, Hadassah-Hebrew University Medical Center.*

**60** 9:10 **An intronic deletion in the *PROM1* gene leads to autosomal recessive cone-rod dystrophy** p. 104

Osnat Eidinger,[1] Rina Leibu,[2] Hadas Newman,[3] Leah Rizel,[1] Ido Perlman,[3,4] Tamar Ben-Yosef[1]

*[1]Department of Genetics and [4]Department of Physiology and Biophysics, The Rappaport Family Institute for Research in the Medical Sciences, Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel, [2] Alberto Moscona Department of Ophthalmology, Rambam Health Care Campus, Haifa, Israel, [3]Department of Ophthalmology, Tel-Aviv Medical Center, Tel-Aviv, Israel*

**61** 9:15 **A single nucleotide polymorphism in ATXN7 gene can cause non-syndromic cone rod dystrophy** p. 105

Shirel Weiss [1,2], Mali Salmon-Divon [3], Lina Basel [4], Rachel Straussberg [2,5], Nitza Goldenberg-Cohen [1,2,6]

*[1]The Krieger Eye Research Laboratory, Felsenstein Medical Research Center and [2]Sackler School of Medicine, Tel Aviv University, [3]Genomic Bioinformatics Laboratory, Molecular Biology, Ariel University, [4]Pediatric Genetics, [5]Pediatric Neurology, and [6]Pediatric Ophthalmology, Schneider Children's Medical Center of Israel, Petah Tiqwa*

**62** 9:20 **Retinal Function in Patients with Achromatopsia Caused by Mutations in the *CNGA3* Gene** p. 106

Boris Rosin [1], Artur Cideciyan[2], Inbar Erdinest[1], Lina Zelinger [1], Dror Sharon[1], Samuel G. Jacobson[2] and Eyal Banin [1]

*[1] Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel [2] Department of Ophthalmology, Scheie Eye Institute, University of Pennsylvania, Philadelphia, Pennsylvania, USA.*

**63** 9:25 **Identification of Homozygous and Hemizygous Genomic Deletions that Cause Inherited Retinal Degenerations by Analyzing Whole Exome Sequencing Data** p. 107

Samer Khateb[1]; Ayat Khalailah[1]; Avigail Beryozkin[1]; Liliana Mizrahi-Meissonnier[1]; Ala Abu-diab[1]; Fathiah Abu-Turkey[1]; Mor Hanany[1]; Tamar Ben-Yosef[2]; Eyal Banin[1] and Dror Sharon[1]

*1. Department of Ophthalmology, Hadassah Medical Center, Jerusalem, Israel. 2. Department of Genetics, Faculty of Medicine, Technion, Haifa, Israel.*

**64** 9:30 **Genome Wide Association Study Analysis on Adult Onset Foveomacular Vitelliform Dystrophy in the Israeli Population** p. 108

Michelle Grunin[1], Liran Tiosano[1], Elior Rahmani[2,3], Gala Beykin[1], Regev Schweiger[2,3], Shira Hagbi-Levi[1], Dror Sharon[1], Eran Halperin[2,3,4], Itay Chowers[1]

*1. Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel, 2. Molecular Microbiology and Biotechnology, Tel Aviv University, Israel, 3. The Blavatnik School of Computer Science, Tel Aviv University, Israel, 4. International Computer Science Institute, ICSI, USA*

**65** 9:35 **Autosomal recessive nonsyndromic retinitis pigmentosa caused by a mutation of the mucopolysaccharidosis type IIIC gene, heparan-alpha-glucosaminide N-acetyltransferase (*HGSNAT*)** p. 109

Leah Rizel,[1] Hadas Newman,[2] Rina Leibu,[3] Hagit N Baris,[4] Eyal Banin,[5] Amir Massarweh,[6] Ofer Isakov,[7] Dror Sharon,[5] Noam Shomron,[7] Tamar Ben-Yosef[1]

*1Department of Genetics and 6Department of Physiology and Biophysics, The Rappaport Family Institute for Research in the Medical Sciences, Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel,2 Department of Ophthalmology, Tel-Aviv Medical Center, Tel-Aviv, Israel, 3 Alberto Moscona Department of Ophthalmology, Rambam Health Care Campus, Haifa, Israel, 4The Genetic Institute, Rambam Health Care Campus, and Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel, 5 Department of Ophthalmology, Hadassah- Hebrew University Medical Center, Jerusalem, Israel, 7 Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel*

**66** 9:40 **A novel platform for minimally invasive delivery of cells and therapeutics to the posterior segment** p. 110

Ygal Rotenstreich[1], Sapir Kalish[1], Adi Tzameret[1], Ifat Sher[1], Avraham Treves[2], Arnon Nagler[3], Michael Belkin[1]

*1Goldschleger Eye Research Institute Sackler Faculty of Medicine Tel Aviv University Sheba Medical Center Tel-Hashomer, 2Center for Stem Cells and Regenerative Medicine Cancer Research Center Sheba Medical Center Tel-Hashomer, 3Hematology Division, Sheba Medical Center Tel-Hashomer, Israel*

9:45 **Discussion**

**Coffee and exhibition** 10:00 – 10:30

## Retina 4: AMD

10:30 – 11:10

### Moderators:

Prof. Itay Chowers
Prof. Ayala Polak

**67** 10:30 **The protective effect of activated protein C (APC) on cell permeability and laser-induced CNV progression** p. 111

Iris Deitch1, Tilda Barliya3, Omer Bialer1,3, Yael Nisgav3, Mor Dachbash3,Dov Weinberger1,2,3, Tami Livnat1,2,3,4
*1Department of Ophthalmology, Rabin Medical Center, PetachTikva, Israel, 2Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel, 3Laboratory of Eye Research, Felsenstein Medical Research Center, Rabin Medical Center, PetachTikva, Israel, 4The Israeli National Hemophilia Center, Sheba Medical Center, Tel Hashomer, Israel*

**68** 10:35 **Suppression of Laser-induced Choroidal Neovascularization Using Promiscuous Cytokine Antagonist** p. 112

Shira-Hagbi-Levi[1], Michal Abraham[2], Liran Tiosano[1], Batya Rinsky[1], Michelle Grunin[1], Amnon Peled[2,3], Itay Chowers[1]
*[1]Department of Ophthalmology, Hadassah-Hebrew University Medical Center,[2]Goldyne Savad Institute of Gene Therapy, Hebrew University Hospital, Jerusalem, 91120 P.O.B 12000, Israel, [3]Biokine Therapeutics Ltd., Science Park, Ness Ziona, Israel.*

**69** 10:40 **TNF-α induced ROS accumulation is mediated by TAK1** p. 113

Zeev Dvashi[1] ,Orit Adir[1] and Ayala Pollack[1]
*1Kaplan Medical Center, Rehovot, affiliated with Hadassah-Hebrew University of Jerusalem, Rehovot.*

**70** 10:45 **Interim Results of the Aflibercept as a Second Line Therapy for Neovascular Age Related Macular Degeneration in Israel (ASLI) study** p. 114

Liran Tiosano[1], Michaela Goldstein[2], Ori Segal[3], Ayala Polack[4], Rita Erlich[5], Itay Chowers[1], Itamar Klemperer[6], Yoreh Barak[7], Nurit Mathalone[8]

*[1]Hadassah-Hebrew University Medical Center, [2] Tel Aviv Medical Center, [3] Meir Medical Center, [4] Kaplan Medical Center, [5] Rabin Medical Center, [6] Soroka Medical Center, [7]*

**71** 10:50 **Structure-Function Correlation Demonstrated by Imaging and Microperimetry in Dry AMD Patients with Geographic Atrophy** p. 115

Shelly Stika, Boris Rosin, Alexey Obolensky, Eyal Banin and Devora Marks Ohana

*CRMD, Hadassah-Hebrew University Medical Center*

10:55 **Discussion**

## Guest lecture 3

11:10 - 11:40

**Rony Paz**

*Dept. of Neurobiology, Weizmann Institute of Science*

**Value modulation of early sensory perception: from neural mechanisms to psychopathology.**

## Awards and ISVER update

11:40 -12:00

## Guest lecture 4

12:00 – 12:30

**Gideon Amichay**

*Former Chief Creative Officer & Joint Managing Partner of Shalmor-Avnon-Amichay*

**"No, No, No, No, No, Yes" - Every "NO" is a great opportunity to search for the next "YES"**

## Lunch

12:30 -13:30

## Glaucoma

13:30 – 14:10

### Moderators:

Prof. Eytan Blumenthal

Dr. Modi Naftali

**72** 13:30 **Indentation gonioscopy during laser Iridotomy, a new concept and lens for treating angle-closure glaucoma** p. 116

Eytan Z. Blumenthal

*Department of Ophthalmology, Rambam Medical Center, Haifa.*

**73** 13:35 **Non Pigmented Ciliary Epithelium derived exosomes and their role within the drainage system as a pharmacological intervention target for glaucoma** p. 117

Natalie Karpenko, Sofia Schreiber-Avissar and Elie Beit-Yannai,

*Ben-Gurion University of the Negev, Beer-Sheva, Israel*

**74** 13:40 **TNF-α and α2M proteins in the aqueous humor of glaucoma patients** p. 118

Michal Schaap-Fogler[1], Pablo F. Barcelona[2], Uri H. Saragovi[2], Maya Eiger-Moscovich[1], Karin Mimouni[1,3], Michal Kramer[1,3]

*[1]Department of Ophthalmology, Rabin Medical Center, Petach Tiqva, [2]Lady Davis Institute-Jewish General Hospital, McGill University, Montreal, [3]Sackler School of Medicine, Tel Aviv University,Tel Aviv*

**75** 13:45 **Pressure vs. Flow characterization of the JET Glaucoma Filtration Device** p. 119

Modi Naftali, Yakir Kushlin[1], Maya Levital[1]

*[1]Hanita Lenses, [2]Technion Biofluids Laboratory*

**76** 13:50 **The effect of nocturnal CPAP therapy on the intraocular pressure of patients with sleep apnea syndrome** p. 120

Yuval Cohen[a], Eyal Ben-Mair[b], Eyal Rosenzweig[b], Dalia Shechter-Amir[b], Arieh S Solomon[a]

*[a] Goldschleger Eye Research Institute, Tel Aviv University, 53621 Tel Hashomer, Israel. [b] The Institute for Fatigue and Sleep Medicine, Chaim Sheba Medical Center, 53621 Tel Hashomer, Israel.*

**77** 13:55 **Sildenafil does not prevent retinal damage in a rat model of acute ocular hypertension** p. 121

Raaya Ezra-Elia[1], Germana Alegro da Silva[2], Diogo Sousa Zanoni[3], Renée Laufer-Amorim[3], José Luiz Laus[2], Ron Ofri[1].

*[1]Koret School of Veterinary Medicine, The Hebrew University of Jerusalem, Rehovot, Israel, [2]Ophthalmology Unit, Dept. of Clinics and Surgery, College of Agronomical and Veterinarian Sciences, São Paulo State University, Jaboticabal, São Paulo, Brazi, l[3]Dept. of Veterinary Pathology, Dept. of Veterinary Clinic, Faculty of Veterinary Medicine and Animal Science, College of Agronomical and Veterinarian Sciences, São Paulo State University, Botucatu, São Paulo, Brazil*

14:00 **Discussion**

## Cataract & Refractive Surgery

14:10– 15:00

### Moderators:

Dr. Guy Kleinmann

Prof. Igor Kaiserman

**78** 14:10 **Accommodative add-on optical implant – a novel concept and preliminary studies** p. 122

Ehud I. Assia [(1, 2)] , Yokrat Ton [(1,2)]

*1. Department of Ophthalmology, Meir Medical Center, Kfar-Saba), 2. Sackler School of Medicine, Tel-Aviv University, Ramat Aviv*

**79** 14:15 **Comparison of three designs of PCO preventing ring** p. 123

Lee Slutzky[1], Guy Kleinmann[2]

*[1]Hebrew University of Jerusalem [2]Kaplan Medical Center, Rehovot, Israel*

**80** 14:20 **Long-term evaluation of hyperopic laser refractive surgery** p. 124

Lily Karmona[1]; Tzahi sela[2]; Oz franco[2]; Avi shoshani[2]; Gur Mitzer[2]; Igor Kaiserman[2,3]

*[1] Department of ophthalmology, Wolfson Medical center, Holon, Israel, [2] Care-Vision Laser center Institute, Tel-aviv, Israel, [3] Department of ophthalmology, Barzilai Medical center, Ashkelon, Israel*

**81** 14:25 **Factors predicting the need for retreatment after refractive surgery** p. 125

Michael Mimouni MD1†, Igor Vainer BScMed1†, Yinon Shapira MD1, Shmuel Levartovsky MD2, Tzahi Sela3, Gur Munzer3, Igor Kaiserman MD, MSc, MHA2,3

*† Both authors contributed equally to this paper, [1]Department of Ophthalmology, Rambam Health Care Campus, Haifa, Israel, [2]Department of Ophthalmology, Barzilai Medical Center, Ashkelon and the Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheba, Israel, [3]Care-Vision Laser Centers, Tel-Aviv, Israel.*

**82** 14:30 **Comparison of three epithelial removal techniques in Photorefractive Keratectomy: mechanical, alcohol-assisted, and transepithelial laser** p. 126

Yinon Shapira1, Michael Mimouni1, Shmuel Levartovsky2, David Varssano3, Igor Kaiserman2

*1 Department of Ophthalmology, Rambam Health Care Campus, Haifa, Israel, 2 Department of Ophthalmology, Barzilai Medical Center, Ashkelon and the Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheba, Israel, 3Department of Ophthalmology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, affiliated to the Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel*

**83** 14:35 **Refractive Surgery: Safety, efficacy, predictability and clinical outcomes** p. 127

Assaf Gershoni, Ofer Daphna, Michael Haims, Andrew Fink, Adi Nahum, Uri Marmur, Michael Mimouni, Irit Bahar

*Assuta Optic Laser Center, Tel Aviv*

14:40 **Discussion**

**Coffee and exhibition:** 15:00 -15:30

## Visual Perception

15:30 – 16:30

### Moderators:

Dr. Shachar Maidenbaum

Prof. Zeev Zalevsky

**84** 15:30 **Rapid tracking of threat during avoidance, by body and eye motion** p. 128

Tidhar Lev-Ari[1], Avichai Lustig[2], Hadas Ketter Katz[2] & Gadi Katzir[1,3]

*1. Department of Evolutionary and Environmental Biology, University of Haifa, Israel. 2. Department of Neurobiology, University of Haifa, Haifa, Israel. 3. Department of Marine Biology, University of Haifa, Israel.*

**85** 15:35 **Binocular dichoptic video content treatment for amblyopia – pilot study** p. 129

Chaim Stolovitch, MD[1]

*Tel Aviv Medical Center, Pediatric Ophthalmology Unit, Department of Ophthalmology[1]*

**86** 15:40 **Criteria for prescribing in cases of borderline refractive errors** p. 130

Einat Shneor[1], Bruce Evans[2], Yael Fine[1], Yehudit Ben Horin[1], Liat Gantz[1] and Ariela Gordon-Shaag[1]

*1. Dept. of Optometry, Hadassah Academic College, 2. Institute of Optometry, London; City University, London*

**87** 15:45 **Prevalence of V Pattern Exophoria in an Academic Institution-Based Optometric Clinic and a Community-Based Optometric Clinic** p. 131

Gary Roth, Michel Millodot, Liat Gantz

*Hadassah Academic College*

**88** 15:50 **Exploring non-visual Allocentric Navigation using Sensory Substitution** p. 132

Shachar Maidenbaum[1,2], Reut Habusha[3], Amir Amedi[1,2,3,4]

*[1]ELSC, Hebrew University of Jerusalem, [2]IMRIC, Department of Medical Neurobiology, Hebrew University of Jerusalem, [3]Departmnt of Cognitive Science, Hebrew University of Jerusalem, [4]Institut de la Vision, UPMC Univ Paris 06,Sorbonne Universités,*

**89** 15:55 **Standardizing functional tests for visual rehabilitation devices using virtual environments** p. 133

Shachar Maidenbaum[1,2], Amir Amedi[1,2,3,4]

*[1]ELSC, Hebrew University of Jerusalem, [2]IMRIC, Department of Medical Neurobiology, Hebrew University of Jerusalem, [3]Departmnt of Cognitive Science, Hebrew University of Jerusalem, [4]Institut de la Vision, UPMC Univ Paris 06,Sorbonne Universités,*

**90** 16:00 **Contribution of color to "visual" acuity using sound** p. 134

Galit Buchs[1,2], Shelly Levy-Tzedek[3,4], Dar Rimer[2], Amir Amedi[1,2,5,6]

*1 The Cognitive Science Program, The Hebrew University of Jerusalem, Jerusalem, Israel, 2 Department of Medical Neurobiology, The Institute for Medical Research Israel-Canada, Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel, 3 Recanati School for Community Health Professions, Department of Physical Therapy, Ben Gurion University of the Negev, Beer-Sheva, Israel, 4 Zlotowski Center for Neuroscience, Ben Gurion University of the Negev, Beer-Sheva, Israel, 5 The Edmond and Lily Safra Center for Brain Sciences (ELSC), The Hebrew University of Jerusalem, Jerusalem, Israel, 6 Institut de la Vision, UPMC Univ*

**91** 16:05 **Core knowledge of geometry develops without visual experience** p. 135

Benedetta Heimler[1,2]*, Tomer Behor[1,2]*, Stanislas Deheane[3,4,5,6] and Amir Amedi[1,2]

*[1]Department of Medical Neurobiology, Institute for Medical Research Israel-Canada, Faculty of Medicine, Hebrew University of Jerusalem, Hadassah Ein-Kerem, Jerusalem, Israel, [2] The Edmond and Lily Safra Center for Brain Research, the Hebrew University of Jerusalem, Hadassah Ein-Kerem, Jerusalem, Israel, [3]Cognitive Neuroimaging Unit, Institut National de la Santé et de la Recherche Médicale,91191 Gif sur Yvette, France, [4]Neurospin Center, Commissariat à l'énergie atomique (CEA), Division Sciences de la Vie(DSV), Institut d'imagerie Biomédicale (I2BM), 91191 Gif sur Yvette, France, [5]University Paris 11, 91405 Orsay, [6]France Collège de France, 75005 Paris, France*

**92** 16:10 **Experimental Quantification of Corneal Tactile Spatial Responsivity for Vision Substitution** p. 136

Zeev Zalevsky[1,2], Yevgeny Beiderman[1], Ygal Rotenstreich[3] and Michael Belkin[3]

*[1]Faculty of Engineering, Bar-Ilan University, Ramat-Gan 52900, Israel, [2]Erlangen Graduate School in Advanced Optical Technologies (SAOT), Friedrich-Alexander Universität Erlangen-Nürnberg, Paul-Gordan-Straße 6, 91052 Erlangen, Germany, [3]Goldshleger Eye Research Institute, Tel-Aviv University, Tel-Hashomer, Israel*

**93** 16:15 **Is Lessepsian fish migration vision based? – The start of a quest** p. 137

Amit Lerner

*National Institute of Oceanography, Israel Oceanographic and Limnological Research Ltd*

16:20 **Discussion**

**Concluding remarks** 16:30 – 16:40

Prof. Avi Solomon

# *Abstracts*

# *תקצירים*

## Correlation between coagulation and inflammatory systems in a rabbit model LPS-induced Uveitis.

Atamney M[1], Barliya T[2], Ehrlich R[1, 2, 3], Weinberger D[1, 2, 3] and Livnat T[1, 2, 4]

*1. Division of Ophthalmology, Rabin Medical Center- Beilinson campus, Petah Tikva, Israel. 2 Laboratory of Eye research Felsenstein Medical Research Center (FMRC). 3. Sackler School of Medicine, Tel-Aviv University, Israel. 4. The Israeli National Hemophilia Center, Sheba Medical Center, Tel Hashomer, Israel*

**Purpose:** The connections between the coagulation and inflammatory systems were well demonstrated in many diseases other than ocular pathologies. The aim of this study is to investigate the possible interplay between these two systems in a rabbit uveitis model.

**Methods:** Panuveitis was induced in 9 New Zealand male rabbits by intravitreal injection of LPS with a 30g needle, under direct visualization of a surgical microscope. The control group (group 1) received sham injection of PBS. Eyes were evaluated at time 0, 2, 4, 6, and 24hrs. Images of the anterior chamber and posterior chambers were acquired by slit lamp and indirect ophthalmoscope, respectively. Eyes were clinically evaluated and scored by the SUM (Standardization of Uveitis Nomenclature scoring). Samples of aqueous humor and vitreous tap were obtained from the right eye at 6hr post injection (group2) and 24hrs (group 1&3). IL-6 and thrombin-anti-thrombin (TAT) levels were determined in these samples using the enzyme-linked immunosorbent assay kits.

**Results:** We confirmed high levels of IL-6 in LPS-induced uveitis, in both the anterior and the posterior chambers as compared to control. IL-6 levels increased over time between the two time points 6hrs (3810 pg/ml) and 24hrs (6824 pg/ml). Levels were slightly higher in the anterior chamber than in the vitreous. Moreover, eyes with LPS-induced uveitis showed high infiltration of white blood cells (PMN) in both chambers. TAT was not found in the control group in either chamber. Interestingly, TAT was detected only in the vitreous samples of LPS-induced uveitis, but not in the aqueous humor samples.

**Conclusions:** In this study we found that the coagulation system is involved in the pathophysiology of uveitis. The coagulation system activation is restricted to the vitreous compartment and does not involve the anterior chamber. Further studies will confirm and clarify the role of the coagulation system in inflammatory diseases of the eye, and might open the door for new therapeutic strategies.

## Early vascular changes in eyes treated with bevacizumab compared with eyes treated with laser for type-1 retinopathy of prematurity

Yuval Cohen [a,f], Domenico Lepore [e], Gui-shuang Ying [b], Clare M. Wilson [c,d] Jiayan Huang [b], Karen A. Karp [a], Agnieshka Baumritter [a], Akosua Nti [a], Giovanni H. Greaves [a], Graham E. Quinn [a,b]

*aDivision of Ophthalmology, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania; bScheie Eye Institute, University of Pennsylvania, Philadelphia; cVisual Science, UCL Institute of Ophthalmology, London, United Kingdom; d Department of Ophthalmology, Great Ormond Street Hospital, London, United Kingdom, eCatholic University of the Sacred Hearts, Rome, Italy, f Hillel Yaffe Medical Center, Hadera, Israel.*

**Purpose:** Most studies assessing treatment outcomes for eyes treated with bevacizumab or laser are based on subjective measures. This study seeks to determine the difference in vascular parameters between eyes treated with bevacizumab and eyes treated with laser objectively by measuring vessel width and tortuosity at one to three weeks after treatment.

**Methods:** Images from 36 eyes (18 infants) with type-1 ROP obtained before and at up to three time points after treatment with bevacizumab in one eye and laser in the fellow eye were analyzed. The tortuosity and width of the vessels were measured in arbitrary units (AU) and pixels, respectively, using computer assisted image analysis of the retina (CAIAR). Statistical comparisons of width and tortuosity were made using paired t-test for pre-treatment vs. post- treatment, and also between bevacizumab vs. laser treated eyes at pre-treatment and post-treatment.

**Results:** At up to three weeks post treatment, decrease in vessel width was significantly greater in bevacizumab treated eyes compared with laser treated eyes for all follow-ups after treatment (-0.15 vs. 0.05 pixels, p=0.02). There was no significant difference in tortuosity between eyes treated with bevacizumab and eyes treated with laser at one to three weeks after treatment.

**Conclusions:** One to three weeks after treatment with bevacizumab, vessel width decrease is greater than in eyes treated with laser. Vasodilatation appears to decrease more rapidly in bevacizumab-treated eyes than in laser-treated eyes. The implication on vasculogenesis of this decreased vessel caliber after treatment is unclear.

## Pax6 role in the regulation of retinal pigmented epithelium maturation

Yamit Cohen-Tayar[1], Ruth Ashery-Padan[1]

*1 Department of Human Molecular Genetics and Biochemistry, Sackler School of Medicine, Tel-Aviv University, Israel*

**Purpose:** Pax6 is a key transcription regulator in early eye development. Haploinsufficiency of Pax6 was long shown to cause microphthalmia, anophthalmia or aniridia in human patients, and therefore led many to investigate its role in eye development. The retinal pigmented epithelium (RPE) is important for the development and maintenance of the photoreceptors and the choroid blood vessels. Somatic mutagenesis of Pax6 in the specified RPE resulted in a phenotype of aniridia and further transcriptomic analysis revealed an up-regulation in expression levels of genes related to RPE maturation. Pax6 is required for establishment of various progenitor subtypes within the central nervous system and was shown to play a role in proliferation, which takes place in early stages of RPE differentiation. Hence, in addition to the known role of Pax6 in executing programs related to early eye development, this study aims to investigate its inhibitory function in regulation of programs related to late differentiation of the RPE.

**Methods:** To this purpose, conditional mutations of Pax6 and genes related to late RPE differentiation will be induced. Gain of function analysis will be conducted using sub-retinal injections followed by electroporation or viral injections. Further investigation of the molecular mechanism involved in this regulation will be performed using RPE cells derived from human embryonic stem cells.

**Results:** Expression patterns of Pax6 and factors established to be required for RPE maturation were determined in course of RPE differentiation. Expressions were examined in wild type mice and mice with Pax6 specific ablation from the RPE and illustrated opposite patterns. Gain of function analysis confirmed this observation since miss-expression of Pax6 in the differentiated RPE resulted in inhibition of late differentiation factors.

**Conclusions:** This study is the first to document Pax6 role in timing RPE differentiation. Pax6 ablation from the RPE resulted in a premature expression of late differentiation factors, and ectopic expression of Pax6 inhibited RPE maturation.

## A SEMA3E mutant resistant to cleavage by furins (UNCL-SEMA3E) inhibits laser induced choroidal neovascularization

Allon Gilad [1], Toledano Shira [2], Kigel Boaz [2], Kessler Ofra [2], Hagbi-Levi Shira [3], Tiosano Liran [3], Schaal Shlomit[4], Neufeld Gera [2], Barak Yoreh[1]

*1.Ophthalmology Department, Rambam Health Care Center, Haifa, Israel. 2.Cancer Research and vascular Biology Center, The Bruce Rappaport Faculty of Medicine, , Technion, Israel Institute of Technology, , Haifa, Israel. 3.Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel. 4. Department of Ophthalmology and Visual Sciences, University of Louisville, Louisville, KY, United States.*

**Purpose:** Abnormal subretinal choroidal neovascularization (CNV) is a major blinding consequence of the exudative form of age-related macular degeneration (AMD). Anti-angiogenic agents may be useful in preventing CNV formation. A point mutated form of semaphorin-3E resistant to cleavage by furin like pro-protein convertases (UNCL-Sema3E) is known to display potent anti-angiogenic properties. UNCL-Sema3E is unique by its action of counteracting activities of angiogenic growth factors other than VEGF, such as affecting receptors of neuropilin and plexin. The purpose of this study is to determine if UNCL-Sema3E may be used in-vivo to inhibit CNV formation.

**Methods:** : Cultured vascular endothelial cells were stimulated with VEGF (10 ng/ml) in the presence or absence of UNCL-Sema3E/Fc (1.5 µg/ml). After 10 min. at room temperature the cells were lysed and ERK1/2 phosphorylation determined. CNV was induced in the eyes of Evans-Long rats by laser photocoagulation (n=128) followed by an intravitreal injection of either UNCL-Sema3E (125 µg/5 µl), avastin (125 µg5 µl), or vehicle (5 µl) as control. After a week flat whole mounts of retinas where used to determine CNV frequency and size. Results were assessed by the staining of blood vessels with isolectin and calculating the area of stained blood vessels using the Image-J morphometric software.

