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

PROGRAM
31st Annual Meeting
Kibbutz Tzuba
March 24-25, 2011

תכנית
הכינוס השנתי ה-31
בית הארחה קיבוץ צובה
24-25 מרץ, 2011

עריכת התוכנית:

ד"ר חני לבקוביץ-ורבין, ד"ר תמר בן-יוסף, פרופ' אריה סולומון

עיצוב והבאה לדפוס: יעקב אלבז, הדסה עין-כרם.

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

ISRAEL SOCIETY FOR VISION AND EYE RESEARCH
XXXI ANNUAL MEETING
KIBBUTZ TZUBA
PROGRAM AT A GLANCE

Thursday, March 24, 2011

Session	Location	Time	Page
Registration and Coffee	**Exhibition Hall**	**08:00 – 08:30**	
Opening Remarks	**Lecture Hall**	**08:30 – 08:35**	
I. Poster Session 1	**Lecture Hall**	**08:35 – 09:30**	**9**
II. Cornea 1	**Lecture Hall**	**09:30 – 10:20**	**14**
Coffee and Posters viewing	**Exhibition Hall**	**10:20 – 10:50**	
III. Highlights in Ophthalmology	**Lecture Hall**	**10:50 – 12:10**	**15**
IV. Retina 1	**Lecture Hall**	**12:10 – 13:00**	**16**
Lunch break and Poster viewing	**Dining Room**	**13:00 – 14:00**	
Guest Lecture 1	**Lecture Hall**	**14:00 – 14:30**	**17**
V. Poster session 2	**Lecture Hall**	**14:30 – 15:40**	**18**
VI. Genetics	**Lecture Hall**	**15:40 – 16:20**	**25**
Awards and ISVER update	**Lecture Hall**	**16:20 – 16:50**	
Poster viewing, Wine & Cheese	**Exhibition Hall**	**16:50 – 17:20**	
VII. Pediatric Ophthalmology and Visual Function	**Lecture Hall**	**17:20 – 18:30**	**26**

Friday, March 25, 2011

Session	Location	Time	Page
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VIII. Glaucoma and cataract	**Lecture Hall**	**08:30 – 09:30**	**28**
IX. Retina 2	**Lecture Hall**	**09:30 – 10:30**	**29**
Guest Lecture 2	**Lecture Hall**	**10:30 – 11:00**	**30**
Coffee and Posters viewing	**Exhibition Hall**	**11:00 – 11:30**	
X. Cornea 2 and Oncology	**Lecture Hall**	**11:30 – 12:30**	**31**
Concluding Remarks	**Lecture Hall**	**12:30 – 12:35**	

יושבי-ראש של האגודה הישראלית לחקר העין והראיה

CHAIRMEN OF THE ISRAEL SOCIETY FOR VISION AND EYE RESEARCH

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Prof. Michael Belkin	1983-1985	פרופ' מיכאל בלקין
Prof. Saul Merin	1986-1989	פרופ' שאול מרין
Prof. Shabtay Dikstein	1990-1993	פרופ' שבתאי דיקשטיין
Prof. Fabian Abraham	1994-1996	פרופ' פביאן אברהם ז"ל
Prof. Ido Perlman	1997-1999	פרופ' אידו פרלמן
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Prof. Ahuva Dovrat	2004-2006	פרופ' אהובה דברת ז"ל
Prof. Mordechai Rosner	2007-2009	פרופ' מרדכי רוזנר
Prof. Eyal Banin	2010-	פרופ' איל בנין

חברי ועד האגודה הישראלית לחקר העין והראיה

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Eyal Banin		יו״ר	**איל בנין**
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Hani Levkovitch-Verbin			**חני לבקוביץ-ורבין**
Arieh Solomon			**אריה סולומון**

מרצים המקבלים פרס על עבודות שהוצגו בכינוס השנתי ה-30, מרץ 2010

RECIPIENTS OF AWARDS FOR THE BEST YOUNG INVESTIGATOR TALKS AND POSTERS PRESENTED AT THE 30TH MEETING, MARCH 2010

1. במקום ראשון (מלגת נסיעה ל-ARVO) – הרצאתה של **לינה זלינגר** (מרכז רפואי הדסה):