**Results:** UNCL-Sema3E inhibits efficiently both VEGF and bFGF induced signal transduction in cultured vascular endothelial cells. UNCL-Sema3E injected into the vitreous cavity reduced the area of laser induced CNV (n=65) by 50% (64040 ± 7321 µm2 for controls (n=61) vs 32720 ±- 2369 µm2, P<0.0001) displaying efficacy similar to that of bevacizumab[SS3] (n=54).

**Conclusions:** UNCL-Sema3E inhibits laser induced CNV formation in the rat model as efficiently as bevacizumab. This suggest that UNCL-Sema3E may be considered as a possible therapeutic agent for the treatment of exudative AMD that is resistant to current anti-VEGF treatments because it acts on a different anti-angiogenic pathway.

## Penetration of Intravitreal Injected Tissue Plasminogen Activator to the Retina - Rats Model Study

Tal, Kfir1, 2; Dotan, Assaf1, 2; Nisgav, Yael3, 2; Mor Dachbash3; Ehrlich, Rita1, 2; Weinberger, Dov1, 2; Livnat, Tami3, 2

*1. Department of Ophthalmology, Rabin Medical Center ,Beilinson Campus Petach Tikva 49101, Israel, Petach Tikva ,Israel. 2. Sackler School of Medicine, Tel Aviv University, Tel Aviv , Israel. 3. Laboratory of Eye Research, Felsenstein Medical Research Center, Petah Tikva, Israel.*

**Purpose:** Tissue plasminogen activator (tPA) is a thrombolytic agent which has the ability to degrade and dissolve fibrin clot. Although the efficacy of intravitreal tPA injections has been shown in clinical practice, the ability of intravitreal Injected tPA to diffuse from the vitreous through the retina and into the subretinal space has been questioned in an experimental models, as tPA conjugated to fluorescein, failed to penetrate the retina. We investigate whether an unconjugated tPA injected into the vitreous could penetrate the neural retina and enter the subretinal space, in a rat model.

**Methods:** 24 rats eyes were used in the study.14 right eyes were injected with intravitreal tPA (0.75 µg/3 µl), 10 right eyes were injected with intravitreal saline, and served as controls. 3, 24, and 48 hours after tPA injection, animals were euthanized and eyes were taken for cryosections and immunohfluorescence staining. Goat anti tPA, followed by alexafluor 568 donkey anti goat (invitrogene) were used for tPA detection.

**Results:** TPA staining was detected in deep retinal layers in all eyes injected with intravitreal tPA. A deeper and more intense staining of tPA was seen after 3 and 24 hours, compared to a decreased staining 48 hours from injection. No staining of tPA was detected in the retina in the eyes injected with saline.

**Conclusions:** We demonstrated that an unconjugated tPA at a dose of (0.75 µg / 3 µl) injected into the vitreous penetrates the retina of rats. We speculate that former rabbit model studies that failed to show penetration of tPA to the retina may be explained by the use of conjugated tPA that doesn't penetrate the retina.

## TNFα- induced TGFβ activation in RPE cells

Orit Adir[1], Zeev Dvashi[1] and Ayala Pollack[1]

*Kaplan Medical Center affiliated to the Hebrew University of Jerusalem, Israel*

**Purpose:** Inflammation is the hallmark of many retinal pathologies and is mediated by cytokines and chemokines such as tumor necrosis factor α (TNFα), transforming growth factor β1 (TGFβ1), monocyte chemoattractant protein-1 (MCP-1) and interleukins. Inflammatory response of the retinal pigment epithelium (RPE) cells is mainly characterized by the transformation of RPE cells into myofibroblasts cells, a process which is manifested by increased motility and contractility, enhanced expression of α- smooth muscle actin (αSMA) and secretion of matrix metalloproteinases (MMPs). TNFα and TGFβ1 are known to play a key role in inflammatory response in RPE cells. This study aimed to investigate a possible cross- talk between TNFα and TGFβ1 in the inflammatory response of RPE cells.

**Methods:** ARPE-19 cells were treated with SB431542 (TGFβ1 receptor kinase inhibitor) followed by TNFα (20ng/ml) stimulation at all experiments, as well as TGFβ1 (2.5ng/ml). Smad2, p38 and p65 activation was determined by western blot analysis; αSMA expression was detected by immunofluorescence staining; cell migration was determined using scratch assay; cell contractility was examined using collagen contraction assay; MMPs levels were quantified by gelatin zymography assay.

**Results:** Stimulation of RPE cells with TGFβ1 activates Smad2/3 proteins, specific TGFβ1 substrates. Surprisingly, treatment with TNFα also increases Smad2/3 activation. Moreover, TNFα treatment increases αSMA expression, cell migration and contractility, all are inflammation features. However, addition of TGFβ1 receptor specific inhibitior abolishes all these processes. A synergistic effect was observed in the combined treatment of TNFα and TGFβ1 induced MMP9 secretion, in addition to elevation in MMP2 secretion.

**Conclusions:** The data presented hereby, demonstrate that TGFβ1 is trans-activated by TNFα, and that TNFα- induced inflammatory response is TGFβ1- dependent. Thus, a better understanding of the cross- talk between TNFα and TGFβ1 might be used to reduce the inflammatory and fibrotic response underlying retinal pathologies.

## Retinal toxicity of intravitreal clindamycin in albino rabbits

Orit Mazza[1], Zohar Habot-Wilner[2], Jonathan Shahar[2], Amir Massarweh[1], Irit Mann[1], Anat Loewenstein[2], Ido Perlman[1]

*Department of Physiology and Biophysics, the Ruth and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology and the Rappaport Institute, Haifa, Israel.[1], Division of Ophthalmology, Tel-Aviv Medical Center, Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel.[2]*

**Purpose:** To evaluate retinal toxicity of intravitreal clindamycin.

**Methods:** Eight albino rabbits were included in the study. In each rabbit, 1 mg/0.1 ml clindamycin was injected into the vitreous of the right (experimental) eye and 0.1 ml saline was injected into the vitreous of the left (control) eye. Electroretinogram (ERG) was recorded before injection, 3-days, 1-, 2- and 4-weeks post injection and Visual Evoked Potential (VEP) was recorded 4-weeks post injection. Clinical examination was conducted at all-time points. Retinal structure and expression of Glial Fibrillary Acidic Protein (GFAP) were derived from histology and immunocytochemistry that were performed on rabbit eyecups, which were enucleated at termination of the follow-up period.

**Results:** ERG and VEP responses recorded following stimulation of the experimental eye were similar to those recorded following stimulation of the control eye. Clinical examination was found normal in all eyes. No histological damage was seen, but GFAP was mildly expressed in 2 out of 8 retina from experimental eyes.

**Conclusions:** Intravitreal injection of 1 mg clindamycin does not cause functional or histological signs of retinal toxicity in albino rabbits, during a period of 1 month post injection. Two eyes had very mild GFAP expression in Müller cells, which may indicate a very low degree of retinal stress.

# Presence of Bevacizumab in the iridocorneal angle following intravitreal injection in a rat model

Orly Gal-Or[1], Assaf Dotan[1], Mor Dachbash[3], Yael Nisgav[3], Dov Weinberger[1,2,3] Rita Ehrlich[1,2] ,Tami Livnat[1,2,3]

*[1] Department of ophthalmology, Rabin Medical Center, Petach-Tikva,[2] Sackler School of Medicine, Tel-Aviv University, Tel Aviv, [3] Laboratory of Eye Research, Felsentatein Medical Research Center, Rabin Medical Center, Petach -Tikva*

**Purpose:** Intravitreal anti vascular endothelial growth factor agents can cause sustained ocular hypertension in treated eyes. Our purpose was to investigate and characterize the presence of intravitreally injected Bevacizumab in the iridocorneal angle in a rat model.

**Methods:** Choroidal neovascularization was induced by diode laser photocoagulation on the right eye of twelve Brown Norway rats. Bevacizumab (25mg/ml) was injected intravitreally following 3 days.

Immediately after Bevacizumab injection and 3,6,24 and 48 hours later, animals were euthanized for immunohfluorescence staining. Donkey anti-human IgG labeled with Alexa Fluor® 488 was used for Bevacizumab immunoreactivity detection. Anti CD31 antibody was used as a marker for schlemm's canal's (SC) endothelial cells. Untreated eyes were used as negative controls. We qualitatively analyzed the intensity of the immunohistochemistry staining.

**Results:** Bevacizumab immunoreactivity was found in the Trabecular Meshwork (TM) and Schlemm's canal (SC) immediately after injection, and declined in a decremented manner within the following hours. Forty eight hours from the injection no bevacizumab staining was detected in the iridocorneal angle structures

**Conclusions:** Our study demonstrated Bevacizumab in iridocorneal angle structures after intravitreal injection in a rat model. Bevacizumab molecules were shown to pass within 48 hours through the iridocorneal angle starting immediately after intravitreal bevacizumab injection.

## Differentiation and paracrine activity of adipose tissue derived mesenchymal stem cells when exposed to normoxic and hypoxic RPE

Aya Barzelay[a], Ran Levy[a], Emmanulle Kohn[a], Meirav Sella[b], Nir Shani[b], Benjamin Meilik[b], Eyal Gur[b], Anat Loewenstein[a], Adiel Barak[a]

*aOphthalmology Laboratory, Department of Ophthalmology Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel, bDepartment of Plastics and Reconstructive Surgery Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel, a,bAffiliated with Sackler Faculty of Medicine Tel Aviv University, Ramat Aviv, Israel*

**Purpose:** Hypoxic stress contributes to various retinal pathologies. We aimed to examine the paracrine activity and differentiation potential of adipose tissue derived mesenchymal stem cells (ASCs) when exposed to hypoxic and normoxic retinal pigment epithelium (RPE) in vitro.

**Methods:** RPE cells were subjected to 1% O2 hypoxia. ASCs were cultured with conditioned medium of hypoxic RPE. ASCs' expression of growth factors was assessed by qRT-PCR and immunoassaying. Differentiation capacity to RPE was examined by culturing ASCs with normoxic RPE conditioned medium, activin A and nicotinamide. Differentiation markers were assessed with qRT-PCR and immunostaining.

**Results:** ASCs increased expression of the trophic factor BDNF (2.2±0.3 folds $p<0.05$) and anti angiogenic agent serpinb5 (2.3±1.6 folds $p<0.05$) when exposed to hypoxic RPE. When exposed to normoxic RPE, ASCs demonstrated differentiation potential to RPE by upregulation of early eye field markers at 1-2 weeks (pax6 2.6±0.8, six3 1.4±0.7, rax 1.4±0.2, otx2 2.2±0.7 folds) and RPE markers at 4 weeks (rlbp1 3.8±0.7, best1 2.3±0.7, emmprin 2±0.2, zo-1 2.2±0.4, tyrosinase 5.5±0.8, RPE65 3.8±1.6 folds).

**Conclusions:** ASCs express trophic and anti angiogenic factors when exposed to hypoxic RPE. Moreover, ASCs exhibit a differentiation capacity to RPE when exposed to normoxic RPE. These data imply to the potential in using ASCs for retinal cell therapy.

## The Effects of the ApoE4 Genotype on the Developing Murine Retina

Idit Maharshak[1,2], Shiran Salomon-Zimri[1], Ran Antes[1],Tami Livnat[3], Arieh S. Solomon[4], Dov Weinberger[5,2], Carol A. Colton[6], Daniel M. Michaelson[1]

*1Department of Neurobiology, George S. Wise Faculty of Life Sciences, Tel Aviv University, Tel Aviv, Israel; 2Department of Ophthalmology, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel; 3Laboratory of Eye Research, Felsenstein Medical Research Center, Rabin Medical Center, Petach Tikva, Israel; 4Goldschleger Eye Institute, Tel-Aviv University, Tel-Hashomer, Israel; 5Department of Ophthalmology, Rabin Medical Center, Petach Tikva, Israel; 6Division of Neurology, Duke University Medical Center, Department of Medicine, Durham, NC*

**Purpose:** Apolipoprotein E4 (apoE4), the most prevalent genetic risk factor for Alzheimer's disease (AD), is associated with neuronal and vascular impairments. The retina is a good model for studying apoE4 effects, since developmentally it is considered an extension of the central nervous system (CNS). The aim of this work was to study the effects of the apoE4 genotype on retinal vasculature, neurons, apoE and vascular endothelial growth factor (VEGF) levels in neonate mice.

**Methods:** Retinal whole mounts and cryo-sections of 4, 7 and 12 days old human-apoE4 and apoE3 targeted replacement mice were stained for endothelial cells, synapses, VEGF and apoE. They were photographed with a confocal microscope and the images were analyzed and quantitated.

**Results:** The results obtained showed a transient increase in vascular density, vascular branching and vascular buds (round vascular elements, 15µX12µ in size, representing sprouting or retracting vessels) in apoE4 mice in the early post-natal days. This effect peaked and ended during the neonatal period. Synaptic immunoreactivity showed a significant decrease on day 12 in apoE4 mice, which was similarly shown in adult mice in a previous work from our lab. Next we found that in correlation to the vascular morphology, VEGF (a known vasculogenic factor) and apoE retinal levels were significantly increased in neonate apoE4 compared apoE3 mice. This is reversed in adults according to a previous study from our laboratory.

**Conclusions:** Our results revealed that apoE4 has a transient vascular effect during retinal development that ends in the neonatal period, a neuronal effect that begins at the end of the neonatal period and is sustained in adult mice. The findings that VEGF and apoE levels are increased in neonate apoE4 mice and decreased in adult apoE4 mice may be related to the observed transient vascular effect in neonates and possibly to reduced retinal neovascular changes in aging.

## The interplay between the coagulation and inflammatory systems in retinal pathologies

Alon Zahavi, [1,2,3] Tami Livnat, [2,3,4] Ruth Axer-Siegel, [1,2] Ayelet Dreznik, [1,2,3] Elinor Megiddo, [1,2] Mor Dachbash, [3] Dov Weinberger, [1,2,3] Rita Ehrlich, [1,2,3]

*[1]Department of Ophthalmology, Rabin Medical Center, Petah Tiqwa, Israel; [2]Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel; [3]Felsenstein Medical Research Center, Rabin Medical Center, Petah Tiqwa, Israel; [4]The Israeli National Hemophilia Center, Sheba Medical Center, Tel Hashomer, Israel*

**Purpose:** To evaluate and correlate the activity of the coagulation and inflammatory systems in the vitreous of patients with different vitreo-retinal pathologies.

**Methods:** Vitreous samples were collected from 91 consenting patients during pars plana vitrectomy surgery. Vitreo-retinal pathologies included macular holes (MH), epiretinal membranes (ERM), rhegmatogenous retinal detachments (RRD), vitreous hemorrhages (VH), and tractional retinal detachments (TRD). Pathologies were grouped to three main categories based on the underlying pathophysiological mechanisms: 1. MH and ERM (n=29); 2. RRD (n=33); 3. VH and TRD (n=29). Key proteins in inflammation and coagulation were assessed by measuring iInterleukin-6 (IL-6) and thrombin anti-thrombin (TAT) levels, respectively, by ELISA.

**Results:** Increased TAT and IL-6 levels measured in the vitreous samples were found highest in patients with RRD followed by VH and TRD and lower levels were measured in patients with ERM and MH. TAT levels were statistically significantly higher in the TRD/VH and RRD groups compared to the MH/ERM group (MH/ERM vs. RRD $p<0.0001$, MH/ERM vs. TRD/VH $p=0.0003$). No significant difference was found between the TRD/VH and RRD groups. IL-6 levels were significantly different in the MH/ERM group and TRD/VH and RRD groups ($p<0.0001$), as well as between TRD/VH and RRD ($p<0.05$). Linear correlation between IL-6 and TAT was found in the MH/ERM group ($p=0.0001$). The RRD group showed a trend towards a linear correlation ($p=0.38$), while the TRD/VH group did not show any significant correlation.

**Conclusions:** Our study demonstrates that TAT levels were significantly higher in the RRD and TRD/VH groups compared to MH/ERM. IL-6 was highest in the RRD patients group. Correlation between TAT and IL-6 levels were not uniform in the different vitreo-retinal pathologies. Future studies will aid in confirming and further revealing the role of the coagulation system in the pathophysiology of different retinal pathologies, and in the development of new treatment strategies.

## Light-induced retinal damage in dark-reared albino rats, its reversibility and the link to acetylcholinesterase

Amir Massarweh, Ronit Heinrich, Olga Medvedev, Ido Perlman

*Department of Physiology and Biophysics, Ruth & Bruce Rappaport, Faculty of Medicine, Rappaport Institute, Technion—Israel Institute of Technology*

**Purpose:** Our goal in this study was to characterize retinal light damage regarding rearing conditions, exposure periods, reversibility and the link to acetylcholinesterase in sprague-dawley rats.

**Methods:** We used albino rats as the experimental model. Rats were divided into three groups depending upon raising conditions. The control group (group A) was kept for two weeks in normal laboratory conditions, 12/12 hours light/dark cycle. The second group of rats (group B) was kept for two weeks in complete darkness. The third group (group C) was kept for two weeks in complete darkness and one week in 12/12 hours light/dark cycle. Then, rats from the three groups were exposed to harmful light for different periods of time. Retinal function was assessed from electrophysiological recordings of the electroretinogram (ERG).

**Results:** No differences in the ERG responses were found between rats of group A and group C. However, significant differences between group A and B were seen in their ERG responses after two hours or more of exposure to bright light. Rats that were raised for two weeks in complete darkness (group B) showed severe functional retinal damage. In fact, we could not record typical ERG responses from these rats. In contrast, rats that were kept for 2 weeks in conditions of 12/12 hours light/dark or two weeks in complete darkness and one week in 12/12 hours light/dark cycle, exhibited mild retinal damage.

**Conclusions:** Our research showed that light causes damage to the retina of albino rats that strongly depends upon the lighting conditions in the two weeks prior to exposure to the bright light. Our findings suggest that complete darkness for two weeks raises the susceptibility of the albino rats' retina to bright light, although dark-rearing without exposure didn't impact the retina, and that the susceptibility of the dark reared retina to bright light is reversible.

## Evaluation of anti VEGF single injection on diabetic retinopathy of non-obese diabetic (NOD) mice

Moshe Ben-Hamou[1,2], Orit Barinfeld[1,2], Tamar Azrad-Leibovich[1,2], Nitza Goldenberg-Cohen[1,2,3].

*[1]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv; Israel, [2]The Krieger Eye Research Laboratory, FMRC, Rabin Campus, Tel Aviv University; [3]Pediatric Ophthalmology Unit, Schneider Children's Medical Center of Israel, Petach Tikva;*

**Purpose:** The aim of this study is to evaluate the effect of intravitreal anti VEGF single injection on retinal architecture and edema in diabetic mice.

**Methods:** The study included 39 Non-obese diabetic (NOD) mice, aged 4-8 months, all examined for glucose levels in the blood. Ten underwent in vivo fluorescein angiography (FA) to demonstrate retinal blood flow and leakage; 8 NOD mice, 4 diabetic and 4 non-diabetics, were perfused with fluorescent gelatin to establish co-localization of vascular stains with vessel lumens. The remaining 21 were divided to 3 subgroups. Seven mice were included in each group which was administered either bevacizumab (Avastin), or saline 0.9% intravitreal injection to the right eye and the left eye served as an internal control. The last group was not treated. All mice were analyzed histologically, stained for Hematoxylin Eosin and Periodic acid–Schiff (PAS) and by immunohistochemistry staining for vascular and neuronal markers (Vimentin, GFAP and NG-2).

The 7 control mice (untreated group) were also analyzed molecularly. Molecular tests were examined for the following gene levels of expression: Vimentin, GFAP, VEGF and VEGF/R-1,2, RAGE, EPO.

**Results:** In vivo FA did not reveal neovascularization. However, perfusion showed tufts suspected for neovascularization, as well as microaneurysms and tortured blood vessels in the diabetic NOD mice only. Retinal thickness was measured in the 3 groups, as follows: without treatment 289$\mu m^{\pm}$20, Saline 308$\mu m^{\pm}$27 in both eyes and Avastin 219$\mu m^{\pm}$51 in the right vs. 270$\mu m^{\pm}$28 in the left eye. Molecular analysis showed an increase only in RAGE (2.7105 vs. 1), while the others remained at baseline levels and VEGF was reduced to 0.5, in the diabetic Vs non diabetic NOD mice.

**Conclusions:** Different thickness of retina was found in treated vs. untreated mice. Although VEGF levels did not increase in the diabetic mice, the anti-VEGF treatment reduced retinal edema and improved diabetic retinopathy in NOD mice.

## Changes in retinal function and cellular remodeling following experimental retinal detachment

Barliya T*[1,2] , Ofri R[*3], Sandalon S[3], Livnat T,[1,2,4], and Weinberger D[1,2,5]

*1.Division of Ophthalmology , Rabin Medical Center- Beilinson campus, Petah Tikva, Israel., 2 Laboratory of Eye research Felsenstein Medical Research Center (FMRC), Rabin Medical Center, Petah Tikva, 3. Koret School of Veterinary Medicine, The R.H. Smith Faculty of Agriculture, Food and Environment, The Hebrew University of Jerusalem, Rehovot, Israel, 4. The Israeli National Hemophilia Center, Sheba Medical Center, Tel Hashomer, Israel, 5. Sackler School of Medicine, Tel-Aviv University, Israel.*

**Purpose:** Rhegmatogenous Retinal Detachment (RRD) is a grave condition associated with acute loss of vision caused by anatomic displacement of the photoreceptor layer. It may also lead to irreversible loss of vision which may be due to retinal remodeling even if reattachment occurred. This study aims to explore functional electroretinographic (ERG) changes and associated retinal cellular remodeling following experimental retinal detachment in a rabbit model.

**Methods:** Retinal detachment was created in the right eye of ten New Zealand rabbits, while left eyes served as intact controls. For the detachment a 25G vitrectomy was performed, and the inferior retina was detached by injecting 0.1ml balanced salt solution between the neural retina and retinal pigment epithelium using a soft tip needle. Indirect ophthalmoscopy was performed pre-operatively and 1, 3, 7 and 14 days postoperatively. ERG recordings were performed pre-operatively and 7 days and 21 days post-operatively. Retinal sections were stained with H&E and studied histopathologically, and immunofluorescence was performed for PKC (All bipolar), mGluR6 (ON bipolar cells) and iGluR4 (OFF bipolar cells) in eyes harvested 21 days post-operatively.

**Results:** Retinal reattachment was seen approximately two weeks following surgery. The amplitude of the scotopic ERG a-wave was decreased significantly in eyes with retinal detachment. While no attenuation was observed in the mean photopic or scotopic b-waves, we noted the disappearance of a secondary b-wave peak in the ERG recordings of eyes with retinal detachment. Immunofluorescence staining demonstrated anatomical changes in bipolar cells, as processes of both ON bipolar and OFF bipolar cells extended into the outer nuclear layer.

**Conclusions:** Retinal detachment and reattachment are associated with functional and anatomical changes. Extensions of the OFF bipolar cells, responsible for hyperpolarization, may be responsible for the changes of the b-wave pattern. Future functional and cellular studies are warranted to more accurately understand the interplay between the 1st and 2nd order retinal neurons, cellular remodeling and ERG patterns.

## Evaluation of experimental carotid stenosis created in laboratory rat

Solomon AS[1], Rudoler N[1], Rotenstreich Y[1],Levi N[1],Tzameret A[1,] Sher I[1],Pointkevitz Y[2],Zilberstein Y[3], Ziv H[1], Pri Chen Sara[1]

*1The Goldschleger Eye Research Institute, Faculty of Medicine, Tel-Aviv University, Sheba Medical Center, Tel Hashomer, Israel;2 Strauss Center for Computational Neuroimaging, TAU;3Sackler Cellular and Molecular Imaging Center, TAU*

**Purpose:** The hypothesis of our study is that long term of carotid stenosis in human, with no symptoms along life, may have an impact on the brain and eye. Our study is intended to find out whether this hypothesis is right.

**Methods:** Adult, male, albino, Wistar rats were used in the presented study. The study was done under the approval of The Committee of Experimental Animal Research of Tel Aviv University and according to the Guidelines of ARVO in Animal Research. The right common carotid artery of each animal was partially narrowed by ligation of the blood vessel with a surgical 6\0 silk suture close to the its bifurcation. MRI, ERG, Doppler Imaging, motoric tests and histology of the brain and eye evaluated the morphologic and functional aspect of the animals.

**Results:** Focal and diffused damage were presented in the MRI examination. ERG deteriorated along the period of follow up, histology presented the damage diagnosed by MRI and retina presented atrophy of receptors. No motoric deficits were find.

**Conclusions:** Asymptomatic carotid stenosis can create damage to the brain structure and retina that may transform later in a pathologic condition of brain and eye leading to dysfunction and invalidity.

## TNF-alpha receptors 1 and 2 play a role in mouse model of optic nerve crush

Moran Fridman,[1,2] Myles Brookman,[2] Orit Barinfeld,[1,2] Nitza Goldenberg-Cohen.[1,2,3]

*1The Krieger Eye Research Laboratory, Felsenstein Medical Research Center, Tel Aviv University 2Sackler School of Medicine, Tel Aviv University, Tel Aviv; Israel, 3Pediatric Ophthalmology, Schneider Children's Medical Center of Israel, Petach Tikva, Israel*

**Purpose:** To examine the role of TNFR1/R2 in optic nerve crush by measuring the expression levels of inflammatory, ischemic, and apoptotic related genes.

**Methods:** Molecular analysis was performed on mRNA extracted from the retina of TNFR1 knock-out (KO) and TNFR2 KO mice (n=3 each). Data was compared to 7 wild type (WT) mice with the same background. All animals underwent ONC of the right eye. The left eye served as control.

Molecular analysis of the retina performed by real time quantitative polymerase chain reaction (RT-qPCR) to study the gene expressions of apoptotic associated Bax, Bcl-2; inflammatory related IL-6, Mip-2, and oxidative stress associated gene SOD.

**Results:** on day 3, apoptosis related genes showed Bax levels of 3.1+0.3 in the TNF-R1 KO as compared to 0.8+0.4 in the TNFR2 KO in the crushed nerves. Bcl-2 was measured 3.84+1.9 and 0.57+0.2 respectively. Control mice had decreased Bax and increased Bcl-2 (0.5 and 1.5, respectively) on day 3. TNFR1 KO showed slight elevation of MIP-2 (1.3) as compared to reduced levels in TNFR2 and control (0.63 and 0.7 respectively). SOD was elevated only in TNFR2-KO (3.71+2.8) and remained in baseline in the TNFR2 and controls.

**Conclusions:** TNFR1 KO differs from TNF2-KO and control groups, suggesting it plays a role in the post crush reaction. Blocking TNFR1 might facilitate a neuroprotection and preserve vision.

## Bioactive magnetic near Infra-Red fluorescent core-shell iron oxide/human serum albumin nanoparticles for controlled release of growth factors for augmentation of human mesenchymal stem cell growth and differentiation.

Ifat Sher[1*], Itay Levy[2]*, Enav Corem-Salkmon[2], Ofra Ziv[2], Amilia Meir[3], Avraham J Treves[3], Arnon Nagler[4], Shlomo Margel[2], Ygal Rotenstreich[1]

*1Goldschleger Eye Research Institute, Sackler Faculty of Medicine, Tel Aviv University Sheba Medical Center, Tel-Hashomer , 2Department of Chemistry, Bar-Ilan Institute of Nanotechnology and Advanced Materials, Ramat-Gan, 3Center for Stem Cells and Regenerative Medicine, Cancer Research Center, Sheba Medical Center, Tel-Hashomer, 4Hematology Division, Sheba Medical Center, Tel-Hashomer.*

**Purpose:** We have previously demonstrated that subretinal transplantation of human bone marrow mesenchymal stem cells (hBM-MSCs) ameliorates photoreceptor degeneration in a rat model of retinal dystrophy. Here we tested whether nanoparticle delivery of fibroblast growth factor 2 (FGF2) can enhance growth and differentiation potential of hBM-MSCs.

**Methods:** FGF2 was covalently conjugated to core-shell near infra-red fluorescent iron oxide magnetic nanoparticles coated with human serum albumin (IO/HSA NPs). Long term stability of free versus conjugated FGF2 in presence of serum was assessed by ELISA. Uptake of FGF2 was determined by microscopy scoring. To evaluate effect of conjugated FGF2 on cell growth, Colony Forming Unit-Fibroblasts assay and MTT proliferation assay were performed. The effect of conjugated FGF2 on cell differentiation toward neurogenic, osteogenic and adipogenic lineage was examined.

**Results:** Covalent conjugation of the FGF2 to the IO/HSA NPs significantly stabilized the growth factor. Human BM-MSCs internalized only FGF2 conjugated NPs and failed to internalize free NPs. Conjugated FGF2 enhanced clonal expansion capacity of hBM-MSCs, to a higher extent compared with free FGF2 ($p=0.005$). Furthermore, conjugated FGF2 was 2-3 fold more efficient in promoting adipogenic and osteogenic differentiation of the cells. Free and conjugated FGF2 promoted the expression of neuronal marker Microtubule-Associated Protein 2 to a similar extent, but conjugated FGF2 was over three fold more effective than free FGF2 in promoting the expression of astrocyte marker Glial Fibrillary Acidic Protein in these cells.

**Conclusions:** These results indicate that stabilization of FGF2 by conjugating to IO/HSA NPs can enhance the biological efficacy of FGF2 and its ability to promote hBM-MSC proliferation and trilineage differentiation. This new system may benefit future clinical use of hBM-MSCs for retinal degeneration.

## Novel methods for the detection of occult metastatic disease in the CSF of children with medulloblastoma

Sivan Gershanov,[1,2] Shalom Michowiz, [3,4] Helen Toledano,[3,5] Dror Fixler,[7] Gilad Yahav,[7] Orit Barinfeld,[2,3] Mali Salmon-Divon,[1] Nitza Goldenberg-Cohen.[2,3,6]

*1Genomic Bioinformatics Laboratory, Molecular Biology, Ariel University, Ariel, Israel, 2The Krieger Eye Research Laboratory, Felsenstein Medical Research Center, and 3Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel, 4Pediatric Neurosurgery, 5Pediatric– Oncology ,and 6Pediatric Ophthalmology, Schneider Children's Medical Center of Israel, Petach Tikva, Israel, 7Faculty of Engineering and Institute of Nanotechnology and Advanced Materials, Bar Ilan University, Ramat-Gan, Israel.*

**Purpose:** Medulloblastoma (MB) is the most common malignant brain tumors in children and is found in the posterior fossa of the brain. Up to 30% will have overt or covert metastatic spread at diagnosis usually within the brain or the spine. Detection of metastatic disease is vital to determining treatment intensity. As yet, imaging and cytology are not sensitive enough for detecting microscopic metastatic spread. The purpose of this study is to combine bioinformatics, molecular methods and fluorescence-lifetime imaging microscopy (FLIM) to improve detection of metastatic disease at diagnosis and during follow up in the hope of improving treatment and prognosis.

**Methods:** DNA was extracted from tumor and blood was analyzed using whole exome sequencing (WES), to identify tumor specific chromosomal aberrations. In addition, cells from the cerebrospinal fluid (CSF) were studied for these aberrations. Real-time PCR was performed for subgrouping of tumors as previously published. Slides with cells from the CSF were studied by DAPI nuclear staining and analyzing the fluorescence lifetime using FLIM method.

**Results:** We studied 19 children diagnosed with MB at a tertiary center, 9 boys and 10 girls; mean age at diagnosis 5.9±3.4 years. 15 of the 19 had localized disease and 4 had metastatic at diagnosis according to imaging or cytology. WES performed on the tumor and blood in 2 overtly metastatic patients (#15 and #18), identified structural variations (SV), 404 and 328 SV's, respectively. We are currently examining the DNA from metastatic cells from the CSF for these unique SVs. In addition, FLIM from 4 patients revealed 3 populations of cells in the CSF: benign, inflammatory and metastatic. One of these patients was thought to be clinically localized disease only.

**Conclusions:** Structural variations and FLIM may improve detection of occult metastatic disease in the CSF at diagnosis and during follow up.

## EGFR overexpression as a prognostic factor in glioblastoma multiforme

Orit Barinfeld,1,2 David Hazon, 3 Shalom Michowiz, 3 Helen Toledano,4,2 Susana Fichman-Horn, 6 Rinat Ankri,7 Ariel Ashkenazy,7 Dror Fixler,7 Nitza Goldenberg-Cohen.1,2,5

*1The Krieger Eye Research Laboratory, Felsenstein Medical Research CenterTel Aviv University, Petah Tikva 2Sackler School of Medicine, Tel Aviv University, Tel Aviv, 3Pediatric Neurosurgery, 4Pediatric– Oncology ,and 5Pediatric Ophthalmology, Schneider Children's Medical Center of Israel, Petach Tikva,. 6Pathology Department, Rabin Medical Center, Beilinson Campus, Petah Tikva 7Faculty of Engineering and Institute of Nanotechnology and Advanced Materials, Bar Ilan University, Ramat Gan, Israel*

**Purpose:** Glioblastoma (GBM) is the most common primary malignant neoplasm of the central nervous system in adults. The molecular mechanisms underlying the development and progression of this tumor remain unclear. The epithelial growth factor receptor (EGFR) may play a role in the level of malignancy of the tumors. The EGFR gene has recently been reported to be overexpressed in primary GBM.

The aim of this study was to investigate the role of polysomy and amplification in the increased level of expression of EGFR in GBM and to try to use its overexpression to stain tumor borders using gold nanoparticles.

**Methods:** Ten GBM frozen and eight paraffin fixated samples from pathology were collected according to Institutional and National IRB approval. DNA was extracted from all fresh samples. Real time PCR was performed using three primers: EGFR, GPER, RNase P. Polysomy and amplification were determined by calculating the differences between each pair of genes. Staining with EGFR gold nanoparticles (GNPs) was performed to distinguish between the tumor (stained area) and normal healthy tissue (unstained) using scattering spectroscopy by hyperspectral camera.

**Results:** Forty percent of the GBM samples showed amplification, 20% polysomy and the remaining 40% had normal levels of EGFR expression. Tumor borders were determined by staining with GNPs, correlating with H& E staining.

**Conclusions:** The high level of expression of EGFR in GBM in the majority (60%) of the samples permitted the localization of tumor borders by staining histological sections with GNPs. We found a very high correlation between the EGFR –GNPs positive staining and the tumor area. This may facilitate the future complete excision of the tumor, in vivo.

## Generation of *in vivo* model for eyelid basal cell carcinoma and characterization of the tumor's microenvironment

Stein Ran, Dvashi Zeev, Milstein Asher and Pollack Ayala

*Ophthalmology department, Kaplan Medical Center, Rehovot, Israel., Affiliated with the Hebrew University, Jerusalem*

**Purpose:** Basal Cell Carcinoma (BCC) is the most common skin malignancy and is also the most common periocular malignancy. Treatment of BCC lesions is usually surgical, with Mohs micrographic surgery (MMS) considered the treatment of choice due to its lowest recurrence rate. Recently, innovative treatment with smoothened inhibitors that interfere with the intracellular hedgehog pathway signaling has been thoroughly investigated. One drug, Vismodegib, has been FDA approved based on activity and tolerability in patients with advanced basal-cell carcinoma, but severe side effect profile still limits its clinical practice. As the search for cure continues, the current available BCC models pose their own limitations. Previous models were conducted by UV or ionizing radiation (IR) in knocked out mice, which resulted in heterogeneity in the tumor's molecular basis and in the time frame needed for its development. The purpose of this study is to generate a novel model system of eyelid BCC in mice. Further, it aims to investigate the tumor's microenvironment and to suggest novel treatments for BCC tumors.

**Methods:** Murine BCC cells were injected into the eyelids of black mice, followed by injection of PBS solution, bevasizumab, or platelet-derived growth factor (PDGF). The mice were monitored for tumor growth and then sacrificed. The tumors were resected and underwent pathological and histological examinations. The cells secretion of pro-inflammatory factors such as Matrix metalloproteinases (MMPs) was investigated by zymography assay.

**Results:** 1x105 BCC cells were injected into the right eyelid of C57 black mice, followed by injections of PBS solution, bevasizumab, or PDGF 48 hours later. BCC tumors were seen in eight out of the nine mice that were treated with PBS, in two out of five mice in the bevasizumab treated group, and in four out of five mice in the PDGF group. In the zymography assay tumor necrosis factor-$\alpha$ (TNF$-\alpha$) had demonstrated increase in the secretion of MMP-2.

**Conclusions:** Eyelid BCC model can be induced by injection of BCC cells. Development of BCC may be regressed by bevasizumab. In contrast, the use of PDGF does not interfere with tumor development. Tumor growth is suggested to be related to MMP-2 secretion. The results of the study should be further investigated to evaluate novel treatment for BCC tumors.

## Diagnosis of vitreoretinal lymphoma: the use of cytology, gene rearrangement, and IL-10/IL-6 ratio

Jacob Pe'er[1], Inna Kalickman[2], Yoav Sherman[3], Bela Maly[3], Dina Ben Yehuda[4], Vivian Barak[2], Shahar Frenkel[1]

*Departments of [1]Ophthalmology, [2]Oncology, [3]Pathology, and [4]Hematology, Hadassah-Hebrew Univ Med Ctr, Mevaseret Zion, Israel.*

**Purpose:** To compare three methods of diagnosis of suspected vitreoretinal lymphoma: cytology, IgH gene rearrangement, and IL-10/IL-6 ratio.

**Methods:** Diluted vitreous fluid obtained in diagnostic vitrectomy from patients with suspected vitreoretinal lymphoma were delivered immediately after the surgery to the cytopathology laboratory; to the hematology laboratory for PCR studies, and to the cancer-markers laboratory for ELISA test for IL-10/IL-6 ratio.

**Results:** Forty-seven specimens were evaluated using the three **Methods:** 21 of them (44.7%) were positive for lymphoma in cytology examination, 13 (27.6%) were positive in Ig-H gene rearrangement evaluation, and 25 (53.2%) were positive by IL-10/IL-6 ratio that was higher than 1.0. Nine of 21 specimens (42.8%) with positive cytology were positive also for Ig-H gene rearrangement and 18 of the 21 (85.7%) were positive also for IL-10/IL-6 ratio. Nine specimens were positive for lymphoma via all three methods. Seven specimens in which the IL-10/IL-6 ratio was positive for lymphoma were negative in cytology, 4 of them developed CNS lymphoma, and 3 that were positive for Ig-H gene rearrangement were negative in cytology.

**Conclusions:** In our series, the examination of the IL-10/IL-6 ratio was much more sensitive and much more comparable to cytology than examination for Ig-H gene rearrangement which showed low sensitivity.

## Novel combinatorial treatment option for metastatic uveal melanoma

Shahar Frenkel [1]; Dudi Shneor [1, 2]; Alik Honigman [2]; Jacob Pe'er [1]

*1. Ophthalmology, Hadassah-Hebrew Univ Med Ctr, Mevaseret Zion, Israel. 2. Biochemistry and Molecular Biology, IMRIC, The Hebrew University-Hadassah Medical School, Jerusalem, Israel.*

**Purpose:** To date, chemotherapy for metastatic uveal melanoma (mUM) is limited to dacarbazine (DTIC) and fotemustine. We tested the effect of the common chemotherapeutic drug doxorubicin (DOX) on cell mortality in order to expand the chemotherapeutic arsenal for mUM.

**Methods:** We examined the effect of both DITC and DOX in five different uveal melanoma cell lines – originating from both metastases (OMM1, OMM2.3 and OMM2.5) and from primary tumors (92.1 and MEL270) and performed dose response tests using both drugs. Based on our previous results, we hypothesized that combining DOX and knockdown of CREB will increase cellular death. To test our hypothesis, we infected cells with replicative competent retroviruses (RCR) expressing shRNA against CREB to create a continuous infective knockdown of CREB.

**Results:** Both chemotherapeutic drugs induced cell death in a dose dependent manner. Knockdown of CREB in these cells increased the effect of DOX on cell mortality.

**Conclusions:** Treatment with DOX is at least as efficient and in some cases even more efficient than DTIC in inducing UM cell mortality in vitro. Moreover, the ability of combining CREB knockdown and DOX treatment to achieve the same amount of cell death in lower concentrations of DOX may result in lower side effects from DOX. This combination is a possible new treatment for metastatic uveal melanoma.

## Stereotactic radiosurgery for uveal melanoma

Shahar Frenkel [1]; Atara Cohen [1], Hadas Rosenne [2], Mark Vigoda [3], Ygal Shoshan [4], Jacob Pe'er [1]

*Departments of [1]Ophthalmology, [2]Social work, [3]Radiotherapy, [4]Neurosurgery, Hadassah-Hebrew University Medical Center, Jerusalem.*

**Purpose:** External beam radiotherapy (EBRT) is being used in several institutions as a primary treatment for all uveal melanomas (UM), but it is mostly used to treat extra-large tumors (instead of enucleations), and for local recurrences. Here we describe our experience with Stereotactic Radiosurgery (SRS) for uveal melanoma, its effectiveness and side effects.

**Methods:** A retrospective analysis of all the UM patients in our database since SRS became available in Hadassah (1/2007 – 12/2014). The patients received fractionated treatment of 5x 12Gy every other day.

**Results:** From Jan, 2007 through Dec 2014, a total of 399 new UM were diagnosed and treated in our institution. Twenty three were referred to SRS. Two were referred for primary treatment, two for orbital control after histopathology revealed a rare intra-optic nerve invasion, and 19 to treat local recurrence that could not be managed by repeated brachytherapy. In one patient the tumor continued to grow after treatment. In 3 patients VA remained unchanged, and the rest VA showed a decrease of 1.37 LogMAR units (range 0.8-2.8). Three patients developed neovascular glaucoma (NVG), 12 had varying degrees of vitreous hemorrhage (VH), and 9 had progression of their cataracts.

**Conclusions:** SRS is effective as both primary and secondary line of treatment, and helps preserve eyes.

# A Biological Tissue Adhesive and Dissolvent System for Intraocular Tumor Plaque Radiotherapy: an *In-vivo* Animal Model Experiment

Ofira Zloto, MD[1]; Dror Alezra, MD[2]; Oded Sagiv, MD[1]; Vicktoria Vishnevskia Dai, MD[1]; Iris Moroz, MD[1]; Gahl Greenberg, MD[3]; Elad Ben-Artsi, MD[1]; Ido Didi Fabian, MD[1,4]

*[1]Goldschleger Eye Institute, [2]Department of Radiation Oncology and [3]Department of Diagnostic Imaging, Sheba Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel. [4]Dr. Pinchas Borenstein Talpiot Medical Leadership Program 2012*

**Purpose:** To examine a novel biological adhesive and dissolvent system for plaque placement and removal using fibrin glue and urokinase, respectively.

**Methods:** In-vivo experiments included 19 rabbit eyes. Of these, 8 underwent technique feasibility and plaque displacement examinations (the latter by ultrasonography), 9 were examined for tissue response to the biological substances (clinically, by magnetic resonance imaging and histopathology), and in 2 intraocular pressure (IOP) was measured. In an ex-vivo experiment the impact of radiation on the glue's adhesive properties was tested on 4 enucleated porcine eyes (sutured vs. glued plaques) using a high dose radiation system and an adhesion-measuring device, and in a non-vivo experiment the glue's attenuation properties were tested by an Oncology EDR-2 film.

**Results:** Plaque horizontal movement throughout follow-up (7-10 days) was negligible (0.5±0.2 mm), and there was no tilting whatsoever. No adverse effects were recorded after application of fibrin or urokinase throughout follow up (21 days). A circumscribed local inflammatory response was noted to surround the fibrin glue and persisted at 21 days after its application. Application of 1cc fibrin glue did not elevate IOP ($P \geq 0.291$). No differences in adhesion strength were found between sutured and glued plaques ($P=0.936$). Radiation readings did not differ statistically with/without glue separation between the radioactive sources and film ($P=0.111$).

**Conclusions:** The adhesive and dissolvent system was feasible and safe for plaque placement and removal. It may be superior to conventional suturing with regard to plaque tilting, a common phenomenon in these cases, and risks related to suturing.

## p63 is essential for mouse eye development

Waseem Nasser[1], Daniel Aberdam[2], Alea Mills[3], Caterina Missero[4], and Ruby Shalom-Feuerstein[1]

*1Department of Genetics and Developmental Biology, The Ruth and Bruce Rappaport Faculty of Medicine, Technion – Israel Institute of Technology, Haifa, Israel; 2INSERM UMR-S976, Université Paris Diderot Hôpital Saint-Louis, PARIS; 3Cold Spring Harbor Laboratory; Cold Spring Harbor, NY USA; 4CEINGE Biotecnologie Avanzate, Napoli, Italy*

**Purpose:** The transcription factor p63, a member of p53 family, plays a significant role in skin development as indicated by p63-deficient mice that fail to develop a stratified epidermis. Interestingly, point mutations in one allele of the human p63 gene are linked with Ectodermal Dysplasia (ED) syndromes which are hallmarked by various abnormalities in the skin and cornea, among other defects. However, although p63 is considered to be a limbal stem cell marker, the role of p63 in eye development has not been defined.

**Methods:** p63-null mice and two new mouse strains containing knocked in alleles of mutated p63 gene which serves as new models for p63-related ED were investigated in collaboration with the teams of C. Missero (Italy) and Alea Mills (USA). Tissue sections of mouse embryos and adult eyes were investigated by histology and immunofluorescent staining.

**Results:** p63-null mice failed to express corneal differentiation marker K12, corneal progenitor markers, K5 and K14, and remained positive for ectodermal markers K8/18, indicating that p63-null epithelia could not develop beyond ectodermal stage. Additional defects included failure in eyelids development, abnormal lens and corneal stromal size. Interestingly, p63-related ED mice displayed several embryonic defects in corneal-epithelial commitment as indicated by reduced levels of expression of essential cytokeratins (i.e.K12). Moreover, p63 mutations were associated with abnormal epithelial proliferation and epithelial thickening.

**Conclusions:** p63 is essential for proper mouse eye development. At the absence of p63, the morphogenesis of the anterior eye segments (cornea, lens) is interrupted. P63 mutations were linked with corneal fate determination as indicated by reduced and punctuated expression of K12 in the developing corneal epithelium. This data suggests that loss of vision in p63-related ED patients is due to autonomous role of p63 in the cornea rather than a secondary effect attributed by defects in other tissue (e.g. meibomian gland dysfunction). Future experiments will elucidate the molecular mechanism that underlies the phenotypes observed in p63-mutated mice. Such knowledge may unravel new pathways in corneal pathophysiology, and pave the way for future therapy of p63-related ED and other p63-related corneal diseases.

## A comparison between bandage contact lenses, punctual plugs and standard measures in preventing corneal injuries related to exposure in patients admitted to the general intensive care unit.

Irena Serov1 MD , Amir Sternfeld1 MD , Lewa Amar1 MD , Idit Dan1 MD , Yonatan Cohen1,2 PROF, Itay Ben Daviv1 MD ,Irit Bahar1,2 PROF, Iftach Yassur1,2 MD, Inbal Avisar1,2 MD

*1.Ophthalmology department, Rabin Medical Center, Petah Tikva, Israel, 2.Sakler faculty of medicine, Tel aviv university, Tel Aviv, Israel*

**Purpose:** A prospective double blinded clinical trial was designed in order to compare the prevention potential of corneal injury of admitted unconscious patients to intensive care unit using contact lenses, punctual plugs and standard lubrication drops.

**Methods: :** The enrolled patients randomized to 3 groups: the bandage contact lens group, the punctual plug group and the control group.

Each patient in each group was checked every 4 days. In the contact lenses group Contact lenses were replaced every 4 days and the patients were treated with topical antibiotics continuously.The control group and the punctual plug group were treated topical lubrication drops. Measures of the palpebral fissure, lagophthalmus, degree of corneal keratopathy and degree of conjuctival edema, were taken each examination

**Results:** The grade of keraopathy and conjuctival edema were compared between the 3 groups. Grade of keraopathy improved in 45% and 43% patients in the plug group and control group respectively and in 37% in contact lens group Grade of keratopathy worsened in 36% of patients in control group (vs 12.5% and 10% in contact lens and plug groups respectively) Conjuctival edema improved in 68% of patients in the plug group (vs 36% and 25% in the control and lens group respectively). No ophthalmic complication was observed in any of the groups.

**Conclusions:** The use of punctual plugs and contact lenses is safe available and useful method therapy for Prevention of dryness complications.

The punctal plugs showed superiority in prevention of conjunctival edema and progression of keratopathy, this was especially shown in patients with increased lagophthalmus.

# Demographic factors, environmental, occupational and infectious exposures in Israeli patients suffering from dry eye syndrome and Sjogren's syndrome

Ben-Eli Hadas[1,2], Solomon Abraham[1], Aframian Doron[3], Mevorach Dror[4], Ben-Chetrit Eldad[5] and Paltiel Ora[2,6]

*1Dep of Ophthalmology, 2 Braun School of Public Health and Community Medicine, 3 Dep of Oral Medicine, 4Dep of Internal Medicine, Unit of Rheumatology and 6Dep of Hematology, Hadassah-Hebrew University Medical Center, Jerusalem*

**Purpose:** To compare demographic parameters and risk factors including infections, environmental and occupational exposures in dry eye syndrome (DES) and Sjogren's syndrome (SS).

**Methods:** The study uses a case-control and a hospital-based cross-sectional design. Referred patients with DES or SS to Ophthalmology, Oral Medicine and Rheumatology Departments in Hadassah Medical Center, answer a validated questionnaire and blood samples for blood counts, serological, immunologic and genetic parameters. Gender, age, ethnicity, occupational, medical history, environmental and viral exposures, family history of cancer and autoimmune diseases were recorded.

**Results:** To date, 122 patients have been recruited (age range 18-86 y.o. mean:54.6±15), of whom 61 with SS (7% males) and 61 with DES (38% males). In both groups 40% were smokers. The SS group consists of 49% with secondary SS, of which 62% have rheumatoid arthritis, 12% have lupus and 26% have other autoimmune disease. The chief complaint of SS patients was dry eyes (35%), joint pain (35%) and dry mouth in 30%. About 20% of cases in both groups combined had a first degree family relative with RA or other immune system related disease. Moreover, 26% of the SS cases and 19% of the DES cases had first degree relative with any autoimmune disease. In the SS group 57% reported a history of infection requiring hospitalization, as apposed to 49% in the DES group. Self-report of Helicobacter pylori infection was noted in 7% and 4% while herpes simplex infection was reported by 44% and 31%, of the SS group and DES groups, respectively. About 70% of DES patients worked in an office environment, as compared to 54% of the SS cases. Mean OSDI questionnaire for dry eye score was 69.3±19.4 in the SS group and 57.4 ±16.3 in DES group by t-test (p=0.000). Preliminary testing of blood counts, based on a partial sample only, showed a tendency towards lower means of hematologic parameters including HGB, WBC, neutrophils and lymphocytes counts, in the SS group compared to DES group.

**Conclusions:** Patients with SS and DES in Israel differ in their demographic parameters. Moreover, SS group had a higher frequency of infections, having a close relative with autoimmune diseases, and lower hematologic parameters. Dry eye symptoms were more severe in the SS group.

## Pyerygium And Human Papilloma Virus In Israel

Shirin Hamed-Azzam M.D.1, Natalia Edison Ph.D.2, Abed Mukari M.D.1 , Irit Elmalah M.D.2 , Daniel Briscoe M.D.1

*1Department of ophthalmology, Emek Medical Center, Afula, Israel. 2The institute of tissue diagnostics and cancer reseach, Emek Medical Center, Afula, Israel.*

**Purpose:** To evaluate the involvement of Human Papilloma Virus (HPV) in primary and recurrent pterygium pathogenesis in Northern Israel .

**Methods:** 100 randomly chosen pterygium specimens from 100 separate patients who underwent surgery over an 18month period between 2012-2013 were examined retrospectively. All the specimens were analyzed for evidence of HPV infection by immunohistochemistry. All patients were operated on at Emek Medical Center.

**Results:** immunohistochemical staining did not detect HPV in any of the 100 pterygia samples. Mean age of patients of 51.5 years and there was a primary: recurrent Pterygium ratio of 8.09: 1.

**Conclusions:** There is controversy in the literature as to the role of Human Papilloma Virus. in the pathogenesis of pterygium. We conclude from our data that in Israel, HPV infection does not appear to be of importance in the pathogenesis of primary or recurrent pterygium.

## Synergism between anticholinergic and oxime treatments against sarin induced ocular insult in rats

Gore A[1]., Brandeis R[1]., Egoz I[1] ., Turetz J[1]., Nili U[1]. and Bloch-Shilderman E[1].

*Dept. of Pharmacology1, Israel Institute for Biological Research, Ness Ziona, 74100, Israel*

**Purpose:** Eye exposure to the extremely toxic organophosphorus irreversible cholinesterase inhibitor sarin results in long-term miosis with visual impairment. Since current treatment using atropine or homatropine eye drops may lead to considerable visual side effects, alternative combined treatments of intramuscular (im) oximes (16.8 µmol/kg, im) with atropine (0.5 mg/kg, im) or with the short acting antimuscarinic tropicamide (0.5%; w/v) eye drops were evaluated.

**Methods:** The combined treatments efficacy following topical exposure of sarin (1 µg) was assessed by measuring pupil width and light reflex using an infra-red based digital photograph system.

**Results:** Results show that the combined treatment of various oximes (im) with atropine (im) or with topical tropicamide eye drops rapidly reversed the sarin induced miosis and presented a long-term improvement of 67-98% (oxime+tropicamide) or 84-109% (oxime+atropine) in pupil widening as early as 10 min following treatment. This recovery was shown to persist for at least 8 h following exposure, with pupil width of 75-109% relative to baseline. The efficacy order of the combined treatments with atropine or tropicamide was HI-6> TMB-4>Obidoxime=MMB-4. All combined treatments facilitated the ability of the iris to contract following sarin insult as tested by a light reflex response.

**Conclusions:** Our findings emphasize the high efficacy of im oxime treatment combined with either atropine im or tropicamide eye drops in counteracting sarin induced ocular insult. Thus, in mass casualty scenario, the systemic combined treatment may be sufficient to ameliorate sarin-induced ocular insult with no need for additional, topical anticholinergic treatment at least in the initial stage of intoxication. In very mild casualties which are not likely to receive im treatment, the combined oxime (im) with topical tropicamide treatment may be sufficient in ameliorating the ocular insult.