" ADAM9 - THE MOST RECENT GENE CAUSING AUTOSOMAL RECESSIVE CONE-ROD DYSTROPHY "

2. הרצאה מצטיינת שנייה (קלינית)– **טון יוקרת** (בתי חולים מאיר, כרמל, קפלן, תה"ש, עין-טל, loptima):

"CARBON DIOXIDE LASER-ASSISTED DEEP SCLERECTOMY (LADS): A PROSPECTIVE CLINICAL STUDY"

3. פוסטר מצטיין – **חן פרחי** (אוניברסיטת ת"א):

" DUAL REQUIREMENT FOR PAX6 IN RETINAL PROGENITOR CELLS"

4. פוסטר מצטיין – **טמילה סדיקוב** (מרכז רפואי רבין, בי"ח שניידר ואוניברסיטת ת"א):

"INTRAVITREAL INJECTION OF ADULT BONE MARROW DERIVED STEM CELLS TO DEVELOPING RETINA OF NEWBORN MICE "

הפרס הראשון הינו מלגת נסיעה ל- ARVO על שמה

של פרופסור אהובה דברת, ז"ל

הפרס השני הינו בחסות חברת לפידות מדיקל Lapidot Medical

פרסים שלוש וארבע הינם בחסות
"לראות"- העמותה למחקר בריאות העין ומניעת עיוורון בישראל

לראות

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

תודה לחברות שתרמו לכינוס:

Our thanks to the sponsoring companies

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לראות
העמותה לחקר בריאות העין ומניעת עיוורון בישראל

מטרות "לראות"

* מציאת מזור למחלות עיניים הגורמות לעיוורון באמצעות הגברת המאמץ המחקרי בישראל.
* העלאת מודעות המוסדות הממשלתיים לחשיבות המכרעת בקידום מחקרים בתחום בריאות העין, כולל מחקרים במחלות "יתומות".
* העלאת המודעות הציבורית לחשיבות הטיפול המונע.

המועצה המדעית של "לראות"

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 רשת מחקרית בינלאומית.
בין חברי המועצה המדעית גורמים בכירים מתחומי הבריאות, האקדמיה והתעשייה.
זהו שילוב ייחודי של מומחים הכולל: רופאים ומדענים בתחומי המחקר ורפואת העיניים, ראשי מחלקות למחקר ופיתוח בחברות פרמצבטיות מובילות, בכירים בסקטור העסקי בעלי ראיה כלכלית ומדעית.
משרד הבריאות בחר בעמותה כגוף מייעץ בתחום תרופות וטכנולוגיות חדשות.

בין יוזמות עמותת "לראות"

* חודש מודעות לרפואה מונעת בעיניים - "אל תהיה עיוור לסכנה-בדיקה פשוטה אחת יכולה להציל את הראייה שלך" הכולל קמפיין תקשורתי, כנס מומחים לבריאות העין לציבור הרחב, פרסום מוסף לבריאות העין בעיתון יומי
* חודש גיוס כספים "תפקחו את העיניים ותפתחו את הלב","התרמה בקופות רשת קמעונאית גדולה, מכירת נרות חנוכה "לראות את האור", אירוע גיוס כספים שנתי של עמותת לראות.
* תכנית פעילה למימון מחקרים, סמינר הרצאות בשידור חי, אתר מידע פעיל כולל פורומים של רופאים בכירים
* הפעלת ניידת לבדיקות עיניים לאוכלוסיות נזקקות – מיזם חדש של חמש שנים.
* קידום בדיקות סקר עיניים לילדים.

כיצד "לראות" פועלת?

העמותה מממשת את מטרותיה באמצעות תרומות מגופים ממשלתיים, מחברות עסקיות ותאגידים, מתורמים פרטיים ומקרנות בישראל ובחו"ל.