## A Novel UBIAD1 Gene Mutation in an Ashkenazi Jewish Family With Schnyder Corneal Dystrophy

Adi Einan-Lifshitz, Isaac Avni, Nadav Shoshany, David Zadok, Eran Pras

*Ophthalmology department, Assaf Harofeh medical center, Zerifin, Israel*

**Purpose:** To describe the phenotype and identify the underlying mutation associated with Schnyder Corneal Dystrophy in a three-generation Ashkenazi Jewish family.

**Methods:** Six members of a family with Schnyder corneal dystrophy were recruited (4 affected members and 2 unaffected members). All patients underwent an ophthalmic examination including; Snellen visual acuity measurments, slit lamp biomicroscopy, corneal photography, and spectral domain anterior segment optical coherence tomography (OCT). Blood samples were obtained from participants for DNA extraction. The coding exons of the UbiA prenyltransferase domain–containing 1 (UBIAD1) gene were screened for mutations by direct sequencing.

**Results:** In vivo corneal morphology analysis, using slit lamp examination and OCT, confirmed the presence of pathologic deposits at the levels of Bowman's membrane and anterior stroma, in affected members of the family.

A novel missense mutation (D106H) was identified in the UBIAD1 gene. The molecular defect co-segregates within the family. Validation studies in order to verify the pathogenicity of this mutation are in process.

**Conclusions:** We report a yet unrecognized mutation in the UBIAD1 gene. This novel mutation expands the spectrum of mutations in UBIAD1 which associates with pathological corneal cholesterol deposition.

## Agreement and reliability in measuring central corneal thickness between a new stationary Scheimpflug camera (VX120) and a rotating Scheimpflug camera (Sirius) in normal and keratoconic corneas

Ariela Gordon-Shaag, David Markov , Tzadok Parnes and Einat Shneor

*Department of Optometry and Vision Science, Hadassah Academic College, Jerusalem, Israel*

**Purpose:** Accurate measurement of central corneal thickness (CCT) is critical for tonometry and in screening for corneal pathology. Rotating Scheimplug devices such as the Sirius (CSO, Italy) have been shown to provide accurate measurements of CCT similar to ultrasound pachymetry. The VX120 (Visionix Luneau, Chartres, France) is a new instrument that measures CCT using a fixed Scheimpflug camera. We tested the agreement of the VX120 with the Sirius, and evaluated the repeatability of both instruments in normal and keratoconic subjects.

**Methods:** Healthy subjects were recruited from the student body of Hadassah Academic College (HAC) while subjects with keratoconus (KC) were recruited from the HAC Optometry Clinic. KC was diagnosed based on clinical presentation and corneal imaging. The right eye was used for the normal cohort, while all keratoconic eyes were used for the KC cohort. CCT was measured three times consecutively with the VX120 and Sirius, by different practitioners masked to one another's results. Using Bland & Altmann analyses, validity and intratest repeatablility was measured on all subjects, while intertest repeatability was assessed after one week on a subset of 31 subjects.

**Results:** 106 normal subjects (106 eyes, 21 men, 85 women, average age 23.12±4.89) participated in this study. The average thickness was 546.88±6.77µm and 543.37±2.70µm for VX120 and Sirius respectively. The averaged difference between the two instruments (3.51±8.56) was statistically, but not clinically, significant ($p < 0.0001$). High Intra-test and inter-test repeatability was demonstrated for all parameters measured. Preliminary data on a small cohort of KC patients (N=5 eyes of four subjects:1 men, 3 women, average ages 27.25±9.88) yielded similar results.

**Conclusions:** The VX120 can be used interchangeably with the Sirius to measure CCT. Both instruments demonstrate high inter and intra test repeatability.

## Pterygium excision with superior conjunctival flap: comparison of fibrin glue with vicryl suture. A randomized control study

Greenbaum Eran[2], Zloto Ofira[1,2] and Ben Simon Guy[1,2]

*Ophthalmology Department, Sheba Medical Center[1], Tel Hashomer, Sackler School of Medicine[2]*

**Purpose:** To compare between two accepted surgical methods in pterygium excision surgeries: fixating the conjunctival flap with 10-0 vicryl sutures versus fixating with fibrin glue – Quixil.

**Methods:** This is a prospective randomized study. The 54 patients that entered the study were randomized to have pterygium surgery using either vicryl 10-0 (25 patients) or fibrin glue (29 patients). During the follow-up of 1 year, the measured outcomes were surgical time, patients discomfort, complications, best corrected visual acuity, refraction. The patients were assessed for complications like recurrence rate or dehiscence.

**Results:** The mean flap time in the fibrin group was significantly shorter with 5.66 minutes, compared with 23.22 in the suture group ($P<0.0001$). The pain grading of the patients at day 1 was lower in the fibrin glue group, but difference did not reach significance ($P=0.08$). In the fibrin glue group we recorded higher recurrence rate with 5 patients (17.2%) compared to 1 in the suture group (4%) ($P=0.123$). Complications rate was higher in the fibrin glue group with 5 cases of dehiscence (17.2%) compared with no recorded cases in the fibrin glue group ($P=0.029$). Significant improvement was achieved in both groups regarding Astigmatic Refraction, Spheric Refraction and BCVA values ($P=0.0067$, $P=0.026$, $P<0.05$ respectively). No group was significantly superior over the other in matter of improving refraction or BCVA values.

**Conclusions:** Our study results suggest that the use of Quixil type fibrin glue for the fixation of the conjunctival flap reduce the operation time, the intensity of the postoperative pain in the day after the surgery and results in a higher rate of recurrence rate of pterygium. The use of fibrin glue shows no significant difference in improvement of the best corrected visual acuity levels and refractive values.

## Risk factors for keratoconus in Israel: a case control study

Ariela Gordon-Shaag[1], Michel Millodot[2], Igor Kaiserman[3], Tzahi Sela[3], Guy Barnett Itzhaki[1], Yaffa Zerbib[1], Efrat Matityahuo[1], Shira Shkedi[1], Svetlana Miroshnichenko[1] and Einat Shneor[1]

*1Department of Optometry and Vision Science, Hadassah Academic College, Jerusalem, Israel; 2 School of Optometry, The Hong Kong polytechnic University, Hong Kong, China; 3 CARE Laser Medical Group, Tel Aviv, Israel*

**Purpose:** Keratoconus (KC) is a progressive corneal thinning disorder with an uncertain etiology. Environmental and genetic factors, including consanguinity, eye rubbing and possibly sun exposure, play a role in the pathogenesis of KC. Here we test for risk factors for KC in an Israeli population with particular emphasis on sun exposure.

**Methods:** This case-control study included KC patients who were diagnosed at Care Laser Medical Group, a refractive surgery clinic with branches throughout Israel. The control group included age, sex and ethnicity matched individuals who were randomly selected from patients presenting at the clinic for refractive surgery, but without KC. Study subjects were asked to fill out a self-administered questionnaire that included demographic and geographic details, questions on ocular and general health and sun exposure. Univariate and multivariate logistic analyses were performed to identify risk factors for KC.

**Results:** 73 KC patients and 146 controls participated in the study. Univariate analyses demonstrated that eye rubbing, positive family history and parental education (<12 years) were significant risk factors for KC . Univariate analyses of sun exposure behavior during teenage years proved equivocal with some behaviors emerging as protective for KC (wearing a hat outdoors) or as risk factors (spending time in the shade), while others showed no association (limiting time in the sun and wearing sunglasses). The same five factors that were significant in the univariate analyses, also emerged as statistically significant in the multivariate model.

**Conclusions:** Eye rubbing and father's education (as a measure of socio-economic status) emerged as environmental risk factors while having family members with KC suggests genetic etiology. The role of sun exposure in KC remains equivocal and warrants further research.

## A retrospective comparison of semi-scleral (ICD) and Hybrid (Ultra Health) Contact Lenses for Keratoconus

Gantz L., Ehrlich E., Nostin L., Fine P.

*Dept. of Optometry and Vision Science, Hadassah Academic College, Jerusalem, Israel*

**Purpose:** This retrospective study reviewed patient files to compare whether semi scleral vs. hybrid contact lenses provide better objective outcomes for keratoconus (KC) patients.

**Methods:** KC patients seen in the clinics between March 2014 and December 2014 and were fit with both lenses were included in the analysis. UltraHealth (UH) are 14.5 mm diameter hybrid contact lenses, with an RGP Si-150 center (DK= 130), and a soft silicone hydrogel skirt (DK= 84). Irregular Corneal Design (ICD) lenses are mini scleral RGP lenses made of a hyperpurified delivery system (DK =100), 16.5 mm total diameter, with a base curve ranging between 6.03-8.65 mm. The saggital height of the initial diagnostic lens for the ICD fitting was selected based on the ectasia of the corneal surface, the presenting pathological condition, and the manufacturer's chart. The UH lens was fit with 50µm more vault than the minimal clearance lens. Snellen decimal visual acuity (VA) was converted to LogMAR values, and compared between the three correction modes (habitual, ICD, UH) using a one-way repeated measures ANOVA with 95% confidence. The peak contrast sensitivity and the spatial frequency of the peak contrast sensitivity (Fact Chart, VSRC, USA) with the habitual and preferred lens were compared using a paired, two-tailed t-test. 95% confidence.

**Results:** Five men and three women (16 eyes; mean age: 31.13 ± 10.26, range: 18-50) were included. Nine eyes had nipple cones, six had oval cones, and one had keratoglobus. All but one patient preferred, and subsequently, ordered, the ICD lens. One patient was not able to insert the UH lens at all. Distance VA improved significantly with the ICD lenses but not with the UH lenses (Mean LogMAR DVA Habitual: 0.31 ± 0.37 UH: 0.27± 0.32 ICD: 0.13 ±0.12, Fdf=2,14=3.51, p=0.04). The peak contrast sensitivity with the preferred correction (63.3 % ± 35.1%) was better than the habitual correction (39.7%± 27.3%), although this was not significantly different (p=0.05), In contrast, the peak spatial frequency of the contrast sensitivity was not significantly different between the preferred (2.5 ± 1.2 cpd) and habitual correction (2.6 ± 3.0 cpd, p=0.9).

**Conclusions:** The ICD lens was preferred by the almost all of the cohort, and provided better visual acuity and contrast sensitivity outcomes. As such, based on this small sample, ICD is recommended over the UH lens.

## Corneal Stiffening by WST-D / and NIR: Near infrared illumination of 1 and 30 minutes

Alexandra Goz 1, 4, Jurriaan Brekelmans5, Alexander Brandis1, Ilan Samish1, Daniel Wagner3, Yoram Salomon2, Arie Marcovich1,4 , Avigdor Scherz1

*Departments of [1]Plant and Environmental Sciences, [2]Biological regulation, [3]Materials and Interfaces, The Weizmann Institute of Science, [4]Department of Ophthalmology, Kaplan Medical Center, Rehovot,Israel, [5]University Eye Clinic Maastricht, Maastricht, The Netherlands*

**Purpose:** To compare the enucleated rabbit eyes stiffening efficacy by treatment with the photosensitizer WST11-D and near infrared (NIR) illumination for 1 and 30 minutes

**Methods:** 22 rabbit eyes were enucleated post mortem. The corneas were de-epithelialized mechanically and treated topically with WST11 2.5 mg/ml combined with dextran-500 (WST-D) for 20 minutes. Next, illumination with NIR at 10mW/cm2 was applied for 30 minutes (11 eyes) and 1 minute (11 eyes) by a diode laser at 755nm. Untreated contralateral eyes served as controls. The corneo-scleral rings were removed post treatment. Corneal strips, 4±0.2mm in width, were cut from the epithelial side with a self-constructed double-blade cutter. Immediately after, the corneal strips were underwent biomechanical test for Stress-strain measurements

**Results:** After 1 and 30-minutes of NIR illumination in a WST-D/NIR treatment protocol the ultimate stress increased over 100% and over 200%, respectively. The increase as well as the difference between the two groups were significant ($P<0.001$). (From 2.66± 1.0 MPa in the non-treated cornea to 9.03 ± 1.38 MPa in the cornea treated for thirty minutes and from 2.43± 0.8MPa to 5.26 ±1.71 MPa after 1 min of illumination).The Young's modulus increased significantly ($P<0.001$) by over 100% for both the 1 and 30-minute illumination protocols. The difference in the Young's modulus increase after 1 and 30 min of illumination was statistically not significant. (From 7.7 ±3.3 MPa to 15.65 ±4.42 MPa after 30 minutes illumination and from 5.84± 2.15 MPa to 13.1 ± 5. MPa after 1 min.ilumination).

**Conclusions:** WST-D/NIR treatment at 1 minute of illumination of 10 mW/cm2 at 753 nm, significantly increases the biomechanical strength of rabbit cornea. After 1 minute of illumination, the increase in ultimate stress was lower than the 30 minutes group; while the increase in Young's modulus was similar in both groups. Hence, WST-D/NIR treatment followed by short illumination (e.g. 1 min) might be sufficient for the treatment of keratoconus and other corneal ectatic diseases even at an overall low energy of illumination.

## Simultaneous topography-guided surface ablation with collagen cross-linking for keratoconus- case series

Lily Karmona1, MD; Tzahi sela *2*; Oz franco*2*; Avi shoshani*2*; Gur Mitzer*2*; Igor Kaiserman2,3

*[1] Department of ophthalmology, Wolfson Medical center, Holon, Israel, [2] Care-Vision Laser center Institute, Tel-aviv, Israel, [3] Department of ophthalmology, Barzilai Medical center, Ashkelon, Israel*

**Purpose:** To present our results of 8 eyes who underwent combined same-day partial Topography guided PTK followed by accelerated CXL procedure at CARE Vision Laser centers to achieve stabilization of corneal ectasia and enhance visual rehabilitation in keratoconus.

**Methods:** This is a retrospective non randomised review of 8 eyes of 6 patients who underwent simultaneous topography guided surface ablation with collagen cross linking for progressive keratoconus. Each patient underwent Topography-guided PRK followed by Collagen CXL Procedure. Patients were followed up on day 1, day 7, and then at 1, 3, 6 and 12 months.

**Results:** There was a rapid and significant improvement in UCVA and BCVA in 100% eyes, a reduction of keratometric values and symmetry between vertical hemimeridians. Topographic evaluation showed a marked improvement in irregularity. There were no signs of keratoconic progression noted in any of the eyes on last follow up. No adverse events were reported in any patient.

**Conclusions:** Simultaneous PRK followed by CXL seems to be a promising treatment capable of offering patients functional vision and halting progression of the disorder.

## The Efficacy of Topical Aflibercept versus Topical Bevacizumab for the Prevention of Corneal Neovascularization in a Rat Model

Ruti Sella1,2, Orly Gal-Or1, Eitan Livny1, Mor Dachbash3,Yael Nisgav3, Dov Weinberger1,2,3, Tami Livnat1,2,3, Irit Bahar1,2

*[1]Department of Ophthalmology, Rabin Medical Center, Petah-Tikva, [2]Sackler School of Medicine, Tel-Aviv University, Tel Aviv, [3]Laboratory of Eye Research, Felsenstein Medical Research Center, Rabin Medical Center, Petah-Tikva*

**Purpose:** To compare the efficacy of topical Aflibercept (VEGF trap) versus topical Bevacizumab for the prevention of corneal neovascularization (NV) in a rat model.

**Methods:** Corneal NV was induced by a chemical burn creation in the central cornea of male Sprague-Dawley rats. Immediately after injury, a drop of Aflibercept (25mg/ml) was instilled in 15 eyes in group 1, a drop of Bevacizumab (25mg/ml) was instilled in 14 eyes in group 2, and a saline drop was instilled in 15 eyes in the control group. Drop volume was identical in all groups (20 microliter). We repeated drop instillation twice daily for 7 days in all groups. Corneal NV was evaluated on days 1, 4, 7 and 10 following injury by corneal photographs. Software analysis (Image J, NIH) of the pictures was performed, and the fraction of corneal vessels from the whole corneal area was calculated by a masked observer. Samples for histological and immunofluorescence analyses were collected on day 10. Additional 6 rats in the Bevacizumab (n=2) or Aflibercept (n=4) groups were euthanized 48 hours after treatment initiation, and Alexa Fluor® 488 donkey anti-human IgG antibody was used for agent immunoreactivity detection in the corneal stroma.

**Results:** Corneal NV was observed clinically on day 4 following injury in all groups. The area of NV increased from 7.38% (±2.23) on day 4 to 31.07% (±23.61) on day 10 in group 1, from 6.04% (±1.81) to 54.42% (±11.33) in group 2, and from 8.99% (±1.93) to 55.15% (±11.54) in the control group. In the Aflibercept group, the area of NV was significantly lower on days 7 and 10 when compared to both the Bevacizumab and the control groups ($p<0.005$). The clinical findings were compatible with the histological data and supported by immunohistochemical staining. Topical application of Bevacizumab and Aflibercep showed variable penetration into the corneal stroma.

**Conclusions:** Topical Aflibercept effectively inhibits corneal NV in a rat model of chemical burn induced NV. These findings are consistent with previous results of our group, showing the effectiveness of subconjunctival Aflibercept injection for NV inhibition in the same model, and may have important therapeutic implications in humans.

## Impression cytology for monitoring ocular surface changes

Tamar Kadar, Hila Gutman, Liat Cohen, Maayan Cohen, Vered Horwitz, Ariel Gore, Adina Amir and Shlomit Dachir

*Department of Pharmacology, Israel Institute for Biological Research, Ness Ziona*

**Purpose:** Impression cytology (IC) is a non-invasive approach used for collection of cells from the ocular surface mostly for diagnosis. Using IC, we have previously shown Limbal Stem Cell Deficiency (LSCD) following chemical ocular injury, clinically expressed by neovascularization (NV) and epithelial defects. The present study aimed to further characterize the ocular surface changes using IC.

**Methods:** Chemical burn was induced in the right eyes of NZW rabbits, using sulfur mustard (SM) vapor. A clinical follow-up was carried out using slit-lamp examination up to 4 weeks. IC samples were obtained from the upper bulbar conjunctiva, limbus and central cornea under general anesthesia. The samples were collected on strips of cellulose acetate filter paper, fixed and stained by Periodic Acid Schiff reagent (PAS) combined with hematoxylin and eosin for identification of goblet cells and for general morphology. Following staining, the filters were viewed under light microscopy and the density of conjunctival goblet cells was measured, using a computerized image analysis software. At the end of experiment (4W) the eyes were processed for histology.

**Results:** IC samples collected during the first days following exposure showed damaged epithelial cells in the cornea and a marked decrease in the number of goblet cells in the conjunctiva that remained significantly lower than control throughout the experiment ($p<0.0001$). Simultaneously, proliferation of non-mucin epithelial cells was noted, expressing early signs of squamous metaplasia in the conjunctiva.

Invasion of conjunctival cells was noted in corneas displaying NV but pathological alterations were observed also in clinically silent corneas, expressed by abnormal giant cells, large PAS positive cells and PMN's. These abnormalities may predict future pathology which was confirmed later on by histology

**Conclusions:** In addition to early clinical diagnosis of LSCD, the IC was found useful for monitoring cytological changes in the ocular surface and especially the conjunctiva where density of goblet cells may serve as an indicator for pathological processes such as mucin deficiency and tear film abnormality. Thus, the analysis of IC highlighted sub-clinical pathology in the ocular surface that may point towards additional therapeutic approach.

## Lineage tracing of stem/progenitor cells of the murine corneal epithelium

Aya Amitai-Lange[1], Anna Altshuler[1], Jeffrey Bubley[1], Noora Dbayat[2], Beatrice Tiosano[2], Ruby Shalom-Feuerstein[1]

*[1]Department of Genetics and Developmental Biology, The Ruth and Bruce Rappaport Faculty of Medicine, Technion – Israel Institute of Technology, Haifa, Israel; [2]Department of ophthalmology – Hillel Yaffe Medical center, Hadera, Israel*

**Purpose:** Accumulating evidence supports the dogma that the corneal epithelium is regenerated by stem cells located exclusively in the limbal niche, at the corneal periphery. Accordingly, limbal stem cells (LSCs) give rise to progenitors that proliferate and migrate centripetally to repopulate the corneal epithelium, which has a short turnover. Accordingly, LSC loss leads to corneal opacity and blindness, while limbal grafting restores patients' vision. However, contradicting data (Majo et al. Nature) suggested that the limbus does not participate in corneal homeostasis and that the corneal stem cells are located over the cornea. This apparently contradicting evidence raised confusion and debate in the field.

**Methods:** We aimed to trace the origin and fate of ocular surface epithelial stem cells through lineage tracing experiments. Using R26R-Confetti mice we followed K14-positive limbal and corneal epithelial cells stochastically induced to express irreversibly one out of four fluorescent genes (GFP, RFP, CFP, YFP). Mouse were sacrificed at 0-4 months following induction and flattened corneas were subjected to automated tile mosaic confocal fluorescent microscopy to visualize clusters of cells that express each fluorophore. Finally, lineage tracing was performed following increasing corneal injury.

**Results:** In homeostasis, radial limbal stripes of slow migrating cells proceeded towards the corneal center while, infrequently, slow cycling limbal clones resembling quiescent stem cells were observed. Interestingly, rare corneal clones that did not migrate centripetally, but survived for over 4 months, were inspected. In contrast to limbal stripes, corneal clusters had minor contribution to tissue replenishment in homeostasis. Corneal cells, however, significantly contributed to mild wound repair while large limbal streaks appeared within a week following severe wounding that coincided with partial loss of corneal transparency.

**Conclusions:** This data indicates that the mouse limbus plays a major role in corneal renewal. Clearly, during corneal replenishment, LSCs undergo slow migration until they reach the corneal center within 4-5 months. Finally, corneal progenitor cells have a long turnover and, therefore, may be able to maintain the corneal epithelium for several months.

# Ocular surface reconstruction using limbal epithelial cells cultivated ex-vivo on contact lenses following limbal stem cell deficiency

Gore A[1]., Horwitz V[1]., Cohen-Jacob O[1]., Gutman H[1]., Cohen M[1]., Cohen L[1].,Zadok D[2]., Turetz J[1]., Dachir S[1]. and Kadar T[1].

*1Dept. of Pharmacology, Israel Institute for Biological Research, Ness Ziona, 74100, Israel and 2Depart. of Ophthalmology, Assaf Harofeh Medical Center, Zerifin 73000, Israel*

**Purpose:** Ocular chemical injury induced by the chemical warfare Sulfur Mustard (SM) is characterized by acute lesions, followed by a delayed pathology, clinically characterized by, corneal opacity and neovascularization (NV). The aim of the present study was to evaluate the potential use of contact lenses (CLs) as a carrier of limbal stem cells (LSC) to the ocular surface to promote corneal reconstruction following SM induced limbal stem cell deficiency (LSCD).

**Methods:** LSCD was induced in rabbits by exposure to SM and confirmed by using impression cytology and based on clinical diagnostic criterion. Eight weeks following exposure, biopsies of limbal tissue were taken from the naïve fellow eye and epithelial cells were isolated and cultured with feeder cells on CLs. Two weeks following seeding, a superficial keratectomy and 360º peritomy, was performed in the injured eye followed by a triple 24 hr interval sequential CL transplantation onto the denuded corneal surface with or without (sham) limbal epithelial cells. Transplanted limbal cell incorporation and survival, cell phenotype and clinical status were monitored by slit-lamp observations, histology sections and evaluated in whole-mount corneal preparation.

**Results:** Proliferation of limbal cultivated cells were observed on CLs, showing retention of viable stem cell phenotype. Non-transplanted sham group showed a poor clinical outcome presenting regenerating NV compared to the SC transplanted group. One month following transplantation, an enhanced re-epithelialization and limbal region reconstruction was observed in the Hematoxylin-Eosin stained sections of the SC transplanted group only. Finally, SC phenotype preservation and no indication of conjunctivalization was observed in the cornea of SC transplanted eyes only.

**Conclusions:** Cultivation of limbal cells with 3T3 feeder-layer on contact lens carrier was beneficial for reconstruction of the ocular surface in experimental LSCD as observed one month following transplantation. A longer follow up may indicate of the success of this method. This novel technique may provide a cheap, available, easy handling and non-immunogenic carrier for SC transplantation in LSCD patients.

## Specular microscopy analysis of post operative central and peripheral endothelial cells following Descemet membrane endothelial keratoplasty (DMEK)

Eitan Livny[1,2], Lisanne Ham[1,3], Silke Ollerich[1], Vasilis Liarakos[1], Gerrit J Melles[1,]

*1. Netherlands institute for innovative ocular surgery, Rotterdam, The Netherlands, 2. Department of Ophthalmology, Rabin medical center, Petach Tiqva, Israel, 3. Amnitrans eye bank, Rotterdam, The Netherlands*

**Purpose:** To evaluate the endothelial cells parameters following Descemet membrane endothelial keratoplasty (DMEK) surgery in different graft areas.

**Methods:** Retrospective, non-randomized clinical study at a tertiary referral center. Thirty eyes with Fuchs' endothelial dystrophy that underwent DMEK surgery were analyzed by specular microscopy in four DMEK graft's areas: central, supero-nasal, supero-temporal and inferior in a 12 months follow up period.

**Results:** In the central area, endothelial cell density (ECD) decreased by 32% (+/- 11.1%) in 12 months compared to pre-operative donor ECD. The central ECD decrement was non significant from one to 12 months follow up period (131 cells/mm2, P = .1490). The inferior, supero-nasal and supero-temporal areas ECD significantly decreased by 186.73, 227.59 and 212.13 cells/mm2, respectively from one to 12 months (P = .0001, <.0001 and = .0001, respectively). After determination in the first follow up the lowest and highest ECD areas, The highest ECD was noted to decrease significantly over time (318 cells/mm2, P < .0001) while the lowest ECD area remained stable throughout the study period (71 cells/mm2, P = .376).

**Conclusions:** The ECD in the peripheral areas and in the high ECD areas of the DMEK graft decreased in a faster rate than the central and the low ECD areas. This may be explained by different cellular death rate in different graft areas or may indicate a cellular migration pattern, possibly by cellular density gradient.

## Descemet's Memebrane Endothelial Keratoplasty- Early Experience

Irit Bahar, MD[1], Eitan Livny,MD[1] , Ofer Daphna,MD, [1] David Rootman,MD [2]

*[1]Ophthalmology Department, Rabin Medical Center, Petach Tiqva, Israel, [2]Ophthalmology Department, Toronto Western Hospital, Toronto,Canada*

**Purpose:** To describe the early experience with Descemet's membrane endothelial keratoplasty (DMEK) at Rabin Medical Center,Petach Tiqva, Israel, and to compare it to the early experience reported by us following the first DSAEK surgeries.

**Methods:** Our first 15 patients were included. Indication for surgery included Fuchs dystrophy (n=**4**), PBK (n=**8**), failed DSAEK (n=2) and decompensated cornea secondary to congenital glaucoma (n=1). Posterior lamellar discs for DMEK were prepared manually before surgery using 4 different techniques. Best-corrected visual acuity (BCVA) , endothelial cell density (ECD) and anterior segment OCT were measured preoperatively and 1-6 months after DMEK.

**Results:** Primary graft failure occurred in 4 eyes. Other 10 cases had a significant improvement of visual acuity as soon as 1 week following surgery. 1 eye developed significant inflammation (TASS) following surgery. Partial, small and peripheral postoperative graft detachment was noted in most of cases (13/15). The loss of donor corneas during preparation was approximately 10% as more experience was acquired with the procedure. A comparison of the first 15 DMEK to the first 15 DSAEK surgeries, performed by the same surgeons, revealed similar outcomes, but significantly less tissue loss during DSAEK donor preparation.

**Conclusions:** Preliminary outcomes show that DMEK is an effective treatment for corneal endothelial dysfunction. Both tissue loss and failure rates are decreasing with the gain of experience in this relatively new technique.

## Bonding surgical incisions using a temperature-controlled laser system based on a single infrared fiber

Ilan Gabay1, Irit Barequet2, David Varssano3, Mordechai Rosner2 and Abraham Katzir1

*1Tel Aviv University, School of Physics and Astronomy, Tel Aviv 69978, Israel. 2Tel Aviv University, Goldschleger Eye Institute, Sheba Medical Center, Sackler School of Medicine, Tel Aviv 52621, Israel. 3Tel Aviv University, Department of Ophthalmology, Tel Aviv Sourasky Medical Center, Sackler School of Medicine Tel Aviv 64239, Israel.*

**Purpose:** Although there has been great interest in laser heating for bonding of surgical incisions in tissues, it has not gained wide acceptance by surgeons. We argue that the main obstacle has been the lack of temperature control, which may lead to a weak bonding. We previously developed a laser bonding system based on two infrared transmitting AgClBr fibers, one for laser heating and one for temperature control.

**Methods:** In view of the inherent limitations of such systems observed in many animal experiments, we developed an improved system based on a single infrared fiber. The laser radiation is delivered through that fiber, to heat a spot on the incised tissue, and simultaneously, the heat from the heated spot travels back through the same fiber, to an infrared detector. The laser and the detector are connected through a computer program, making sure that the tissue temperature is stabilized on a predefined value, typically around 60ºC. Besides the decreased dimensions, this system offers many advantages over the two-fiber system. It is less sensitive to accuracy of height and tilt of the fiber distal tip above the tissue, ensuring more accurate heating that can potentially lead to stronger bonding with minimal thermal damage.

**Results:** The system is successfully tested in the soldering of 15 corneal incisions, of ex vivo bovine eyes. The average surface temperature is stabilized by the computer program to 60ºC ± 2ºC. The Histopathology shows little thermal damage and good wound apposition. The thermal damage is confined to ~1 mm in width and ~100 µm in depth. It is estimated that for human cornea, which is half the thickness, the thermal damage could be eliminated. The average burst pressure is 100 ± 30 mmHg.

**Conclusions:** These findings indicate the usefulness of the system for ophthalmic surgery as well as other surgical procedures, including endoscopic and robotic surgery.

## Pupillary responses of healthy subjects to chromatic light stimuli at incremental intensities at central and peripheral visual field locations

Soad Haj Yahia[1], Ron Chibel[1], Daniel Ben Ner[1], Ifat Sher[1], Michael Belkin[1], Ygal Rotenstreich[1]

*1Goldschleger Eye Research Institute Sackler Faculty of Medicine Tel Aviv University Sheba Medical Center Tel-Hashomer, Israel*

**Purpose:** A second-generation chromatic multifocal pupillometer was developed with 76 LEDs of 30 degree visual field and a small spot size (2.5 mm diameter) resembling the Humphrey's 30-2 perimetry. The aim of the research was to determine the pupillary responses of healthy participants to chromatic light stimuli presented at increasing intensities in central and peripheral locations.

**Methods:** A computerized infrared video pupillometer was used to record changes in pupil diameter in response to short- and long-wavelength stimuli (peak 485 nm and 620 nm, respectively) presented by 76 LEDs, 2.5 mm target diameter, at 12 increasing light intensities (0.3 - 5623 cd/$m^2$). Stimulus duration was 1 sec. The pupillary responses to chromatic stimulus presented at 4 peripheral (18 degree) and 4 central (6 degree) locations of the visual field were recorded in 18 normal subjects (ages 24-51).

**Results:** The pupillary responses showed a monotonic increase with increasing light intensities. Substantial pupillary response in central locations (over 15% change in pupil size) was obtained using light intensities of 100 cd/m2 and 1000 cd/m2 for short and long wavelength stimuli, respectively. By contrast, in peripheral locations higher light intensities were required to obtain similar pupillary responses (316 and 1778 cd/m2 for short and long wavelength, respectively).

**Conclusions:** The chromatic pupillometer enabled differential assessment of pupillary responses at different peripheral and central locations of the visual field. These data will be used for setting an age matched clinical protocol for objective chromatic multifocal visual field testing.

## Chromatic multifocal pupillometer for objective perimetry in patients with macular degeneration

Daniel Ben-Ner[1], Ron Chibel[1], Mohamad Mahajna[1], Ifat Sher[1], Michael Belkin[1], Ygal Rotenstreich[1]

*[1]Goldschleger Eye Research Institute, Sackler Faculty of Medicine, Tel Aviv University, Sheba Medical Center, Tel-Hashomer, Israel*

**Purpose:** To objectively assess visual field (VF) defects and retinal cell function in healthy subjects and patients with macular degeneration using a chromatic multifocal pupillometer.

**Methods:** A computerized infrared video chromatic pupillometer was used to record pupillary responses of 17 healthy subjects and 5 Vitelliform Macular Dystrophy patients. Short- and long-wavelength stimuli (peak 485 nm and 620 nm, respectively) were presented at light intensities of 400 and 1000 cd /m2, respectively for duration of 1 sec at 76 different points in a 18 degree VF. The pupillary responses of patients were compared with their findings on Humphrey's 24-2 perimetry and with the pupillary responses obtained from healthy subjects. Three parameters were determined automatically: percentage of change of pupil size between initial pupillary size and minimum pupillary size recorded following the light stimulus, the maximal constriction velocity (in pixels/sec) and the time point at which maximal constriction velocity was recorded (in sec).

**Results:** Patients with Best Vitelliform Macular Dystrophy demonstrated more than two standard deviations (SD) away from the mean of healthy subjects in percentage of pupillary contraction and slower maximal contraction velocity in response to long wavelength stimuli in majority of 18 degree visual field locations. In response to short wave length stimuli, the percentage of pupillary contraction was lower (by over two SD) compared with normal controls only in several central points and the maximum speed of pupillary contraction was lower in the center as compared with the periphery. Surprisingly, the time point of maximal contraction velocity was recorded earlier in patients compared with healthy subjects in response to both wavelength stimuli.

**Conclusions:** This study demonstrates the potential feasibility of using pupillometer-based chromatic perimetry for objectively assessing visual field defects in patients with BEST'S vitelliform macular dystrophy. Our finding also suggests that chromatic perimetry may differentiate between pupillary responses mediated by cones or rods, and can specifically detect defects in macular cones.

## Chromatic multifocal pupillometer for objective perimetry in healthy subjects and patients with retinal dystrophies

Ron Chibel [1], Ifat Sher [1], Mohamad Mahajna [1] Michael Belkin[1] , Ygal Rotenstreich [1]

*1Goldschleger Eye Research Institute Sackler Faculty of Medicine Tel Aviv University Sheba Medical Center Tel-Hashomer, Israel*

**Purpose:** To objectively assess visual field (VF) defects and retinal cell function in healthy subjects and patients with retinal dystrophies using a chromatic multifocal pupillometer.

**Methods:** A computerized infrared video chromatic pupillometer was used to record pupillary responses of 17 healthy subjects and 11 retinitis pigmentosa (RP) patients. Short- and long-wavelength stimuli (peak 485 nm and 620 nm, respectively) were presented at light intensities of 200 and 1000 cd /m2, respectively for duration of 1 sec at 76 different points in a 18 degree VF. The pupillary responses of patients were compared with their findings on Goldmann dark adapted subjective perimetry and with the pupillary responses obtained from healthy control subjects. Three parameters were determined automatically: percentage of change of pupil size between initial pupillary size and minimum pupillary size recorded following the light stimulus, the maximal constriction velocity (in pixels/sec) and the time point at which maximal constriction velocity was recorded (in sec).

**Results:** Comparison between control and RP patients demonstrated statistically significant differences ($p<0.05$) in amplitude and constriction velocity in majority (46) of locations in response to short-wavelength stimuli and mostly in peripheral targets in response to long-wavelength stimuli. High consistency was observed in pupillary responses recorded in serial testing of healthy subjects ($P<0.001$, $R=0.74$ for long-wavelength and $P<0.001$, $R=0.683$ for short-wavelength).

**Conclusions:** This study demonstrates the feasibility of using pupillometer-based chromatic perimetry for objective assessment of VF defects. The device requires minimal patient cooperation, demonstrates high reproducibility in test-retest and enables the identification of defects in rods or cones preferentially according to the light stimulus wave length.

## Prevalence and Risk Factors for Epiretinal membrane in patients with type-2 Diabetes Mellitus Screened with a Digital Non-Mydriatic Fundus Camera

Perach Osaadon MD[1,2], Orit Schachter MD[1], Jaime Levy MD[1,2], Ygal Plakht RN, PhD [3], Yonathan Serlin MD[1], , Tova Lifshitz MD [1,2], Boris Knyazer MD [1,2]

*1Joyce and Irving Goldman Medical School, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel. 2Department of Ophthalmology, Soroka University Medical Center, Ben-Gurion University of the Negev, Beer-Sheva, Israel. 3 Nursing Research Unit, Soroka University Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel*

**Purpose:** To determine the prevalence of epiretinal membrane (ERM) and its risk factors in patients with diabetes mellitus type 2 (DM2).

**Methods:** A retrospective cross sectional study included 1550 patients with DM2, who underwent a digital non-mydriatic retinal photography for the detection of diabetic retinopathy as an annual follow up during the years 2009-2010. ERMs were defined by the assessment of the retinal photography by a retina specialist.

**Results:** ERM was present in 102 of 1550 patients with DM2 (6.5%; 95% confidence interval [CI] 5.5 -8.1). Age-standardized prevalence as calculated by using World Health Organization world population was 4.7% (95% CI: 3.8-5.7). The mean age of the study population was 64 ± 12.2 years and 69 ± 8.7 years for patients with ERM (P<0.001). The prevalence of ERM was significantly associated with age, [P<0.001 (1.2% for <49 years, 4% for 50-59 years, 8.2% for 60-69 years and 9.6% for >70 years)], cataract surgery (P <0.001), diabetic nephropathy (P<0.001) and chronic renal failure (P=0.039). Prevalence was similar for males and females (53% females, 47% males, P =0.33). In logistic regression models, the prevalence of ERM was significantly associated with increasing age (P=0.018), cataract surgery (P<0.001), and diabetic nephropathy (P =0.011).

**Conclusions:** The prevalence of ERM in patients with DM2 screened with a digital non-mydriatic fundus camera was not significantly higher than the prevalence among the general population. ERM was significantly associated with age, diabetic nephropathy and cataract surgery.

# Diameters of large retinal blood vessels in hypertensive patients as measured by spectral domain optical coherence tomography

Amit Meshi MD[1], Jonathan Shahar MD[2], Yaron Arbel MD[3], Shlomo Berliner MD[3], Anat Loewenstein MD[2], Dafna Goldenberg MD[2]

*1. Department of Ophthalmology, Meir Medical Center, Kfar Saba, affiliated to the Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel. 2. Department of Ophthalmology, Tel Aviv Medical Center, Tel Aviv, affiliated to the Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel.3. Department of Internal Medicine "D" and "E", Tel Aviv Medical Center, Tel Aviv, affiliated to the Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel.*

**Purpose:** To measure retinal blood vessels diameters in hypertensive patients using spectral domain optical coherence tomography (SD-OCT).

**Methods:** A cohort of 47 hypertensive patients (94 eyes) underwent an SD-OCT exam (Spectralis, Heidelberg Engineering, Heidelberg, Germany). Two cubes of seven high-resolution horizontal scans each were placed at the superior and inferior borders of the disc to include the large temporal retinal vessels. Inter-scan interval was 240 µm. The outer diameter of the main temporal arteriole and venule was measured manually (Image J software, National Institute of Health, USA) at distances 480 µm, 720 µm, 960 µm, 1200 µm and 1440 µm from the optic disc border, superiorly and inferiorly. Previously reported results from 29 healthy subjects (58 eyes) were used as controls.

**Results:** The mean age ± SD of the hypertensive cohort was 57.3 ± 8.85 years. The mean ± SD diameters of the arterioles and venules in hypertensive patients steadily decreased from 130.85 ± 13.7 µm and 162.02 ± 16.04 µm at 480 µm from the optic disc to 119.7 ± 13.45 µm and 151.35 ± 15.44 µm at 1440 µm from the optic disc, respectively. The overall mean artery-to-vein ratio (AVR) in hypertension was 0.81. Uncontrolled hypertensive patients had narrower mean arteriolar diameters compared to controlled hypertensive patients at all points of measurement, reaching statistical significance in the superior arterioles ($P = 0.009$). Compared to healthy controls, mean arteriolar diameters and AVR were decreased ($P < 0.04$), whereas mean venular diameters were increased ($P < 0.01$) in hypertensive patients at all points of measurement.

**Conclusions:** Measurement of large temporal retinal vessel diameters by SD-OCT may be used as an adjunctive tool for the assessment of hypertension.

## Sub Retinal Fluid Optical Density in Rhegmatogenous Retinal Detachment

Ari Leshno[1], Adiel Barak[1], Anat Loewenstein[1], Amit Weinberg [1] and Meira Neudorfer[1]

*1Department of Ophthalmology Sourasky Tel-Aviv medical center*

**Purpose:** Investigation of the changes over time in optical density characteristics of sub retinal fluid (SRF) in rhegmatogenous retinal detachment (RRD) and its clinical relevance.

**Methods:** Patients with first onset RRD with no history of intra-ocular illness or surgery apart from cataract extraction who underwent optical coherence tomography (OCT), and whose earliest OCT scans showed sufficient SRF for sampling that did not include tissue edges, were included in the study. The highest quality B-scan containing SRF (as graded by the OCT image acquisition software) was analyzed. Optical density (OD) measurements were obtained using ImageJ, an open code Java-based image processing software. Optical density ratios (ODRs) were calculated as SRF OD divided by vitreous OD.

Time from onset of RRD was determined by first signs of visual loss as described in the patient's anamnesis. To apply parametric statistical testing patients were divided into 3 groups: acute duration (a week or less); sub-acute duration (between a week and a month) and chronic duration (more than a month).

**Results:** Overall 35 eyes (34 patients) met the inclusion criteria. Mean ODR was significantly ($p<0.05$) higher in eyes who were diagnosed with RRD more than a month after onset compared to those diagnosed before a month after onset. In addition, ODR was found to have a significant association with 3 months post-operative visual acuity ($p<0.0001$). There was no significant difference in vitreous optical density between the groups.

**Conclusions:** ODR of the SRF increases in RRD over time. This increase might reflect a change in the composition of the SRF and state of the retina. Our finding correlate with previous studies on the effect of RRD duration and the SRF. In addition we found a significant association between preoperative ODR values and 3-months postoperative BCVA, suggesting its future role as a biological marker for the prediction of postoperative visual results. Further investigation is needed to evaluate the use of this parameter in determining both treatment and prognosis in RRD patients.

## Spectrally-resolved retinal imaging

Oded Sagiv, GenadyKostenich, Gidi Arbel, Iris Moroz, Arie Orenstein, Michael Belkin

*The Chaim Sheba Medical Center*

**Purpose:** The development of a new device for non-invasive imaging of retinal microvasculature that may partially replace the standard fluorescein angiography (FA) which necessitates intravenous injection and is fraught with side-effects and logistics impediments.

**Methods:** The device is based on spectrally resolved imaging. It utilizes simultaneous acquisition of images in two predefined spectral regions.Image processing, using an appropriate algorithm, then enhances the signal-to-background ratio (i.e. contrast ratio, CR) between blood vessels and the adjacent tissues. Clinical study was carried comparing the new device to FA and other retinal photography methods. Several algorithms of imaging processing based on integration of both spectral images were developed and tested. The images were analyzed using imageJ software and CR values were compared to standard color and red-free photography as well as FA.

**Results:** Retinal images were obtained from 16 patients using a low resolution system prototype (1 megapixel camera). CR values were found to be dependent on the blood vessels' diameters and were different for veins and arteries. Images were therefore analyzed for different blood vessel diameters ("order"). Significant improvement in blood vessels CR and visualization of small capillaries were obtained after application of mathematical algorithms.

**Conclusions:** We proposed, developed and clinically validated a novel method improving visualization of retinal blood vessels on fundus photographs. A study using standard 5 megapixel cameras is underway. In the future, this system may be used to improve retinal vascular imaging without the need for injection of contrast material.

## Define the surgical orbital apex using CT scans of the orbit

Olga Zurinam, Dmitry Lumelsky, Ziv Neeman, Daniel Briscoe

*Technion Faculty of Medicine, Department of Ophthalmology, Department of Radiology, Emek Medical Center, Afula, Israel*

**Purpose:** The orbital surgical apex is the area wherein the volume of the pyramidal shaped orbit decreases so significantly that any mass in this location can cause crowding of the optic nerve. The surgical apex area has never been specifically defined although it is understood in concept by orbital surgeons. Our goal was to define its location by determining the area where the volume decrease ratio changes significantly.

**Methods:** We performed a retrospective analysis of CT's measuring the right orbital retrobulbar volume in 100 normal patients. Retrobulbar volume was measured between optic nerve attachment to the globe and the location of optic nerve exit from the orbit. The measured length between these two points was divided into five equal segments, from the anterior to posterior orbit; V1, V2, V3, V4 and V5. All 5 segments were compared and the most significant area of volume depletion established.

**Results:** The mean numeric value of measured orbital volumes was compared. A ratio difference of V1/V2 was less than 2, V2/V3 was 2.32 (±0.27), V3/4 was 3.26 (±0.39), and V4/V5 was 5.72 (±1.67). The most remarkable difference in ratio was between V4 and V5 (mean 5.72 ±1.67 with $p<.0001$). Our data demonstrated that the V3 segment (the posterior 3/5 of the orbital volume) was the location where the decrease in orbital volume impacted, and measured ratios were statistically significant.

**Conclusions:** We defined the surgical apex as the posterior 3/5 of the retrobulbar orbital space, the area where significant decrease in volume peaks. This area is important to recognize and defines the “high risk location” of optic nerve compression more accurately. This definition should help alert radiologists and ophthalmologists to recognize those patients needing urgent treatment or surgery.

## Publication outcomes of abstracts submitted to the annual American Academy of Ophthalmology Meeting

Michael Mimouni MD[1], Mark Krauthammer MD[2], Hamza Abualhasan MD[1], Hanan Badarni MD[1], Kamal Imtanis MD[1], Gilad Alon MD[1], Liron Berkovitz MD[1], Gil Amarilyo MD[3]

*1Department of Ophthalmology, Rambam Health Care Campus, Haifa, Israel,2Department of Ophthalmology, Sourasky Medical Center, Tel Aviv, Israel, 3Schneider Children's Hospital, Tel Aviv, Israel*

**Purpose:** The American Academy of Ophthalmology (AAO) annual meeting is an important forum for early dissemination of novel ideas. While in peer-reviewed journals studies are selected according to the merit of the complete article, abstracts are selected for presentation in the meeting solely on a general summary of the research. The current study aimed to characterize the publication outcomes of abstracts presented at the AAO annual meeting.

**Methods:** We identified all abstracts accepted for oral or poster presentation at the 2008 AAO annual meeting. Two independent investigators conducted a manual PubMed search for each abstract and recorded whether or not the abstract was published as a full length manuscript, the resulting journal's title, impact factor and time to publication.

**Results:** A total of 690 abstracts were analyzed. The overall publication ratio was 39.1%. The mean ± SD time from abstract presentation to publication was 19.3 ± 16.6 months with a mean ± SD impact factor of 3.03 ± 1.79. One quarter of the studies were published in the journal "Ophthalmology". Those published in "Ophthalmology" had a shorter publication time (18 versus 9.9 months, p=0.002). Oral presentations were published more often than poster presentations (57.84% versus 35.88%, p<0.001) and in journals with a higher impact factor (3.24 versus 2.83, p=0.02). The median publication rate (27.37% to 52.17%) and impact factor (1.98 to 5.27) varied among subspecialties (p=0.004 and p=0.003 respectively). Rare diseases were published more often (49.37% versus 37.95%, p=0.49) and in journals with a higher impact factor (3.71 versus 2.86, p=0.03) within a shorter period of time (15 versus 11.9 months, p=0.02). Additional factors associated with publication in journals with a higher impact factor were sample size greater than 1000 (p=0.01), affiliation with an institute located in the United States (p=0.02) and funded studies (p=0.01).

**Conclusions:** Nearly 40% of abstracts presented at the AAO meeting are eventually published, a quarter of them in the AAO affiliated "Ophthalmology" journal within half of the publication time of other journals. Abstracts were published in journals with a mean impact factor above the fields. Characteristics such as rare diseases, large sample size, affiliation to a USA institute and being funded were associated with higher impact factors.

## Giant Cell Arteritis associated with night sweats may be protective from vision loss

Joshua Kruger[1], Joseph Rizzo[2]

*1) Department of Ophthalmology, Hadassah Medical Center, 2) Department of Ophthalmology, Harvard Medical School*

**Purpose:** To assess whether the occurrence of night sweats in Giant Cell Arteritis (GCA) is associated with a different visual prognosis.

**Methods:** A retrospective review of all GCA cases presenting to a neuro-ophthalmologist at the Massachusetts Eye and Ear Infirmary between the years 2007 and 2014.

**Results:** Four cases were identified. In all cases, there were no symptoms of vision loss. The reason for referral in all cases was to screen for subclinical ophthalmic GCA-manifestations. The assessment was negative in all cases and remained negative in the course of follow-up.

**Conclusions:** Night sweats may be part of a GCA variant that is protective from vison loss. This may be due to a unique cytokine profile involving altered IL-6 production.

## Knobloch syndrome masquerading as albinism

Libe Gradstein[1], Gerald F. Cox[2], Pablo Altschwager[3], Anne B. Fulton[3]

*1 Department of Ophthalmology, Soroka Medical Center and Clalit Health Services, Faculty of Health Sciences, Ben Gurion University, Beer Sheva, Israel, 2 Division of Genetics and Department of Pediatrics, Boston Children's Hospital and Harvard Medical School, Boston, Massachusetts, USA, and Clinical Development, Genzyme, a Sanofi company, Cambridge, Massachusetts, USA, 3 Department of Ophthalmology, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts, USA*

**Purpose:** In a girl who presented in infancy with ocular features of albinism and gradually developed choroidal sclerosis and patchy atrophy leading to a diagnosis of Knobloch syndrome (KS, OMIM 267750, *COL18A1*), we present for the first time evidence of progressive electroretinographic abnormalties.

**Methods:** In an infant whose parents were first cousins, nystagmus and esotropia prompted ophthalmic evaluation and identification of albinotic fundi, absent foveal reflexes, myopia of 14 D and normal cutaneous pigmentation. Genetics consultation was obtained in infancy and again at age 8.5 years as retinal findings evolved. Ophthalmic features, including electroretinographic responses to full-field stimuli, were monitored. Brain MRI to evaluate a new-onset seizure disorder at age 6 years showed bifrontal polymicrogyria.

**Results:** The ERG in infancy showed mild deficits in scotopic b-wave sensitivity and prolonged photopic b-wave implicit times. Tyrosinase gene sequencing revealed one novel mutation, S466F, and the temperature-sensitive polymorphism, R402Q, suggesting the diagnosis of OCA1. Because of the appearance of choroidal sclerosis and atrophic retinal patches, ERG testing was repeated at age 8 years and showed significant attenuation of scotopic and photopic responses. At age 8.5 years retinal detachment was found. Genetic re-analysis led to the identification of a homozygous mutation in the COL18A1 gene, c.3213dupC, which predicts a frameshift with premature protein termination. This result confirmed the diagnosis of Knobloch syndrome, a rare autosomal recessive disorder originally defined in 1971 by the triad of high myopia, occipital skull defects, and vitreo-retinal degeneration with retinal detachment, but since then shown to express a more variable phenotype.

**Conclusions:** Our patient's features illustrate the significant clinical variability observed in KS. In retrospect, the mild ERG changes in infancy likely represented early stages of choroioretinal degeneration. Similar to the ERG results in *col18a1* knockout mice, we have documented progressive diminution of the photopic and scotopic responses in KS.

## Ophthalmic disease associated with natural and experimental infection with Tilapia Lake Virus in fish

Asaf Berkowitz[1], Avi Eldar[1], Ron Ofri[2]

*1 Department of Avian and Fish Diseases, Kimron Veterinary Institute, Ministry of Agriculture, Beit Dagan, Israel, 2Koret School of Veterinary Medicine, The Hebrew University of Jerusalem, Rehovot, Israel*

**Purpose:** In the past 5 years, a significant population decline of certain species of Tilapines (a generic term for fish belonging to the family Chiclidae) has been documented in the Sea of Galilee in northern Israel. The decline was associated with a high prevalence of ocular lesions in affected fish. A novel RNA virus named Tilapia Lake Virus (TiLV; Eyngor et al., 2014) was isolated from morbid fish, and the disease was reproduced by experimental infection of naïve tilapia. The purpose of this study was to compare pathologic findings observed in the natural disease to the findings in an experimentally-induced disease.

**Methods:** Viral isolation and molecular detection in affected fish was performed using nested PCR. Naïve tilapia fish were inoculated with an intracoelomic injection of isolated TiLV. A gross pathological examination of morbid fish was performed, and affected tissues were studied histopathologically.

**Results:** Over 90% of the morbid fish with natural infection had a distinct unilateral ophthalmic disease. Affected eyes were phthisical, and chronic optic neuritis, mature corneal fibrosis with distortion of the anterior chamber and anterior synechia were observed. In experimentally-inoculated fish, the disease had two manifestations: 1. An acute, lethal disease with no significant pathologic lesions 2. A subacute disease, with anterior uveitis, diffuse inner layer atrophy of the retina (including the nerve cell layer, the inner plexiform layer, and the inner nuclear layer) and optic neuritis observed in affected eyes. Other recorded lesions in the subacute form of the experimentally induced disease included multifocal gliosis and necrosis in the brain, meningomyelitis and ganglioneuritis. No significant lesions were observed in any other tissue.

**Conclusions:** The targeting of the optic nerve observed in both the natural and experimental diseases suggests that optic neuritis is a primary lesion, which also leads to retinal inner layer atrophy in the experimentally induced disease. Further study of the pathogenesis is warranted for a better understanding of this disease.

## Time trends reveal a decrease of childhood blindness in Israel

*Eedy Mezer MD[1,2], Angela Chetrit MHA[3], Ofra Kalter-Leibovici MD[3,4], Michael Kinori MD[4,5], Itay Ben-Zion MD[4,5], Tamara Wygnanski-Jaffe MD[4,5]*

*1Department of Ophthalmology, Rambam Health Care Campus, Haifa, Israe, l2Ruth and Bruce Rappaport Faculty of Medicine, Technion–Israel Institute of Technology, Haifa, Israe, l3Unit of Cardiovascular Epidemiology, Gertner Institute for Epidemiology & Health Policy Research, Tel Hashomer, Israel, 4 Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel, 5 The Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, Israel*

**Purpose:** To explore trends in the incidence and causes of legal childhood blindness in Israel, one of the few countries worldwide that maintain a national registry of the blind.