מחקרים ממומנים ע"י עמותת לראות 2007-2011

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

א. **דר' רות אשרי-פדן**, הפקולטה לרפואה ע"ש סאקלר, אוניברסיטת ת"א: "חקר המנגנונים המולקולאריים המעורבים בבקרת התפתחות תאי הפיגמנט בעין יונקים".

ב. **פרופ' איל בנין**, מחלקת עיניים, בית החולים האוניברסיטאי הדסה ע"כ, ירושלים: "תאי גזע עובריים אנושיים כמקור לתאי אפיתל פיגמנטי ברשתית".

ג. **דר' תמר בן יוסף**, המחלקה לגנטיקה, הפקולטה לרפואה ע"ש רפפורט, הטכניון, חיפה: "מפוי גנים וזהוי מוטציות בגנים האחראיים לרטיניטיס פיגמנטוזה במשפחות ערביות ויהודיות מצפון הארץ".

ד. **דר' דרור שרון**, מחלקת עיניים, בית החולים האוניברסיטאי הדסה ע"כ, ירושלים: "אפיון גנטי של מחלות ניוון מקולרי תורשתיות באוכלוסיה הישראלית".

ה. **פרופ' אידו פרלמן**, הפקולטה למדעי הרפואה, המחלקה לפיסיולוגיה, הטכניון חיפה: "התפשטות תהליכים ניוונים מפוטורצפטורים חולים מסוג קנים לפוטורצפטורים בריאים מסוג מדוכים במודל חולדה לרטיניטיס פיגמנטוזה".

ו. **פרופ' אריה סולומון**, הפקולטה לרפואה, אוניברסיטת תל אביב: "שילוב ננו טכנולוגיות וחומרים ביו-טכנולוגיים חדשים ליצירת טיפול אינטגרטיבי לרפוי עצב הראייה לאחר חבלה או מחלה".

ז. **פרופ' איתי חוברס**, מחלקת עיניים, בית החולים האוניברסיטאי הדסה ע"כ, ירושלים: "אפיון מעורבות תתי אוכלוסיות של תאי דם לבנים והרצפטורים לכמוקינים CCR2 ו-CXECR בפתוגנזה של ניוון מקולרי גילי (נמ"ג).

ח. **דר' ניצה גולדנברג-כהן**, מרכז רפואי שניידר לרפואת ילדים בישראל: "הזרקה תוך עינית של תאי גזע ממח עצם בוגר לרשתית מתפתחת בעין של עכברים בני יומם".

ט. **דר' מיכאל ויסבורד**, מחלקת עיניים, המרכז הרפואי איכילוב, ת"א: "שימוש טופיקלי באבסטין למחלות עיניים".

י. **פרופ' רון עופרי**, ביה"ס לווטרינריה, האוניברסיטה העברית: "מודל חדשני לעיוורון יום: מחקר היתכנות לקראת טיפול גנטי בחולי אכרומטופסיה".

יא. **דר' שחר פרנקל**, מחלקת עיניים, בית החולים האוניברסיטאי הדסה ע"כ, ירושלים: "גרורות ממלנומה של הענביה: עיכוב גורמי התיעתוק NFkB ו-USF2 כטיפול נגד מיקרו-גרורות".

יב. **דר' דרור שרון**, מחלקת עיניים, בית החולים האוניברסיטאי הדסה ע"כ, ירושלים: "אפיון גנטי ותפקודי של גן חדש שהינו גורם עיקרי לרטיניטיס פיגמנטוזה באוכלוסיה הישראלית".

יג. **דר' רות אשרי-פדן**, אוניברסיטת תל-אביב: "חקר התפקידים של מיקרו-רנ"א בהתפתחות העין ביונקים".