**Methods:** A historical cohort study of annual reports of the National Registry of the Blind (NRB) between 1999 and 2013 included children 0-18 years of age registered for blind certification. All data regarding demographic information, year of registration and cause of blindness were obtained from the annual reports of NRB. Causes of legal blindness analyzed were optic atrophy, retinitis pigmentosa (RP), retinopathy of prematurity (ROP), albinism, other retinal disorders, cataract and glaucoma. The main outcome measure was the incidence of new cases of certified legal blindness.

**Results:** The incidence of newly registered legally blind children in Israel almost halved from 7.7 per 100,000 in 1999 to 3.1 per 100,000 in 2013. The decline was mainly attributable to a decreased incidence of blindness resulting from RP and ROP. The incidence of registered cases due to cerebral visual impairment increased.

**Conclusions:** During the past decade, there was a decline in childhood blindness in Israel. A continuous decline in consanguineous marriages among the Jewish and Arab populations in Israel may have contributed to the decrease in the rate of blindness due to RP in the pediatric population. The lower incidence of blind certification due to ROP could have been secondary to improved postnatal growth in preterm very low birth weight infants.

## Generation and characterization of Fam161a Conditional Knockout mice

Avigail Beryozkin (1), Alexey Obolensky (1), Ayat Khalaileh (1), Carlo Rivolta (2), Yvan Arsenijevic (3), Eyal Banin (1), Dror Sharon (1)

*1.Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel, 2.Department of Medical Genetics, University of Lausanne, CH-1005 Lausanne, Switzerland,3.Department of Ophthalmology, University of Lausanne, Jules-Gonin Eye Hospital, FAA, Unit of Gene Therapy & Stem Cell Biology, Avenue de France 15, 1004 Lausanne, Switzerland*

**Purpose:** We previously reported that FAM161A mutations are the most common cause of inherited retinal degenerations in the Israeli population. The FAM161A gene is an excellent candidate for gene therapy since the mRNA length is relatively short and all reported mutations are expected to be null. The purpose of the study is to generate a homozygous line of mice with knockout of the Fam161a gene and examine whether this genetic defect mimics the one identified in humans with retinitis pigmentosa due to mutations in FAM161A.

**Methods:** Mice were produced for us by the KOMP Company. Genotyping of mutations was performed by PCR followed by Sanger sequencing. The retinal localization of the construct was evaluated by LacZ staining. Retinal function was evaluated by ERG and structure by histological analysis at 1 and 2 months-old mice. RT-PCR was performed on RNA isolated from mice eyes.

**Results:** Our initial colony included five mice who were heterozygous for a conditional allele carrying a Fam161a-KO construct. The mice were found to carry a known CRB1 mutation and were bred with C57BL/6J mice in order to filter out this mutation. Then, the mice were inbred to create a homozygous line containing the non-activated Fam161a-KO construct. LacZ staining revealed that Fam161a is expressed in the ganglion cells, inner and outer nuclear layer in these mice. In photoreceptors, LacZ expression was noted in the inner and outer segments. ERG analysis of mice homozygous for the non-activated construct at ages 1 and 2 months revealed lower a-wave and b-wave amplitudes comparing to wt mice. Light-adapted ERG showed a trend for lower responses that is correlated with light intensity. RT-PCR analysis revealed an unexpected insertion of a 115bp fragment (c.8267_8268ins115, p.Ser139ArgfsX11) that is originated from the construct, causing a frameshift and a premature stop codon.

**Conclusions:** Our preliminary data indicate that a Fam161a frameshift mutation can affect retinal function. We will crossbreed these mice with Flp and Cre mice aiming to obtain a conditional Fam161a KO allele that will be used for Fam161a gene therapy.

## The Genetics of Usher Syndrome in the Israeli and Palestinian Populations

Ayat Khalaileh (1), Tamar Ben-Yosef (2), Annick Raas-Rothschild (2), Itay Chowers (1), Eyal Banin (1), Dror Sharon (1), Samer Khateb (1)

*(1) Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel. (2) Genetics Department, Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel.*

**Purpose:** To characterize the set of mutations and genes that cause Usher syndrome (USH) in the Israeli and Palestinian populations.

**Methods:** All participants in the study signed an informed consent that adhered to the tenets of the declaration of Helsinki before drawing a blood sample for molecular analysis. Patients underwent clinical examination including electroretinography and retinal imaging. Genetic analysis included Sanger sequencing for the detection of founder mutations, homozygosity mapping in some consanguineous families, and whole exome sequencing (WES) in large families.

**Results:** Our cohort contains about 1300 families with inherited retinal diseases, 78 of the index cases were diagnosed with Usher syndrome (30 with USH type 1 (USH1), 37 with USH2, 8 with USH3, one with atypical USH, and in 2 families the type could not be determined). In 55 of the families (71 %), the inheritance pattern was determined as autosomal recessive (AR) and the remaining were isolate cases. A comprehensive mutation detection analysis (including homozygosity mapping, screening for founder mutations and WES analysis in 7 cases) lead to the identification of the cause of disease in 31 (38%) of the families: (13 families with USH2A mutations, 9 MYO7A, 7 USH3A, 1 GPR98 and 1 CEP250). In an Ashkenazi Jewish family with USH3 (MOL1021), we identified a novel nonsense mutation (p.Tyr1768*) in the USH3A gene that is in a compound heterozygous state with the known founder mutation (p.N48K). In Muslim families from the vicinity of Jerusalem (MOL1019, MOL1191, MOL406), we identified two novel founder MYO7A mutations: p.G1298R and c.2187+1G>T (IVS18+1G>T). Finally, we report here of the first GPR98 mutation in the Israeli population: a homozygous frameshift mutation (p.K5l65fs) identified by WES analysis.

**Conclusions:** The cause of disease in most USH families is still unknown and further analyses are needed to identify mainly family-specific mutations. Our data support previous studies indicating that MYO7A is the major USH1 gene, USH2A is the major USH2 gene, and USH3A the major USH3 gene.

# Molecular, physiological and morphological effects of DHDDS knockdown in photoreceptors of Drosophila

Liliana Mizrahi-Meissonnier[1], Rachel Zaguri[2], Elisheva Rhodes[2], Vladimir Katanaev[3], Baruch Minke[2], Dror Sharon[1]

*1. Department of Ophthalmology, Hadassah Medical Center, Jerusalem, Israel. 2. Faculty of Medicine, Hebrew University, Jerusalem, Israel. 3. Faculty of Biology and Medicine, University of Lausanne, Lausanne, Switzerland.*

**Purpose:** In 2011, others and we reported the identification of a founder mutation in the dehydrodolichyl diphosphate synthase (DHDDS) gene in Ashkenazi Jews with non-syndromic retinitis pigmentosa (RP). The DHDDS enzyme is known to be involved in dolichol synthesis, a lipid molecule that is important for various biological functions, including N-glycosylation and membrane fluidity. The fact that the patients do not suffer from other clinical problems is surprising since genetic defects in related enzymes cause a systemic phenotype with involvement of multiple organs. The purpose of the current study was to construct and analyze a Drosophila strain in which DHDDS expression is knocked-down in photoreceptors using RNAi.

**Methods:** The DHDDS-RNAi (CG10778-RNAi) Drosophila strain under the control of photoreceptor specific promoter was generated by crossing w-;P[UAS: CG10778-RNAi]; Sb+flies with a Gal4 strain to drive maximal suppression of CG10778-RNAi. Flies were raised under on a 12H:12H dark/light cycle, in complete dark or in 24H intense light in 25C and collected 1 and 7 days after eclosion. Electroretinogram (ERG) was recorded using standard techniques. The Prolonged Depolarizing Afterpotential (PDA) was used as an assay for in vivo electrophysiological test. Transmission electron microscopy (TEM) analysis was performed on fly eye. Western blot analysis was performed with several antibodies.

**Results:** Western Blot analysis revealed that DHDDS expression is downregulated in the CG10778-RNAi fly photoreceptors. ERG analysis of CG10778-RNAi flies showed an abnormally small and short PDA indicating that rhodopsin (Rh1) level was drastically reduced in the transgenic fly, as verified directly by Western blot analysis. TEM analysis revealed an abnormal retinal structure indicating an early-onset and strong severe photoreceptor degeneration. Interestingly, not all photoreceptor were equally affected by the degenerative process and developmentally-dependent specific subtype were spared.

**Conclusions:** CG10778-RNAi Drosophila is an excellent model to study DHDDS function. We were able to show by molecular (Western blot analysis), physiological (ERG) and morphological (TEM) methods that DHDDS knockdown specifically disrupts the Rh1 protein causing severe degeneration in Drosophila photoreceptors.

## Immunological Properties and Interactions of Retinal Pigment Epithelium derived from Human Embryonic Stem Cells

Ayala Ejzenberg(1), Ruslan Alper-Pinus (1), Alexey Obolensky(1), Maria Idelson(2), Benjamin Reubinoff(2), Eyal Banin(1).

*(1)Department of Ophthalmology, Hadassah-Hebrew University Medical Center. (2)The Hadassah Human Embryonic Stem Cell Research Center, The Goldyne Savad Institute of Gene Therapy & Department of Gynecology, Hadassah-Hebrew University Medical Center.*

**Purpose:** Blinding diseases such as Age-related macular degeneration (AMD), Best disease, and some sub-types of retinitis pigmentosa are due to dysfunction of retinal pigment epithelium (RPE) cells which lie underneath and support the photoreceptors. Transplantation of RPE cells is considered as a potential therapeutic approach that may delay, halt or perhaps even reverse degeneration, improve retinal function and prevent blindness in these conditions. We previously reported the development of a directed differentiation protocol which allows for efficient derivation of RPE cells from hESCs, and our goal is to transplant such cells in patients with RPE disease. The purpose of this study is to explore the immune properties of hESC-derived RPE cells and their interaction with the host immune system. Such interactions may lead to acute or chronic immune rejection and collateral injury to surrounding tissue by the inflammatory response, which may significantly influence the safety, efficacy, and survival following transplantation.

**Methods:** The potential of hESC-derived RPE cells to induce immune responses was studied by co-culturing hESC-derived RPE with activated peripheral blood monocytes (PBMCs), and their cytokine secretion profile was explored. The influence of hESC-derived RPE cells on proliferation and apoptosis of activated T cells was studied. To examine possible immune responses against transplanted RPE cells in-vivo, transplantation experiments were performed in RCS rats with a mutation in the MERTK gene with and without systemic cyclosporine treatment. Levels of the pro-inflammatory cytokine IFNγ and the anti-inflammatory cytokine IL-10 were measured in serum.

**Results:** In-vitro, hESC-derived RPE cells inhibited the proliferation of activated T cells and their secretion of the pro-inflammatory cytokine IFNγ. In addition, they induced apoptosis of activated T cells. In-vivo, transplantation of hESC-derived RPE into the subretinal space induced an immune tolerant state as reflected by an increase in the IL-10/ IFNγ ratio. Interestingly, this effect was enhanced in the absence of cyclosporine.

**Conclusions:** RPE cells may induce an immune tolerant state in-vitro and in the RCS rat model.

# An intronic deletion in the PROM1 gene leads to autosomal recessive cone-rod dystrophy

Osnat Eidinger,[1] Rina Leibu,[2] Hadas Newman,[3] Leah Rizel,[1] Ido Perlman,[3,4] Tamar Ben-Yosef[1]

*[1]Department of Genetics and [4]Department of Physiology and Biophysics, The Rappaport Family Institute for Research in the Medical Sciences, Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel, [2] Alberto Moscona Department of Ophthalmology, Rambam Health Care Campus, Haifa, Israel, [3]Department of Ophthalmology, Tel-Aviv Medical Center, Tel-Aviv, Israel*

**Purpose:** To investigate the genetic basis for autosomal recessive cone-rod dystrophy (CRD) in a consanguineous Israeli Jewish family.

**Methods:** Patients underwent a detailed ophthalmic examination, including funduscopy, electroretinography (ERG), visual field testing and optical coherence tomography (OCT). Genome-wide homozygosity mapping using a SNP array was performed to identify homozygous regions shared among two of the affected individuals. Mutation screening of the underlying gene was carried out by direct sequencing. *In silico* and *in vitro* analyses were used to predict the effect of the identified mutation on splicing.

**Results:** The affected family members are three siblings suffering from progressive visual deterioration, glare, deficient color vision and night vision abnormalities. Visual field tests revealed central scotomas of different extension. Both cone and rod ERG responses were reduced, with cones being more severely affected. Homozygosity mapping revealed several homozygous intervals shared among two of the affected individuals. One of them included the *PROM1* gene. Sequence analysis of the 26 coding exons of *PROM1* in one affected individual revealed no mutations in the coding sequence or in intronic splice-sites. However, in intron 21, proximate to the intron-exon junction, we observed a homozygous10 bp deletion between positions -26 and -17 (c.2281-26_-17del). This deletion co-segregated with the disease in the family, and was not detected in public databases nor in 101 ethnically-matched control individuals. *In silico* analysis predicted that this deletion would lead to altered intron 21 splicing. Bioinformatic analysis predicted that a recognition site for the SRSF2 splicing factor is located within the deleted sequence.

**Conclusions:** Here we report a novel and unique intronic mutation of *PROM1*, underlying autosomal recessive CRD in a consanguineous Israeli family. Altered splicing probably results from deletion of a recognition site for the SRSF2 splicing factor. This report expands the spectrum of pathogenic mutations of *PROM1* and further demonstrates the importance of intronic mutations.

## A single nucleotide polymorphism in ATXN7 gene can cause non-syndromic cone rod dystrophy

Shirel Weiss [1,2], Mali Salmon-Divon [3], Lina Basel [4], Rachel Straussberg [2,5], Nitza Goldenberg-Cohen [1,2,6]

*1The Krieger Eye Research Laboratory, Felsenstein Medical Research Center and 2Sackler School of Medicine, Tel Aviv University, 3Genomic Bioinformatics Laboratory, Molecular Biology, Ariel University, 4Pediatric Genetics, 5Pediatric Neurology, and 6Pediatric Ophthalmology, Schneider Children's Medical Center of Israel, Petah Tiqwa*

**Purpose:** The prevalence of cone rod dystrophy (CRD) is about 1/40,000, characterized by primary cone involvement or concomitant loss of both cones and rods. Several genes are specifically associated with CRD, such as ABCA4, ADAM9, CERKL, CNGA3, RDH5, RPGRIP1, TTLL5AIPL1, CRX, GUCA1A, GUCY2D. Trinucleotide repeat expansion in another gene, ATXN7, is known to cause CRD in spinocerebellar ataxia syndrome (SCA7). Here we describe a novel dominant mutation in the ATXN7 gene in a child, leading to CRD.

**Methods:** Complete eye examination was performed, including fundus photography, optical coherent tomography, and electroretinography combined with neurological evaluation. Genomic DNA was extracted from peripheral blood leukocytes and sent for whole-exome sequencing (WES). Bioinformatics analysis was performed using the BWA and GATK software.

**Results:** Except for impaired vision (BVC 1/60), high myopia (BE -7.0), esotropia and mild temporal pallor of the optic discs, the fundus appearance and the retinal thickness measured by OCT were normal. Parents and brothers were healthy with normal eye examination results. WES revealed no compound heterozygosity or recessive mutations. The dominant mutation in ATXN7 (S574F) was not detected in the parents.

**Conclusions:** Here we described a boy with severely impaired vision, diagnosed with unspecified CRD based on ERG responses, with healthy unrelated parents and normally seeing brothers. His neurology examination results were normal, with no ataxia. Whole exome trio analysis revealed de novo autosomal dominant mutation in ATXN7 gene. Apparently, PolyQ (CAG) expansion in the ATXN7 gene is the cause for the SCA7 syndrome with CRD and ataxia. Recently it was associated with RNA toxicity and repeat-associated non-ATG (RAN) translation. We describe a novel dominant mutation leading to CRD without ataxia (not shown yet) via a different mechanism, which is now under investigation.

Foundation Fighting Blindness (FFB) BR-GE-0214-0639-TECH; the Zanvyl and Isabelle Krieger Fund, Baltimore, MD (NGC), the Claire and Amedee Maratier Institute for the Study of Blindness and Visual Disorders, the Sackler Faculty of Medicine, Tel-Aviv University (SW)

# Retinal Function in Patients with Achromatopsia Caused by Mutations in the CNGA3 Gene

Boris Rosin [1], Artur Cideciyan[2], Inbar Erdinest[1], Lina Zelinger [1], Dror Sharon[1], Samuel G. Jacobson[2] and Eyal Banin [1]

*1Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel 2 Department of Ophthalmology, Scheie Eye Institute, University of Pennsylvania, Philadelphia, Pennsylvania, USA.*

**Purpose:** Achromatopsia (ACHM), or Rod monochromatism, is a debilitating disorder of vision clinically manifested by photophobia, decreased visual acuity and absence of color perception. To date, five genes were found to cause the disease, with CNGA3 (encoding a subunit of a Na+ voltage-gated ion channel) accounting for over 80% of patients in Israel. The disease leads to complete absence of cone function, as evidenced by ERG testing, while structurally the cone photoreceptors remain relatively preserved, as evidenced by OCT as well as by adaptive optics imaging. The purpose of the present study was to better characterize retinal function in patients with CNGA3 ACHM.

**Methods:** Disease phenotype of CNGA3 ACHM patients was analyzed by electrophysiological as well as psychophysical techniques including electroretinography, dark- and light-adapted chromatic perimetry, and by a novel method to quantify photoaversion. Plots of threshold intensity as a function of stimulus wavelength were constructed to assess the type of photoreceptors mediating vision in CNGA3 ACHM patients. Severity of photoaversion was quantified by measuring the interpalpebral distance in patients exposed to increasing background light intensities.

**Results:** In addition to complete cone dysfunction, in close to 60% of patients rod ERG abnormalities were detected on full field ERG testing. Chromatic perimetry revealed that patients use rod-mediated pathways under both scotopic and photopic conditions, including under background light levels that would normally suppress rod photoreceptor function. Upon transition from dark to a dim light background, pronounced photoaversion was observed in the patients as compared to normal seeing controls.

**Conclusions:** Visual function of CNGA3 ACHM patients is mediated by rod photoreceptors even under photopic conditions, as our data suggests that these do not undergo bleaching under background light intensities known to induce such bleaching in normal subjects. A characteristic pattern of photoaversion response was demonstrated. These tests can be utilized for disease characterization and for assessment of treatment outcomes in future treatment trials.

# Identification of Homozygous and Hemizygous Genomic Deletions that Cause Inherited Retinal Degenerations by Analyzing Whole Exome Sequencing Data

Samer Khateb[1]; Ayat Khalailah[1]; Avigail Beryozkin[1]; Liliana Mizrahi-Meissonnier[1]; Ala Abu-diab[1]; Fathiah Abu-Turkey[1]; Mor Hanany[1]; Tamar Ben-Yosef[2]; Eyal Banin[1] and Dror Sharon[1]

*1. Department of Ophthalmology, Hadassah Medical Center, Jerusalem, Israel. 2. Department of Genetics, Faculty of Medicine, Technion, Haifa, Israel.*

**Purpose:** Inherited retinal degenerations (IRDs) are a common cause of visual disturbance with a high clinical and genetic heterogeneity. Various mutations in more than 200 genes were identified and/or mapped causing this disease. The development of next-generation sequencing techniques such as whole exome sequencing (WES) contributed to the discovery of many of these genes during the last few years. The aim of the current study was to utilize WES data in order to identify large deletions that include at least one exon in known retinal disease genes.

**Methods:** Patients diagnosed with different inherited retinal degenerations underwent a comprehensive ophthalmic evaluation, including ophthalmic ancillary tests. Index cases who were found to be negative for the already known mutations were selected for WES analysis. WES was performed using the NimbleGen V2 paired-end kit and Illumina HiSeq2000 (Otogenetics). An analysis of exon coverage data was performed.

**Results:** We analyzed data of 81 WES samples from index patients with inherited retinal diseases. By calculating the average coverage for all exons in the human genome, we were able to identify homozygous or hemizygous deletions of at least one exon in 6 families (7.5%). In one family we identified a single-exon deletion in the EYS gene, in two families we identified deletions of three consecutive exons (in the MYO7A and NPHP4 genes), in two families we identified different RPGR deletions of four and eight consecutive exons, and in one family with the original diagnosis of retinitis pigmentosa we identified a multi-gene deletion on the X-chromosome, including the CHM gene. By using PCR-walking analysis, we were able to identify the borders of two of the deletions and to screen our set of patients for the presence of additional patients with either heterozygous or homozygous deletions.

**Conclusions:** To the best of our knowledge, this is the first study in which WES data are systematically analyzed to identify large deletions in WES data of patients with IRDs. Our analysis indicates that large deletions (including at least one exon) are relatively frequent (about 7.5 % in our cohort) and should be screened when analyzing WES data.

# Genome Wide Association Study Analysis on Adult Onset Foveomacular Vitelliform Dystrophy in the Israeli Population

Michelle Grunin[1], Liran Tiosano[1], Elior Rahmani[2,3], Gala Beykin[1], Regev Schweiger[2,3], Shira Hagbi-Levi[1], Dror Sharon[1], Eran Halperin[2,3,4], Itay Chowers[1]

*1. Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel, 2. Molecular Microbiology and Biotechnology, Tel Aviv University, Israel, 3. The Blavatnik School of Computer Science, Tel Aviv University, Israel, 4. International Computer Science Institute, ICSI, USA*

**Purpose:** The genetic cause of majority of cases of adult-onset foveomacular vitelliform dystrophy (AOFVD) is currently unknown. We have amassed a cohort of patients with AOFVD from the Israeli population to evaluate for its genetic causes.

**Methods:** Fifty one consecutive patients with a clinical diagnosis of AOFVD without known family history of retinal disease were evaluated versus a cohort of 247 unaffected age-matched controls from the same referral center. PCR and Sanger sequencing was performed for PRPH2 and BEST1, and for known mutations in IMPG1/2. Samples were also run on a custom Illumina SNP array chip with ~500,000 variants.Quality control (QC) was performed with Illumina Bead Studio and PLINK. Examination of GWAS results was performed using R, PLINK, ANNOVAR, Haploview, Integrative Genome Viewer (IGV), and other bioinformatics programs.

**Results:** No known mutations were found in sequencing of IMPG1/2 along with PRPH2 and BEST1. GWAS evaluation after QC indicated 522 variants with Bonferroni- corrected P<1x10^-5, with several variants relating to possible retinal disease genes, including variants related to age-related macular degeneration (AMD), and several novel variants ranging across the genome. DAVID functional annotation indicated 7 main clusters, such as membrane-signaling pathways, glycosylation pathways, or iron oxidation pathways (FDR-P<0.05).

**Conclusions:** GWAS indicates variants that may comprise part of the pathogenesis of AOFVD, including both known and novel variants. These genome-wide SNPs, or a risk burden of a large proportion of risk variants, may comprise a portion of the genetic architecture of the disease in the Israeli population. Further research of these variants is needed to investigate their role in the pathway or pathogenesis of the disease.

## Autosomal recessive nonsyndromic retinitis pigmentosa caused by a mutation of the mucopolysaccharidosis type IIIC gene, heparan-alpha-glucosaminide N-acetyltransferase (HGSNAT)

Leah Rizel,[1] Hadas Newman,[2] Rina Leibu,[3] Hagit N Baris,[4] Eyal Banin,[5] Amir Massarweh,[6] Ofer Isakov,[7] Dror Sharon,[5] Noam Shomron,[7] Tamar Ben-Yosef[1]

*[1]Department of Genetics and [6]Department of Physiology and Biophysics, The Rappaport Family Institute for Research in the Medical Sciences, Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel,[2] Department of Ophthalmology, Tel-Aviv Medical Center, Tel-Aviv, Israel, [3] Alberto Moscona Department of Ophthalmology, Rambam Health Care Campus, Haifa, Israel, [4]The Genetic Institute, Rambam Health Care Campus, and Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel, [5] Department of Ophthalmology, Hadassah- Hebrew University Medical Center, Jerusalem, Israel, [7] Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel*

**Purpose:** Retinitis pigmentosa (RP) is a genetically heterogenous condition, which can appear as both syndromic and nonsyndromic. We aimed to identify the cause for nonsyndromic RP in an Ashkenazi Jewish (ASH) patient.

**Methods:** Patient's DNA was subjected to whole exome sequencing. The effect of the mutation on splicing was studied by RT-PCR analysis. Patients underwent complete physical and ophthalmic evaluation, including funduscopy, optical coherence tomography and electroretinography. HGSNAT activity and glycosaminoglycan levels were measured in leukocytes and in urine, respectively.

**Results:** A homozygous mutation **(**c.370A>T**)** was identified in the *HGSNAT* gene, which is usually associated with a severe and lethal disorder, Mucopolysaccharidosis type IIIC (MPS IIIC). A subsequent screen of 66 ASH RP index cases revealed an additional family with two siblings homozygous for the same mutation. All three patients were adults diagnosed with nonsyndromic RP. The oldest patient was 60 years old and did not exhibit cognitive or neurological deterioration nor did she have any phenotypic features consistent with MPS IIIC. c.370A>T leads to partial skipping of *HGSNAT* exon 3, resulting in reduced HGSNAT activity and to increased levels of incompletely degraded mucopolysaccharides.

**Conclusions:** Most MPS IIIC patients manifest symptoms during childhood with progressive neurological deterioration, including retinal degeneration, and die in early adolescence. This report broadens the spectrum of phenotypes associated with *HGSNAT* mutations, and adds *HGSNAT* to the list of over 40 genes associated with autosomal recessive nonsyndromic RP.

## A novel platform for minimally invasive delivery of cells and therapeutics to the posterior segment

Ygal Rotenstreich[1], Sapir Kalish [1], Adi Tzameret [1], Ifat Sher[1], Avraham Treves[2], Arnon Nagler[3], Michael Belkin[1]

*1Goldschleger Eye Research Institute Sackler Faculty of Medicine Tel Aviv University Sheba Medical Center Tel-Hashomer, 2Center for Stem Cells and Regenerative Medicine Cancer Research Center Sheba Medical Center Tel-Hashomer, 3Hematology Division, Sheba Medical Center Tel-Hashomer, Israel*

**Purpose:** One of the major limitations in clinical cellular therapy is the current surgical approach that involves invasive pars plana vitrectomy. A limited amount of cells can be injected and therapeutic effect is restricted to the transplanted area. Here we evaluate a novel minimally invasive posterior eye delivery system by means of injection of cells and therapeutics in a thin layer across the extravascular spaces of the choroid covering 70 percent of the sub retinal pigment epithelium (RPE) surface in a rabbit animal model.

**Methods:** A novel system comprised of a syringe with a blunt needle and an adjustable pin was developed. New Zealand White Rabbits (n=12) were injected with human cells and 3 rabbits were injected with near infra-red (NIR) human serum albumin (HSA) core-shell iron oxide nanoparticles (IO/HSANs) of very narrow size distribution (15-200 nm). No immunosuppressants were used. The efficacy of technique and safety profile, were determined using Optical Coherence Tomography (OCT), Electroretinogram (ERG) and histopathology.

**Results:** Transplanted cells and injected nanoparticles were identified as a thin layer across the extravascular spaces of the choroid, covering 70 percent of the sub RPE surface. Cells and nanoparticles could be identified in the posterior eye up to 2 weeks following injection. OCT scans revealed no retinal detachment or choroidal hemorrhage. No changes in retinal functions were recorded in rabbits following injection. Histopathology demonstrated normal anatomy with no signs of inflammation up to 2 weeks post injection.