Moderators and committee members please note: You should select four presentations for the Young Investigator Award, for the two best oral and the two best poster presentations. The candidates are marked by AC (AC: Award Candidate)

PROGRAM

Thursday, March 24, 2011

Registration 08:00 – 08:30

Opening Remarks 08:30 – 08:35

Eyal Banin

Session I – Poster presentations 1 08:35 – 09:30

Moderators: Tamar Ben Yosef and Arieh Solomon

GOLDFARB DANIEL (2) * KNYAZER BORIS
(1) FACULTY OF MEDICAL SCIENCES, BEN-GURION UNIVERSITY IN THE NEGEV, BEER SHEVA, ISRAEL (2) OPHTHALMOLOGY DEPARTMENT, SOROKA UNIVERSITY MEDICAL CENTER, BEN-GURION UNIVERSITY IN THE NEGEV, BEER SHEVA, ISRAEL (3) CLALIT HEALTH SERVICES, SOUTHERN DISTRICT, BEER SHEVA, ISRAEL

4. **THE DIAGNOSTIC SIGNIFICANCE OF THE ERG A/B RATIO IN RETINAL DISORDERS** **36**
(1) * FERMAN-ATTAR GILI (1) ROTENSTREICH YGAL
(1) GOLDSCHLEGER EYE INSTITUTE, SHEBA MEDICAL CENTER, TEL-HASHOMER, ISRAEL

5. **INTRAVITREAL BEVACIZUMAB TREATMENT FOR MACULAR EDEMA DUE TO CENTRAL RETINAL VEIN OCCLUSION** **37**
(1) AXER SIEGEL RUTH (1) * DOTAN ASSAF (1) BOURLA DAN (1) MIMOUNI KARIN (1) BOR ELITE (1) WEINBERGER DOV
(1) DEPARTMENT OF OPHTHALMOLOGY, RABIN MEDICAL CENTER, BEILINSON CAMPUS

6. **SUB-RETINAL INJECTION OF HUMAN ADULT STEM CELLS PRESERVES ERG RESPONSE IN RCS RATS** **38**
AC
(1) BELKIN MICHAEL (2) TREVES AVRAHAM J (1) * TZAMERET ADI (3) BLUM NIRA (3) NAGLER ARNON (1) ROTENSTREICH YGAL
(1) TEL-AVIV UNIVERSITY, TEL-HASHOMER, ISRAEL , GOLDSCHLEGER EYE RESEARCH INSTITUTE (2)TEL-HASHOMER, ISRAEL, CANCER RESERCH CENTER (3)TEL-HASHOMER, ISRAEL, HEMATOLOGY DEVISION

7. **THE ROLE OF LIM-DOMAIN BINDING PROTEINS IN RETINAL DEVELOPMENT** **39**
AC
(1) * GUETA KEREN (2) COHEN TSADOK (2) WESTPHAL HEINER (1) ASHERY-PADAN RUTH
(1) SACKLER FACULTY OF MEDICINE, TEL-AVIV UNIVERSITY, RAMAT AVIV, TEL AVIV, ISRAEL (2) LABORATORY OF MAMMALIAN GENES AND DEVELOPMENT, EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT, NATIONAL INSTITUTES OF HEALTH, HHS, BETHESDA, MD 20892, USA.

8. **ERECTILE DYSFUNCTION IS ASSOCIATED WITH RETINOPATHY IN DIABETIC MEN: TWO MANIFESTATIONS OF A SYSTEMIC MICRO-VASCULAR DISEASE** **40**
(1) * SHAHAR JONATHAN (2) HENIS OREN (3) STENVEIL ARIE (4) FINN TALIA (5) HERUTI RAFI (6) LOEWENSTEIN ANAT (7) JUSTO DAN
(1) OPHTHALMOLOGY TEL AVIV MEDICAL CENTER (2)

SACKLER FACULTY OF MEDICIN TEL AVIV UNIVERSITY (3) MEDICINE D TEL AVIV MEDICAL CENTER (4) MEDICINE D TEL AVIV MEDICAL CENTER (5) SEXUAL HEALTH CLINIC, REUTH MEDICAL CENTER, TEL-AVIV (6) OPHTHALMOLOGY TEL AVIV MEDICAL CENTER (7) DEPARTMENT OF GERIATRIC MEDICINE, TEL AVIV MEDICAL CENTER