**Conclusions:** Targeting cells and pharmaceuticals to the posterior segment can be achieved using a novel injection platform in a safe and reproducible manner. This surgical system enables placement of therapeutics and cells in high dosage in close proximity to the RPE and retina as a thin layer, across the extravascular spaces of the choroid without insertion of surgical instruments under the macula, with no vitrectomy, no retinal detachment, choroidal hemorrhage or inflammation. This new transplantation system is predicated to increase the therapeutic effect and safety of cell-based therapies and pharmaceuticals for a wide variety of macular and retinal diseases.

# The protective effect of activated protein C (APC) on cell permeability and laser-induced CNV progression

Iris Deitch[1], Tilda Barliya[3], Omer Bialer[1,3], Yael Nisgav[3], Mor Dachbash[3],Dov Weinberger[1,2,3], Tami Livnat[1,2,3,4]

*[1]Department of Ophthalmology, Rabin Medical Center, PetachTikva, Israel, [2]Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel, [3]Laboratory of Eye Research, Felsenstein Medical Research Center, Rabin Medical Center, PetachTikva, Israel, [4]The Israeli National Hemophilia Center, Sheba Medical Center, Tel Hashomer, Israel*

**Purpose:** Choroidal neovascularization (CNV) is the leading cause of severe vision loss in various ocular diseases such as age-related macular degeneration (AMD), angioid streaks and high myopia. A rupture of Bruch's membrane which follows by a damage to the blood retinal barrier (BRB) induces CNV formation and progression. Activated protein C (APC) is a plasma serine protease with systemic anticoagulant, anti-inflammatory and antiapoptotic activity. Our aim is to explore the barrier protective effect of APC treatment in both an in vitro and a laser-induced CNV animal models.

**Methods:** In vitro model: human Retinal pigment epithelial cells (ARPE-19) were cultured for a month to achieve definite polarity properties. APC-induced cell permeability was evaluated based on spectrophotometric monitoring of the transport across the cell layer of labeled dextran. Cellular localization of the tight junction protein Zonula Occludens 1 (ZO-1) was studied using immunofluorescence staining with anti-ZO1 antibody. In vivo model: CNV was induced by indirect diode laser photocoagulation on male C57BL/6J mice. Immediately following injury mice were injected intravitreally with 1µl APC at 1µg/animal or 1µl bevacizumab at 25 µg/animal. CNV area of flat choroid was determined by using anti CD31 antibody immunofluorescence staining on days 5 and 14 post laser injury. CNV area was evaluated by image J.

**Results:** In vitro: APC induced translocation of ZO-1 protein to the ARPE-19 cell membrane and reduced RPE permeability as compared to untreated cells. In vivo: APC treatment dramatically reduced CNV area. The CNV area on days 5 and 14 post laser application, as indicated by CD31 staining was 34% and 50%, respectively as compared to untreated control eyes. APC effect was to a similar extant as compared to bevacizumab outcome.

**Conclusions:** APC was found to reduce cell permeability in RPE cells, and change the re-organization of ZO1 into a membranal position. This is the first study to show that intravitreal injection of APC lead to a significant reduction in CNV area compared to the treatment of choice, bevacizumab. This study offers an innovative approach that may lead to the development of novel therapeutic strategies targeting CNV. APC should be considered as a good candidate for such strategies though future studies are warrant to fully explore its beneficial potential.

# Suppression of Laser-induced Choroidal Neovascularization Using Promiscuous Cytokine Antagonist

Shira-Hagbi-Levi[1], Michal Abraham[2], Liran Tiosano[1], Batya Rinsky[1], Michelle Grunin[1], Amnon Peled[2,3], Itay Chowers[1]

*[1]Department of Ophthalmology, Hadassah-Hebrew University Medical Center,[2]Goldyne Savad Institute of Gene Therapy, Hebrew University Hospital, Jerusalem, 91120 P.O.B 12000, Israel, [3]Biokine Therapeutics Ltd., Science Park, Ness Ziona, Israel.*

**Purpose:** Monocytes/macrophages were suggested to exert a proangiogenic effect in the context of neovascular age-related macular degeneration (nvAMD). Several cytokines in addition to vascular endothelial growth factor may potentially mediate such an effect. We aim to explore simultaneous perturbation of several cytokines as a potential therapeutic strategy for choroidal neovascularization (CNV).

**Methods:** Laser injury induced CNV was generated in Long-Evans rats (n=15). BKT130, a promiscuous antagonist of several cytokines including MCP1, MIP-3A, IP-10, Mig, I-TAC, TARK and RANTES, was delivered via intraperitoneal (IP) injection (4 mg) at the day of laser injury and five days later. Control rats received IP PBS. CNV was evaluated via fluorescein angiogram (FA) that was performed 10 days following the laser injury. Retina flatmounts immunostained for CD11b served to quantify subretinal macrophages, and retinal pigment epithelium-choroid flatmounts stained with isolectin were utilized to quantify CNV.

**Results:** Masked quantification of isolectin staining showed a mean suppression of CNV area of 26% (p=0.0058; Mann Whitney test). CD11b immunostaining showed a mean of 23% reduction of subretinal macrophages number following BKT130 therapy (p=0.0011; Mann Whitney test). Systemic or ocular side effects were not identified.

**Conclusions:** These data further supports the putative pathogenic role of macrophages and their cytokine products in CNV growth. It also suggests that targeting multiple cytokines simultaneously using a single compound (polypharmacology) may potentially serve as a therapeutic strategy for the disease.

## TNF-α induced ROS accumulation is mediated by TAK1

Zeev Dvashi1 ,Orit Adir1 and Ayala Pollack1

*1Kaplan Medical Center, Rehovot, affiliated with Hadassah-Hebrew University of Jerusalem, Rehovot.*

**Purpose:** Oxidative damage has a key role in retinal pathologies such as age related macular degeneration (AMD). Accumulation of reactive oxidative species (ROS) in the retinal pigment epithelial (RPE) cells may affect the viability of the cells and may eventually lead to cell death and atrophy. It is known that accumulation of ROS alters RPE cells morphology and hemostasis, thus can contribute to the development and progression of AMD. Several proteins were suggested to be involved in the generation and the accumulation of ROS in RPE cell. Still, the mechanism underlying this phenomenon needs to be studied. The research presented hereby aims to investigate the role of tumor necrosis factor-α (TNF-α) and transforming growth factor β activated kinase (TAK1) in the process of generation and the accumulation of ROS.

**Methods:** ARPE-19 cells were treated with TNF-α (20ng/ml) as well as TAK1 specific inhibitor (5Z-7 oxozeaenol 1μM). p65 activation was determined by western blot analysis. Cells were washed with serum free medium, treated with 2',7'-dichlorodihydrofluorescein diacetate (H2DCFDA) DCFDA, trypsinized and subjected to flow cytometry (FACS).

**Results:** Stimulation of RPE cells with TNF-α resulted in an increase of ROS generation and accumulation and finally cells death demonstrated by cell proliferation assays. In contrast, employing TAK1 inhibitor prior to TNF-α stimulation reduced the generation and accumulation of ROS seen by DCFDA staining.

**Conclusions:** This study demonstrates that TNF-α is involved in the generation of ROS in RPE cells and that this response is mediated by TAK1. RPE cells which were treated with TNF-α display abnormal morphology and increased accumulation of ROS, phenotypes similar to those associated with dry AMD. This study demonstrates for the first time the link between TNF-α and oxidative damage in RPE cells via TAK1 activation. The data presented hereby suggest a potential novel approach to prevent RPE cells death, thus may halt the progression of dry AMD.

## Interim Results of the Aflibercept as a Second Line Therapy for Neovascular Age Related Macular Degeneration in Israel (ASLI) study

Liran Tiosano[1], Michaela Goldstein[2], Ori Segal[3], Ayala Polack[4], Rita Erlich[5], Itay Chowers[1], Itamar Klemperer[6], Yoreh Barak[7], Nurit Mathalone[8]

*1Hadassah-Hebrew University Medical Center, 2 Tel Aviv Medical Center, 3 Meir Medical Center, 4 Kaplan Medical Center, 5 Rabin Medical Center, 6 Soroka Medical Center, 7 Rambam Medical Center, 8 Carmel Medical Center*

**Purpose:** To evaluate the use of Aflibecept in patients with neovascular age-related macular degeneration (nvAMD) showing partial or lack of response for initial therapy with bevacizumab.

**Methods:** The ASLI study is a prospective, multi-center, open-label, clinical trial. Three monthly intravitreal aflibercept (2mg) injections were administered followed by two bi-monthly injections (weeks 16 and 24), and a final examination at week 28th. According to the investigator decision, additional injection was given at week 20. All patients underwent a complete ophthalmic examination, including measurement of Early Treatment Diabetic Retinopathy Study (ETDRS) best-corrected visual acuity (BCVA), and spectral-domain optical coherence tomography (SD-OCT) at every visit**.** Baseline and final fluorescein angiography were performed. Change in the central sub-field macular thickness (CST) from baseline to week 28 on OCT was considered the primary end-point. Secondary end-points included the mean change in BCVA, and structural changes in OCT and FA.

**Results:** After 6 months from initiation of the study, 34 patients were recruited with mean±SD age of 76±8 years. Ten (29%) patients completed the study. The mean±SD number of bevacizumab intravitreal injections prior to enrollment to the study was 5.2±2.3 (range 3-9). After 2 loading injections the CST improved significantly and reduced from mean±SD of 465±137 microns at baseline to 358±114 microns at week 8 (n=20, p=0.04; paired T-Test). Mean BCVA for the 10 patients who completed the study improved from 0.43±0.3 LogMAR at baseline to 0.34±0.1 LogMAR at week 28 (p=0.01, paired T-Test).

**Conclusions:** Interim results from the ASLI study demonstrate decrease in CST after the first 2 aflibercept injections, and improved BCVA at the end of the study. These preliminary results suggest that intravitreal aflibercept may be effective in nvAMD eyes with lack or partial response to bevacizumab treatment. Further follow-up on the entire study cohort is required to validate the findings.

## Structure-Function Correlation Demonstrated by Imaging and Microperimetry in Dry AMD Patients with Geographic Atrophy

Shelly Stika, Boris Rosin, Alexey Obolensky, Eyal Banin and Devora Marks Ohana

*CRMD, Hadassah-Hebrew University Medical Center*

**Purpose:** To examine correlation between retinal structure and function in areas of Geographic Atrophy (GA) due to dry AMD using different imaging modalities and microperimetery (MP).

**Methods:** 15 dry AMD patients with extensive Geographic Atrophy in both eyes were recruited. Retinal structure was evaluated by OCT, Auto fluorescence, InfraRed and Multicolor imaging at six month intervals. At the same time points macular microperimetry was performed using the MAIA system (CenterVue, Padova, Italy). Analysis of GA size and expansion over time was correlated with visual sensitivity at specific retinal locations as measured by MP.

**Results:** GA area showed expansion over time at a mean rate of xx±yy mm2 per year. MP showed absolute scotomas centered over the areas of GA, surrounded by a transition area of reduced light sensitivity. In patients with over one year of follow-up, expansion of the absolute scotoma correlated with GA progression, showing loss of vision in regions of transition that previously had reduced light sensitivity. The progress of transition zones to complete atrophy could also be demonstrated on OCT.

**Conclusions:** There is close correlation between retinal structure and function in areas of GA associated with dry AMD.

## Indentation gonioscopy during laser Iridotomy, a new concept and lens for treating angle-closure glaucoma

Eytan Z. Blumenthal

*Department of Ophthalmology, Rambam Medical Center, Haifa.*

**Purpose:** To describe a concept and lens, used for widening the angle during routine Iridotomy procedures, thus distancing the peripheral iris from the overlying cornea.

**Methods:** Iridotomy is a common procedure performed in cases of narrow angles as well as angle-closure glaucoma. A novel lens design was developed, aimed at improving the visualization and safety of this laser procedure. Indentation-gonioscopy-iridotomy is thus enabled for the first time, owing to the smaller contact area, the shallower contact surface curvature, and the unique optical design of the lens.

**Results:** A new Iridotomy lens, the 'Volk Blumenthal Iridotomy lens', recently launched, provides several advantages stemming from the ability to widen the angle during the laser procedure, distancing the area of treatment from the overlying cornea.

**Conclusions:** The overall design provides a tighter laser spot, enabling less "collateral damage" to adjacent iris tissue. In addition it distances the area of "laser explosion" from the overlying endothelium and provides easier tissue penetration.

## Non Pigmented Ciliary Epithelium derived exosomes and their role within the drainage system as a pharmacological intervention target for glaucoma

Natalie Karpenko, Sofia Schreiber-Avissar and Elie Beit-Yannai,

*Ben-Gurion University of the Negev, Beer-Sheva, Israel*

**Purpose:** Our goal is to provide insights into the role of Non Pigmented Ciliary Epithelium (NPCE) derived exosomes in the ocular drainage system. In addition, to identify possible new interfering sites for Primary Open Angle Glaucoma treatment within the ocular drainage system based on intervention in the signaling pathways regulated by NPCE derived exosomes.

**Methods:** Exosomes were purified from cell culture medium of NPCE cell line by ultracentrifugation. The vesicular nature and size of the purified exosomes were confirmed by electron microscopy (EM) and sucrose density gradient centrifugation. Western immunoblotting was performed to assess changes in key mediators of relevant signaling pathway. Confocal microscopy was used for intracellular visualization of labeled exosomes. The exosomes proteomes were examined using two-dimensional polyacrylamide gel electrophoresis (2DE PAGE) and LC-MS/MS approach.

**Results:** The NPCE cell derived exosomes were round and mostly 100±10 nm in diameter as measured by EM. The exosomal marker proteins TSG 101 and Alix were detected in the exosomes preparation. The range of density was between 1.05 g/ml and 1.23 g/ml. The results of confocal microscopy indicated that exosomes were internalized into resting human trabecular meshwork (TM) cells through an unknown pathway and transported to the perinuclear region. Exosome uptake was found to be specific and time dependent. γ-catenin, a close homolog of β-catenin that shares with β-catenin common protein partners and can fulfill some of its functions, was identified using 2DE-MS approach. Preliminary data indicating the involvement of signal transduction regulators will be presented.

**Conclusions:** Our data demonstrate that NPCE cells release exosome-like vesicles and that these structures can be transferred into TM cells, suggesting a potential role in regulating intraocular pressure. Findings on the involvement of NPCE cell derived exosomes in the drainage system of the eye will promote a better biological understanding, diagnostic applications and advance future glaucoma management.

## TNF-α and α2M proteins in the aqueous humor of glaucoma patients

Michal Schaap-Fogler[1], Pablo F. Barcelona[2], Uri H. Saragovi[2], Maya Eiger-Moscovich[1], Karin Mimouni[1,3], Michal Kramer[1,3]

*1Department of Ophthalmology, Rabin Medical Center, Petach Tiqva, 2Lady Davis Institute-Jewish General Hospital, McGill University, Montreal, 3Sackler School of Medicine, Tel Aviv University,Tel Aviv*

**Purpose:** The proteins α2M and TNF-α, are known mediators of the apoptotic processes in ganglion cells. The purpose of our work was to study their involvement in the pathogenesis of primary open-angle glaucoma (POAG) and pseudo-exfoliation syndrome (PXF) by measuring their levels in the aqueous humor of these patients.

**Methods:** Samples from the aqueous humor were collected from patients during standard cataract surgery. Levels of α2M and TNF-α were studied in the samples using standardized versus human immunoglobulin as loading control. Ten micrograms of total aqueous humor protein were combined with 2X SDS loading buffer and transferred to nitrocellulose membranes. The α2M protein was detected using rabbit polyclonal antibodies against α2M and TNFα protein was detected using rabbit polyclonal antibodies against TNF-α. Goat anti-rabbit antibodies conjugated with horseradish peroxidase were used as secondary reagents. For digital quantification, membranes were scanned and analyzed using ImageJ software. Data were subjected to ANOVA and Dunnett's Post Hoc Contrasts.

**Results:** Overall 27 samples were collected, with 7 samples collected from POAG patients, 8 from PXF patients (only one with glaucoma) and 12 controls. In patients with POAG, both α2M levels and TNF-α levels were significantly elevated compared to control eyes (0.93±0.28 versus 0.089±0.087, and 0.77±0.32 versus 0.058±0.037, respectively ($p < 0.001$)). Mean levels of proteins in samples taken from patients with PXF were not significantly different from control levels, (0.13±0.19 for α2M and 0.42±0.33 for TNF-α levels).

**Conclusions:** This work further documents a potential novel mechanism of the apoptotic process in ganglion cells and a potential biomarker for glaucoma, in contrast to PXF alone. If verified in larger studies, these proteins may further serve as a therapeutic target for glaucoma.

## Pressure vs. Flow characterization of the JET Glaucoma Filtration Device

Modi Naftali, Yakir Kushlin[1], Maya Levital[1]

*1Hanita Lenses, 2Technion Biofluids Laboratory*

**Purpose:** Evaluate the Pressure vs. Flow characteristics of the JET Glaucoma shunt. The JET Glaucoma Filtration Device is intended to reduce intraocular pressure in glaucoma patients by creating a 170 micron filtration bypass from the anterior chamber to a scleral bleb. The device is manufactured from a hydrophilic co-polymer; implanted in a Micro Incision Glaucoma Surgery (MIGS) with its hook and bullet inside the anterior chamber, wings embedded inside a scleral pocket.

**Methods:** Porcine cadaver eyes were obtained from Lahav CRO, Israel. The eyes were harvested with intact conjunctiva at the same day of the experiment. The perfusion system incorporated a syringe pump (Fusion 400 Touch; Chemyx, Stafford, TX, USA). Pressure was monitored via pressure transducer (Disposable Pressure Transducer, Elcam Medical; Israel) connected to a two channel chart recorder (ETH-256; iWorx Systems, Dover, NH, USA). After implantation of the device, the eye was injected with saline and connected with a 21G needle to the pressure transducer and syringe pump. Initial flow of 7.5 micro liters per minute was supplied to the eye for a period of 20-15 minutes. Subsequently, the flow was reduced to 2.5 micro liters per minute and the pressure was monitored until a steady state was obtained for a period of 30-40 minutes.

**Results:** The first device was implanted under a scleral pocket with no penetration to the conjunctiva. Pressure was approaching 11mmHg, no bleb observed. It was decided by the surgeon to reopen the scleral pocket and create a penetration to the conjunctiva; average steady state pressure of 6.48mmHg was observed. The second eye was implanted with minor penetration to the conjunctiva, average steady state pressure of 10.17mmHg was observed. A low, diffuse bleb was seen. The third eye was implanted with penetration to the conjunctiva, average steady state pressure of 5.82mmHg was observed. A bleb was seen at the site of penetration to the conjunctiva.

**Conclusions:** The JET Glaucoma filtration device was successfully implanted in porcine cadaver eyes and was seen to reduce pressure in the range between 5.82 to 10.17 mmHg depending on the degree of penetration to the conjunctiva.

## The effect of nocturnal CPAP therapy on the intraocular pressure of patients with sleep apnea syndrome

Yuval Cohen[a], Eyal Ben-Mair[b], Eyal Rosenzweig[b], Dalia Shechter-Amir[b], Arieh S Solomon[a]

[a] *Goldschleger Eye Research Institute, Tel Aviv University, 53621 Tel Hashomer, Israel.* [b] *The Institute for Fatigue and Sleep Medicine, Chaim Sheba Medical Center, 53621 Tel Hashomer, Israel.*

**Purpose:** Few studies have documented that nocturnal continuous positive airway pressure (CPAP) therapy is associated with an increase in intraocular pressure (IOP) in patients with severe obstructive sleep apnea syndrome (OSAS). We re-examined the effect of CPAP therapy on the IOP of OSAS patients.

**Methods:** The IOP of two different groups of newly diagnosed OSAS patients was compared at their first sleep lab exam without CPAP treatment (non-CPAP treated group; n=20) and at their second sleep lab exam with CPAP treatment (CPAP treated group; n=31). The sleep lab exam (sleep period: from 11:00 pm until 6:00 am) included IOP measurements, a complete ophthalmologic exam and nocturnal hemodynamic recordings. The IOP was measured serially using rebound tonometer (IOP; ICARE® PRO) performed while in sitting and supine positions before, during and after the sleep period. We compared the difference in IOP of CPAP and non-CPAP groups.

**Results:** The mean IOP of the non-CPAP and CPAP groups measured in sitting position before the sleep period was 14.14±2.41 mmHg and 13.62±2.07 mmHg, respectively (p=0.48). Assuming a supine position for 1 minute, significantly increased the IOP by 2.18±2.46 mmHg and 1.91±2.16 mmHg for both the non-CPAP and CPAP groups (Paired t-test; p=0.027, p=0.034, respectively), but this IOP rise showed no difference between the two groups. The IOP increased significantly further after 7 hours of sleep in the supine position, and the mean IOP of the non-CPAP and CPAP groups was 19.41±4.11 mmHg and 19.69±5.61 mmHg, respectively (independent t-test p=0.76). The rise in IOP for both groups was not correlated with any hemodynamic parameters.

**Conclusions:** OSAS patients have a significant rise in IOP during the sleep period when comparing measurements before and after the sleep period; however, CPAP therapy did not affect the measurements of IOP. In our study, the rise in nocturnal IOP in OSAS patients is not related to changes in hemodynamic parameters.

## Sildenafil does not prevent retinal damage in a rat model of acute ocular hypertension

Raaya Ezra-Elia[1], Germana Alegro da Silva[2], Diogo Sousa Zanoni[3], Renée Laufer-Amorim[3], José Luiz Laus[2], Ron Ofri[1].

*[1]Koret School of Veterinary Medicine, The Hebrew University of Jerusalem, Rehovot, Israel [2]Ophthalmology Unit, Department of Clinics and Surgery, College of Agronomical and Veterinarian Sciences, São Paulo State University, Jaboticabal, São Paulo, Brazi, I[3]Department of Veterinary Pathology, Department of Veterinary Clinic, Faculty of Veterinary Medicine and Animal Science, College of Agronomical and Veterinarian Sciences, São Paulo State University, Botucatu, São Paulo, Brazil*

**Purpose:** Mounting evidence suggests that reduced blood flow in the inner retina and optic nerve might play a role in the pathogenesis of glaucomatous neuropathy. Nitric oxide (NO) is known to increase blood flow by decreasing vascular resistance in ocular circulation. Consequently, impaired NO synthesis and release are considered potential pathogenic factors in glaucomatous neuropathy of some patients. We therefore hypothesized that treatment with sildenafil, a phosphodiesterase inhibitor which prolongs the effect of NO, may be neuroprotective in glaucomatous neuropathy.

**Methods:** Anterior chamber cannulation was performed to induce acute intraocular pressure (IOP) elevation for 60 minutes in one randomly- chosen eye of 38 Lewis rats. Twenty rats received sildenafil (0.5 mg/kg) or saline intraperitoneally (IP) for 7 days. Eighteen rats received double dose of sildenafil (1 mg/kg) or saline IP for 18 days. Treatment began three days before IOP elevation in both experimental groups to evaluate prophylactic effect. Full-field electroretinography (ERG) recordings were conducted using both dark- and light-adapted protocols. Seven days prior to IOP elevation RGC were retrogradely labeled by bilateral stereotaxic injection of fluorogold and counted following retinal flatmount preparation.

**Results:** Mean ±SE IOP of cannulated eyes was 70.1 ±1.5 mmHg. ERG confirmed significant functional deficits, and RGC counts were significantly lower, in hypertensives eye compared with fellow un-cannulated eyes of saline treated animals, thus validating the cannulation model. No significant differences in ERG or RGC counts were observed between sildenafil- and saline-treated animals in either experimental group.

**Conclusions:** Both RGC counts and ERG failed to show any (prophylactic or therapeutic) neuroprotective effect of sildenafil in a rat acute ocular hypertension model, implying that treatment may not be beneficial for glaucoma patients.

This study was supported by the Joseph Alexander Foundation.

## Accommodative add-on optical implant – a novel concept and preliminary studies

Ehud I. Assia [1, 2] , Yokrat Ton [1,2]

*1. Department of Ophthalmology, Meir Medical Center, Kfar-Saba), 2. Sackler School of Medicine, Tel-Aviv University, Ramat Aviv*

**Purpose:** To present a novel concept of a sulcus fixated optical element to restore natural accommodation.

**Methods:** The optical element is positioned in the ciliary sulcus of eyes following in-the-bag implantation of conventional IOL targeted to emmetropia. The ciliary muscle is utilized to change the anterior curvature of the optical system to provide the additional optical power needed for near vision. Ex-vivo laboratory studies in animal and human eyes were done to study feasibility of implantation of the accommodative element and determined the desired shape and configuration of the device.

**Results:** Experimental studies were done on post-mortem eyes of pigs, rabbits and human eyes and a preliminary live study was done on rabbit eyes. Prototypes of the optical system were implanted in pseudophakic eyes through a relatively small incision (3.5 mm) and positioned in the sulcus in direct contact with the ciliary muscle. UBM studies helped determine lens dimension and design.

**Conclusions:** Preliminary studies suggest that the concept of an add-on sulcus fixated optical system to restore natural accommodation is feasible and may have the potential for clinical use.

## Comparison of three designs of PCO preventing ring

Lee Slutzky[1], Guy Kleinmann[2]

*1Hebrew University of Jerusalem 2Kaplan Medical Center, Rehovot, Israel*

**Purpose:** To investigate three designs of open capsule ring (OCR) with different size and density of side wall apertures on PCO and Soemmering's ring formation

**Methods:** 24 NZW rabbits' eyes were divided to 3 groups. 3 different OCRs were implanted into the capsular bag after crystalline lens evacuation. Group A (n=8): 190 degrees of large side wall apertures, group B (n=9): 90 degrees of small side wall apertures, and group C (n=7): 175 degrees of small side wall apertures. The same intraocular lens was then implanted into the OCR. A weekly slit lamp exam was performed for the 6 weeks of the study duration. After 6 weeks the rabbits were sacrificed; the eyes were enucleated and fixated and then evaluated using the Miyake-Apple view and histology.

**Results:** Similar low levels of PCO and Soemmering's ring formation were found in all the study groups. Six weeks slit lamp PCO level were: A:0.4±0.7, B:0.8±0.8, C:0.5±0.8; p=0.5, Histology PCO level were: A:0±0, B:0.7±0.1, C:0.4±1.1; p=0.25, Soemmering's Ring area(%): A:24±14, B:23±12, C:20±14; p=0.85. Area of Soemmering's ring protrusion over the OCR (%): A:12±10, B:10±9, C:9±9; p=0.87.

**Conclusions:** The three OCR designs showed similar PCO and Sommering's ring prevention. The difference in size and density of the side wall apertures was not proven to influence results.

## Long-term evaluation of hyperopic laser refractive surgery

Lily Karmona[1]; Tzahi sela [2]; Oz franco[2]; Avi shoshani[2]; Gur Mitzer[2]; Igor Kaiserman[2,3]

*1 Department of ophthalmology, Wolfson Medical center, Holon, Israel, 2 Care-Vision Laser center Institute, Tel-aviv, Israel, 3 Department of ophthalmology, Barzilai Medical center, Ashkelon, Israel*

**Purpose:** To evaluate the efficacy, safety, and predictability of hyperopic laser in situ keratomileusis (H-LASIK) and hyperopic Photorefractive keratectomy (H-PRK).

**Methods:** In this retrospective study the records of consecutive patients who had LASIK and PRK for hyperopia during 2006-2012 were reviewed . For analysis, the patients were divided into 5 groups based on preoperative hyperopia: low hyperopia ( 0-2.00 D), low-moderate hyperopia (≥+2.00 to 4.00 D), moderate hyperopia ( +4.00-6.00 D), high hyperopia ( +6.00-7.00 D ) and very high hyperopia (≥+7.00 D).

**Results:** 1856 consecutive eyes of 930 patients received Hyperopic refractive surgery in the years 2006-2012. 1367 eyes received H-LASIK and 489 eyes had H-PRK. 683 eyes had a follow-up of at least 12 months. Thirty three eyes had a follow-up period of 6-7 years and 25 eyes had 7-8 years follow-up. The mean MSE refraction in the 1856 eyes was +1.94 ± 1.77 D preoperatively and -0.08 ± 0.9 D (range +5.50 to −3.6 D) postoperatively . At the final examination, 1267 eyes (68.3%) had a mean MSE refraction within ±0.5 D of emmetropia and 1484 eyes (80.0%) and 1780 eyes (95.9%) had a mean MSE within ±1.00 and ±2.00 D, respectively. Predictability in the low hyperopia group and the moderate hyperopia group ( until 6.0 Diopers of hyperopia) was significantly higher (P<.0001) than in the high hyperopia group (>6.0 Diopters of hyperopia).

Preoperatively, the BCVA was 20/20 or better in 1103 eyes (59.4%) and 20/40 or better in 1846 eyes (99.46%). At the final examination, it was 20/20 or better in 850 eyes (45.8%) and 20/40 or better in 1728 eyes (93.1%). At the final examination, the UCVA was 20/20 or better in 561 eyes (30.2%) and 20/40 or better in 1717 eyes (92.5%). Up to Pre-operative MSE of 6.0 Diopters the Efficacy Index is maintained at an average of 0.83. As the Pre-operative MSE gets higher, the Efficacy Index drops down. Untill Pre-operative MSE of 7.0 diopters, the safety Index doesn't change with regards to the Pre-operative MSE and is maintained at an average of 0.95. When the pre-operative MSE is 7.00 D of hyperopia or higher, the Safety Index climbes to 1.07.

**Conclusions:** Laser in situ keratomileusis was a safe, effective, and predictable procedure for hyperopia up to +6.0 D and less predictable for higher hyperopia.

## Factors predicting the need for retreatment after refractive surgery

Michael Mimouni MD[1]†, Igor Vainer BScMed[1]†, Yinon Shapira MD[1], Shmuel Levartovsky MD[2], Tzahi Sela[3], Gur Munzer[3], Igor Kaiserman MD, MSc, MHA[2,3]

*† Both authors contributed equally to this paper, [1]Department of Ophthalmology, Rambam Health Care Campus, Haifa, Israel, [2]Department of Ophthalmology, Barzilai Medical Center, Ashkelon and the Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheba, Israel, [3]Care-Vision Laser Centers, Tel-Aviv, Israel.*

**Purpose:** To identify the potential risk factors that increase the likelihood of requiring retreatment following refractive surgery.

**Methods:** A retrospective study of patients who underwent laser in situ keratomileusis (LASIK) or photorefractive keratectomy (PRK) between January 2005 and December 2012 at the Care-Vision Laser Centers, Tel-Aviv, Israel. Patients were divided into two groups according to whether or not they underwent additional refractive surgery (retreatment) during the study period.

**Results:** Overall, 41,504 eyes of 21,313 patients were included in the final analysis of this study. Throughout the study period there was a significant reduction in the corrected annual retreatment rates with a decline from 8.1% for primary surgeries done in 2005 to 0.87% for surgery done in 2012 (Quadratic R2=0.95, P=0.01). The retreatment group had significantly higher preoperative age, maximum keratometric power, sphere, cylinder, and best corrected visual acuity. They were more likely to have preoperative hyperopia and have been treated with PRK in higher humidity conditions and lower temperature and higher ablation depths. Significant differences in retreatment rates were found between surgeons ranging from 0.48% to 3.14% (P<0.0001). Multiple logistic regression analysis demonstrated that age, astigmatism, hyperopia, temperature and surgeon's experience all significantly predicted the need for retreatment.

**Conclusions:** Several factors significantly predict the need for refractive retreatment such as preoperative age, astigmatism, hyperopia, operating room temperature and surgeon. These factors may be incorporated into nomograms in order to reduce future retreatment rates.

## Comparison of three epithelial removal techniques in Photorefractive Keratectomy: mechanical, alcohol-assisted, and transepithelial laser

Yinon Shapira1, Michael Mimouni1, Shmuel Levartovsky2, David Varssano3, Igor Kaiserman2

*1 Department of Ophthalmology, Rambam Health Care Campus, Haifa, Israel, 2 Department of Ophthalmology, Barzilai Medical Center, Ashkelon and the Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheba, Israel, 3Department of Ophthalmology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, affiliated to the Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel*

**Purpose:** To compare visual and refractive results following Photorefractive Keratectomy (PRK) using three different epithelial removal techniques.

**Methods:** The medical files of consecutive eyes with myopia and myopic astigmatism that underwent mechanical PRK, alcohol-assisted PRK or transepithelial (t)PRK between May 2000 and December 2013 at Care-Vision Laser Centers, Tel-Aviv, Israel, were reviewed.

**Results:** Overall, 14,489 eyes were included. tPRK technique resulted in a significantly better visual Efficacy Index ($p<0.01$) and Safety Index ($p<0.0001$) up to 1 month postoperative, while alcohol-assisted PRK was superior in Efficacy Index ($p<0.01$) and Safety Index ($p<0.05$) at >3 months postoperative. At long follow up (>1 year), tPRK exhibited inferiority in terms of Efficacy Index outcome that corresponded to a mean uncorrected visual acuity of approximately 1 Snellen line lower than the other groups ($p<0.0001$). While all three techniques exhibited a clinically acceptable Safety Index, at all times mechanical PRK technique was significantly inferior to the other groups ($p<0.01$). At short term follow up a hyperopic shift was evident in the alcohol-assisted PRK and mechanical PRK groups, while at longer follow up times a significant and progressive myopic regression was evident in the tPRK group ($p<0.0001$).

**Conclusions:** Significant differences were detected in the visual outcomes as well as in the refractive results of these epithelial removal techniques. These trends depend on the time that elapsed since treatment.

## Refractive Surgery: Safety, efficacy, predictability and clinical outcomes

Assaf Gershoni, Ofer Daphna, Michael Haims, Andrew Fink, Adi Nahum, Uri Marmur, Michael Mimouni, Irit Bahar

*Assuta Optic Laser Center, Tel Aviv*

**Purpose:** The purpose of the study is to analyze the safety, efficacy, predictability and clinical outcome of corrective eye surgery, using one of three Methods: Photorefractive Keratectomy (PRK), Transepithelial Photorefractive Keratectomy (TRANS PRK) and Ziemer-Laser In Situ Keratomileusis (Z-LASIK) for the correction of myopia, hyperopia and astigmatism.

**Methods:** We retrospectively reviewed the medical records of all patients who underwent corrective eye surgery in our institution, between 1/1/2013 and 31/10/2014. The collected data includes age, sex, operating physician, follow-up time, patient's refractive status and visual acuity prior to surgery and throughout the available follow-up, operative data, corneal thickness and post surgery complications.

**Results:** Of 2117 eyes that met the inclusion criteria 2065 eyes were myopic and 52 were hyperopic. The efficacy index in the myopic group was 0.98 ± 0.12 and 0.92 ± 0.17 in the hyperopic group (P=.028). The safety index in the myopic group was 0.98 ± 0.10 and in the hyperopic group 0.95 ± 0.11 (P=.029). The final spherical equivalence was -0.03 ± 0.01 and 0.22 ± 0.69, respectively (P=.014).

Of 2065 myopic eyes that met the inclusion criteria, 1560 had PRK or TRANS PRK and 505 had Z-LASIK. The efficacy index in the PRK group was 0.97 ± 0.12 and 0.98 ± 0.12 in the Z-LASIK group (P=.051). The safety index in the PRK group was 0.98 ± 0.10 and in the Z-LASIK group 0.99 ± 0.10 (P=.013). The final spherical equivalence was 0.01 ± 0.68 and -0.15 ± 0.50, respectively (P<0.000).

**Conclusions:** Our vast experience and enormous database of patients have allowed us to demonstrate that laser refractive surgery using the SCHWIND AMARIS 500E and Ziemer LDV Femtosecond Laser machines are safe, effective, and predictable for treatment of ammetropia.

## Rapid tracking of threat during avoidance, by body and eye motion

Tidhar Lev-Ari[1], Avichai Lustig[2], Hadas Ketter Katz[2] & Gadi Katzir[1,3]

*1. Department of Evolutionary and Environmental Biology, University of Haifa, Israel. 2. Department of Neurobiology, University of Haifa, Haifa, Israel. 3. Department of Marine Biology, University of Haifa, Israel.*

**Purpose:** A chameleon on a perch will hide from a moving threat by performing a smooth counter-rotation of its body, in synchrony with the threat's change in position, while compressing its body bilaterally. The response is visually guided, innate and functions to increase concealment. Here we ask: (i) How precise is the avoidance response in relation to the threat? (ii) Do the eyes perform equally in tracking the threat?

**Methods:** To determine the precision of counter-rotation and eye use, we analyzed the motion patterns of the head and eyes during avoidance from. For three angular velocities of a horizontally moving threat (36°, 60°, 90°/sec) we measured the angle α between the sagittal plane of the chameleon's head and the threat, and angle β between the center of the head, the pole and the threat. We further measured gaze direction of each eye.

**Results:** The chameleons showed an extremely rapid and precise tracking of the threat, reaching > 90 deg/sec. The threat is tracked virtually exclusively by the "Leading eye" (i.e. the eye towards which the threat approached) while the contralateral eye scans the environment.

**Conclusions:** The capacity of chameleons to maintain a highly precise position relative to a moving stimulus is, to our knowledge, the first reported for a non - flying terrestrial vertebrate. The results highlight the capacity of ectotherms to "share attention" under highly independent eye movement and low inter-tectal connectivity.

# Binocular dichoptic video content treatment for amblyopia – pilot study

Chaim Stolovitch, MD[1]

*Tel Aviv Medical Center, Pediatric Ophthalmology Unit, Department of Ophthalmology*[1]

**Purpose:** Our objective was to assess a novel device for treatment of Amblyopia, using dynamically altered dichoptic presentation of video contents without patching.

**Methods:** We used a dedicated software that alter dynamically video content presented dichoptically binocularly, using Reviview™ video goggles, in which reduced contrast of the video content is presented to the good eye compared with enhanced contrast video content to the amblyopic eye. Eighteen subjects, age 4-8 years, diagnosed with refractive or strabismic amblyopia, with VA worse than 6/15 (20/50) in the amblyopic eye were enrolled. All the children were reluctant for further patching or using atropine and their compliance was bad. All used the device for 30-60 min daily while watching animated TV shows at home without patching. Visual Acuity and Randot stereoacuity were assessed at baseline and after 4,8 and 12 weeks of treatment.

**Results:** 16 patients completed 12 week of treatment. Two of our patients stopped treatment after 4 weeks. At the 4-week visit, visual acuity improved significantly (mean 0.1828 ± 0.1443 logMAR) in the amblyopic eye, (T value=5.4175,P=0.001), at 8 weeks visit (N=16,mean 0.2475 ± 0.1267 logMAR) (Anova=F value=7.373, P=0.0017) and at 12 weeks (N=16,mean 0.2681 ± 0.1645 logMAR) (Anova=F value=6.61211,P=0.0066 from base line Visual Acuity.)

**Conclusions:** Our device and protocol of treatment achieved promising results at 4 weeks of treatment 0.1828 ± 0.1443 logMAR with continuous improvement towards the 12 week visit 0.2681 ± 0.1645 logMAR.

## Criteria for prescribing in cases of borderline refractive errors

Einat Shneor1, Bruce Evans2, Yael Fine1, Yehudit Ben Horin1, Liat Gantz1 and Ariela Gordon-Shaag1

*1. Dept. of Optometry, Hadassah Academic College, 2. Institute of Optometry, London; City University, London*

**Purpose:** Perhaps the most frequent decision that optometrists make is whether or not to correct a refractive error, whether it be with spectacles or contact lenses. This decision is generally an easy one if a large uncorrected anomaly is present, but becomes much more difficult in marginal or borderline cases. This study aimed at assessing prescribing decisions for borderline prescriptions by Israeli optometrists and whether working environment, gender and years of experience influence this.

**Methods:** A questionnaire was distributed via email and social media. The questionnaire included demographic information (age, gender), alongside professional information (years of experience, work environment and economic incentive). There were 12 questions regarding prescribing philosophies for different refractive errors, for various age ranges, and in the presence and absence of symptoms. Statistical significance was assessed with the Mann-Whitney test ($p<0.05$ considered significant) using Bonferroni correction where appropriate.

**Results:** Of the ~1000 optometrists in Israel, 124 participated in the survey. Respondents (66.1% female) averaged 7.8 ± 8.0 years of work experience, mostly worked in a private optical store (58.9%), were in salaried positions (85.5%), worked both as optometrists and in sales (44.4%), and without sales incentives (62.9%). Cumulative frequency distributions reveal that 75% of optometrists would prescribe glasses for symptomatic patients in the following situations:

Hyperopia: 1.50D for age 4-6years (y), 1.25D for age 6-10y, 1.00D for age 10-20y, 0.75D for age 20-40y; Myopia: 0.75D for age 6-10y, 0.50D for age 10-20y & 20-40y; Astigmatism 0.75D for age 6-10y, 10-20y and 20-40y; Presbyopia: 1.00D for age 40-50y, 1.50D for age 50-70y.

For all types of refractive errors there was a statistically significant shift to prescribe for lower powers in symptomatic vs. asymptomatic cases. No statistically significant differences were observed in prescribing behavior between practitioners who were male vs. female, with vs. without financial incentive and working in chain stores vs clinic.

**Conclusions:** Symptoms are the most important factor in influencing prescribing criteria. It is reassuring that the differences between different modes of practice were non-significant.

## Prevalence of V Pattern Exophoria in an Academic Institution-Based Optometric Clinic and a Community-Based Optometric Clinic

Gary Roth, Michel Millodot, Liat Gantz

*Hadassah Academic College*

**Purpose:** Dissociated phoria is a deviation from the orthovergence position that occurs when no fusionable contours are provided. In V Pattern exophoria (V-XP), the divergence is larger by at least 15 prism diopters at upgaze as opposed to downgaze. To the best of our knowledge, V-XP prevalence has not been reported, though a V pattern is common in approximately 64% of vertical incomitance strabismus cases. This study examined the prevalence of V-XP in academic vs. community based clinics in Jerusalem, Israel.

**Methods:** In this retrospective analysis, the files of patients from Hadassah Academic College's Optometry clinics (HAC) and the community-based Samuel Bliss Eye Clinic (SBE) in Jerusalem, were reviewed. All patients underwent a cover test at 35 cm without correction in three positions: primary (straight-ahead), upgaze and downgaze (each 45 degrees from primary), as well as a full subjective refraction (in + cylinder format). Data from the right eyes only, were analyzed as a group and separately for each clinic, and compared.

**Results:** A total of 590 patients (307 males, 283 females, mean age: 28.98 ± 16.20, range: 5-84) were analyzed: 231 HAC patients (95 male, mean age 32.60± 17.60) and 359 SCE patients (212 male, mean age 27.00± 18.38). The Spherical equivalent refractive error for the entire group was -2.25 ± 3.12 DS, for the males was -2.92 ± 3.17 DS and for the females, -1.52 ± 2.89 DS. 159 subjects (101 male, 58 female) presented with V-XP (26.95%). The prevalence was lower in HAC (20.34%) compared with SBE (31.20%). There was no statistically-significant correlation between V-XP and age, gender, or spherical nor cylindrical ametropia.

**Conclusions:** V-XP is present in approximately one-quarter of patients. This study emphasizes the importance of incorporating the cover test in three positions of gaze (u, primary, down) as part of the routine binocular examination. It is therefore recommended to perform the cover test as part of the routine binocular examination.

## Exploring non-visual Allocentric Navigation using Sensory Substitution

Shachar Maidenbaum[1,2], Reut Habusha[3], Amir Amedi[1,2,3,4]

*[1]ELSC, Hebrew University of Jerusalem, [2]IMRIC, Department of Medical Neurobiology, Hebrew University of Jerusalem, [3]Departmnt of Cognitive Science, Hebrew University of Jerusalem, [4]Institut de la Vision, UPMC Univ Paris 06,Sorbonne Universités,*

**Purpose:** When people who are blind navigate the lack of visual information causes a tendency to egocentric navigation, based mainly on nearby cues. Previous research has shown that this tendency is reflected in their basic spatial representation – while they are able to form spatial cognitive maps, the frame of reference used is mainly egocentric. Is this tendency due to a current-situation perceptual lack of the visual information, or has the lack of visual experience led to more fundamental changes?

**Methods:** We explored this with a Sensory Substitution Device (SSD) called the EyeMusic, which conveys whole-scene visual information via auditory cues, thus enabling recognition of visual landmarks. We used this device in a virtual adaptation of the classical Water-Maze in which users must learn a target's location based on visual landmarks, forcing them to rely upon an allocentric mapping of their environment.

**Results:** We show here that congenitally blind and sighted-blindfolded users are indeed able to perform this task, and do so in both 3rd person and 1st person paradigms in a manner replicating effects from the water maze literature such as the effect of environment rotation.

**Conclusions:** These results conform with the current amodal/multimodal view of spatial representation and suggest the commonly reported deficiency in allocentric navigation in the blind may be mainly perceptual to the point that when relevant information is offered they will indeed utilize such strategies.

## Standardizing functional tests for visual rehabilitation devices using virtual environments

Shachar Maidenbaum[1,2], Amir Amedi[1,2,3,4]

*[1]ELSC, Hebrew University of Jerusalem, [2]IMRIC, Department of Medical Neurobiology, Hebrew University of Jerusalem, [3]Departmnt of Cognitive Science, Hebrew University of Jerusalem, [4]Institut de la Vision, UPMC Univ Paris 06,Sorbonne Universités,*

**Purpose:** Many visual rehabilitation approaches are currently attempting to restore vision to the blind and severely visual impaired. These methods include among others bionic-eye prosthesis, gene therapy and sensory substitution. There is a growing need for standardized tests for these approaches, as traditional vision tests are often not sensitive enough in the range of extreme low vision, and focus more on specific visual parameters then on functional abilities such as object localization or orientation and mobility. Current suggestions for such standard tests require large, expensive and difficult to identically build setups, especially excluding environmental factors and the advanced compensatory skills of the users being tested. They also require a team to assemble and run. Thus there is currently no good way to comparatively explore the advantages and disadvantages of each, nor practical way to use them in the clinic to assess users abilities.

**Methods:** We suggest that the use of standardized virtual environments can be an important part of this testing toolkit, as they are easy to share, flexible, affordable, safe, identical wherever run, can be run by a single operator and offer control over specific parameters enabling a focus on the restored vision alone. We will demonstrate the results of a virtual setup based on a common real-world behavioral test currently in use as a standard.

**Results:** We transformed several real-world tests into virtual environment tasks, successfully tested them and offer them online. Using the "find-the-door" test we show that EyeMusic users are indeed capable of performing this task within the given timeframe in a manner significantly above chance.

**Conclusions:** We have indeed been able to create a functional visual rehabilitation virtual test and we call upon users of other visual rehabilitation methods to perform these same tasks.

## Contribution of color to "visual" acuity using sound

Galit Buchs[1,2], Shelly Levy-Tzedek[3,4], Dar Rimer[2], Amir Amedi[1,2,5,6]

*1 The Cognitive Science Program, The Hebrew University of Jerusalem, Jerusalem, Israel, 2 Department of Medical Neurobiology, The Institute for Medical Research Israel-Canada, Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel, 3 Recanati School for Community Health Professions, Department of Physical Therapy, Ben Gurion University of the Negev, Beer-Sheva, Israel, 4 Zlotowski Center for Neuroscience, Ben Gurion University of the Negev, Beer-Sheva, Israel, 5 The Edmond and Lily Safra Center for Brain Sciences (ELSC), The Hebrew University of Jerusalem, Jerusalem, Israel, 6 Institut de la Vision, UPMC Univ*

**Purpose:** Testing the "visual" acuity achieved while using the EyeMusic visual to auditory sensory substitution device. The use of both monochromatic (white) and colored stimuli was aimed at determining whether color constitutes a perceptual advantage in sensory substitution as in vision.

**Methods:** An adaptation of the Snellen tumbling-E test was used for testing the "visual" acuity. This adaptation was initially performed for testing "visual" acuity in the vOICe sensory substitution device. We now adjusted the stimuli to accommodate the EyeMusic's lower resolution. In addition to these monochromatic stimuli, we created a set of colored stimuli. In this version, the vertical line in the upright letter E was drawn in red, with the three horizontal lines remaining white. Twenty three individuals participated in this study, of them 13 have visual impairments, and 10 were blindfolded sighted individuals. Each participant was tested twice, once with the monochromatic version, and once with the colored stimuli. The order of the tests was counterbalanced between participants.

**Results:** We found no significant differences in performance between blind and the sighted groups of participants. We found a significant effect of the added color on the “visual” acuity. The highest acuity participants reached in the monochromatic test was 20/800, whereas with the added color, acuity doubled to 20/400.

**Conclusions:** we conclude that color, represented by timbre, can be used to increase the effective resolution of auditory sensory substitution devices.

## Core knowledge of geometry develops without visual experience

Benedetta Heimler[1,2]*, Tomer Behor[1,2]*, Stanislas Deheane[3,4,5,6] and Amir Amedi[1,2]

*1Department of Medical Neurobiology, Institute for Medical Research Israel-Canada, Faculty of Medicine, Hebrew University of Jerusalem, Hadassah Ein-Kerem, Jerusalem, Israel, 2 The Edmond and Lily Safra Center for Brain Research, the Hebrew University of Jerusalem, Hadassah Ein-Kerem, Jerusalem, Israel, 3Cognitive Neuroimaging Unit, Institut National de la Santé et de la Recherche Médicale,91191 Gif sur Yvette, France, 4Neurospin Center, Commissariat à l'énergie atomique (CEA), Division Sciences de la Vie(DSV), Institut d'imagerie Biomédicale (I2BM), 91191 Gif sur Yvette, France, 5University Paris 11, 91405 Orsay, 6France Collège de France, 75005 Paris, France*

**Equal contributions*

**Purpose:** In the last decade the presence of core geometry intuitions has been demonstrated in young children as well as in adults completely lacking geometrical language or geometrical education. However, it remained still unknown whether such intuitions can arise without any access to visual experience throughout the lifespan.

**Methods:** To unravel this issue, we took advantage of a visual deviant detection task consistently used in previous works to test sensitivity to geometric invariants, and we tested a group of congenitally blind adults in a tactile version of the same task.

**Results:** We found that congenitally blind participants spontaneously used geometric concepts such as curves, parallelism, right angles, quadrilaterals, relative distances among elements, to detect intruders in the tactile displays. Interestingly, geometric concepts requiring complex spatial transformations such as mental rotations, homothecy, symmetry and rotation were the least detectable among blind participants, similarly to what has been previously reported with young children and with uneducated adults.

**Conclusions:** These results provide evidence suggesting that core geometry intuitions do develop also in the absence of visual experience.

# Experimental Quantification of Corneal Tactile Spatial Responsivity for Vision Substitution

Zeev Zalevsky[1,2], Yevgeny Beiderman[1], Ygal Rotenstreich[3] and Michael Belkin[3]

*[1]Faculty of Engineering, Bar-Ilan University, Ramat-Gan 52900, Israel, [2]Erlangen Graduate School in Advanced Optical Technologies (SAOT), Friedrich-Alexander Universität Erlangen-Nürnberg, Paul-Gordan-Straße 6, 91052 Erlangen, Germany, [3]Goldshleger Eye Research Institute, Tel-Aviv University, Tel-Hashomer, Israel*

**Purpose:** To develop a sensory substitution device in which corneal stimuli are used to generate neural input to the brains of visually compromised people to substitute for absent retinal input.

**Methods:** The device is composed of spectacles-mounted cameras wirelessly transmitting processed images to a special contact lens translating the visual information into tactile stimulation of the corneal nerves. In order to improve the spatial resolution of the constructed image, the camera will also time multiplex, compress and encode the captured image before transmitting it to the stimulating contact lens.

**Results:** The full vision substitution system was constructed including special contact lens to perform the corneal tactile stimulus. Preliminary quantified experiments were performed and we were able, for the first time to the best of our knowledge, to demonstrate with preliminary human trials that the tactile sensing of the cornea has two points discrimination capability which is better than 2.5mm and that this sensing capability can be used to identify basic spatial shapes and images. Those shapes and images were transmitted to the subjects' cornea through 3 X 3 stimulation matrix. The recognition rate obtained for the two-point discrimination was relatively high around 81%-86% and it was obtained after only a few minutes of training. However, it is still difficult to show an improvement over the canonical Braille method due to the spatial resolution limitation of our preliminary device.

**Conclusions:** We propose novel concept of solving some of the vision problems of blind people via non-retinal stimulation of the cornea. Preliminary quantified mapping of the spatial responsivity of the human cornea was clinically demonstrated and used for transmission of visual spatial information.

## Is Lessepsian fish migration vision based? – The start of a quest

Amit Lerner

*National Institute of Oceanography, Israel Oceanographic and Limnological Research Ltd*

**Purpose:** To determine if Lessepsian fish species that migrated from the Red Sea to the Mediterranean Sea through the Suez Canal differ in their eye size and therefore in sensitivity and acuity from their local Mediterranean family members.

**Methods:** Fish were collected by using a trawl at depths varying between 15-100 m in front of the Ashdod shore of the Mediterranean Sea, and their eye diameter and body weight were measured. The slope and intercept values calculated from the eye diameter - weight log-log correlation of the Lessepsian fish migrants were compared to those of their Mediterranean related species from the same family.

**Results:** In the families Carangidae and Scombridae, which include open water visual predators, the Lessepsian migrants had smaller intercepts than their Mediterranean relatives. In the family Mullidae, which includes less visual species that mostly feed on benthic prey, detecting it by touch or smell, no difference was found in either the intercept or the slope. The Intercept and slope of the same species caught at different depths did not differ either.

**Conclusions:** The eye size of the Lessepsian open-water predators was smaller than that of their Mediterranean Sea relatives from the same family. The non-predator benthic feeding species of the Mullidae family did not differ in its eye size from its Mediterranean Sea family member. Eye size did not depend on depth, in all the species examined. The shallowness of the Suez Canal (a max. depth of 25 m) provides a highly illuminated environment that dictates only the passage of species, and individuals within the species, with low sensitivity to light. As light sensitivity positively correlates with eye size, only fish with small eyes may pass and migrate. Any further deepening of the canal in the future may allow deep-water species or highly sensitive individuals to invade the Mediterranean Sea from the Red Sea. This may lead to competitive exclusion and the possible extinction of local deep-water Mediterranean species. The independence of eye-size from depth observed in this study is explained by the fact that open-water predators cross the studied depth-range rapidly and constantly during their time of activity. Adaptation to the decreased light intensity that occurs with increased depth may take part in the retina. Future research should test for differences in the retina and the photoreceptor structure, e.g. photoreceptor length, diameter, and density, as well as perform behavioral studies comparing the vision abilities of both migrants and locals.