9. **POLY-LACTIC-CO-GLYCOLIC ACID (PLGA) - IS IT TOXIC TO THE RETINA?** **41**
(1) * SHAHAR JONATHAN (2) ZEMEL ESTHER (3) GILERT ARIEL (3) MACHLUF MARCELLE (1) LOEWENSTEIN ANAT (2) PERLMAN IDO
(1) OPHTHALMOLOGY DEPARTMENT, TEL AVIV MEDICAL CENTER (2) DEPARTMENT OF PHYSIOLOGY AND BIOPHYSICS, RUTH & BRUCE RAPPAPORT FACULTY OF MEDICINE, TECHNION (3) FACULTY OF FOOD ENGINEERING AND BIOTECHNOLOGY, TECHNION

10. **IMMUNE INTERACTIONS OF HUMAN EMBRYONIC STEM CELL-DERIVED RPE CELLS IN DYSTROPHIC RCS RATS** **42**
AC
(1) * ALPER RUSLANA (2) IDELSON MARIA (1) HEMO ITSHAK (1) PIONTEK ELENA (1) BARZEL ISRAEL (1) SHULMAN MARINA (2) REUBINOFF BENJAMIN (1) BANIN EYAL
(1) CENTER FOR RETINAL AND MACULAR DEGENERATIONS, DEPARTMENT OF OPHTHALMOLOGY,HADASSAH-HEBREW UNIVERSITY MEDICAL CENTER, JERUSALEM, ISRAEL. (2) CENTER FOR HUMAN EMBRYONIC STEM CELLS, HADASSAH-HEBREW UNIVERSITY MEDICAL CENTER, JERUSALEM, ISRAEL.

11. **ROLE OF SIRT6 IN RETINAL AGING** **43**
AC
(1) * OBOLENSKY ALEXEY (2) PESHTI VICTORIA (2) COHEN HAIM Y (1) BANIN EYAL
(1) CENTER FOR RETINAL AND MACULAR DEGENERATIONS, DEPARTMENT OF OPHTHALMOLOGY, HADASSAH-HEBREW UNIVERSITY MEDICAL CENTER, JERUSALEM (2) THE MINA & EVERARD GOODMAN FACULTY OF LIFE SCIENCES, BAR-ILAN UNIVERSITY, RAMAT-GAN

12. **DIFFERENTIATION OF PAX6- RPCS IS PROLONGED AND SKEWED TOWARDS EARLY AMACRINE TYPES** **44**
(1) * FARHY CHEN (1) ASHERY-PADAN RUTH
(1) 1SACKLER FACULTY OF MEDICINE, HUMAN MOLECULAR GENETICS AND BIOCHEMISTRY, TEL AVIV UNIVERSITY, TEL AVIV, ISRAEL.

13. **HYPERGLYCEMIA INDUCES MICROPARTICLES FORMATION AND AFFECTS THEIR ANTIGENIC EXPRESSION AND THROMBOGENICITY** **45**
AC
(1) * BACHAR ZIPORI ANAT (2) BRENNER BENJAMIN (3)

Session II – Cornea 1 09:30 – 10:20

Moderators: Igor Kaiserman and Irit Bachar

Coffee and Posters 10:20 – 10:50

Session III – Highlights in Ophthalmology 10:50 – 12:10

Dedicated to the memory of Prof. Ahuva Dovrat

Moderators: Hani Levkovitch-Verbin and Eyal Banin

Prof. Ido Perlman - In memory of Prof. Dovrat 10:50-11:00

Time	TITLE	Page
11:00-11:10	**THE USE OF BIOLON DURING DONOR'S CORNEAL HARVESTING FOR PRESERVATION OF THE ENDOTHELIUM** (1) * BOR ELITE (2) KAISERMAN IGOR (1) BOURLA DAN (1) BAHAR IRIT (1) DEPARTMENT OF OPHTHALMOLOGY, BEILINSON HOSPITAL, RABIN MEDICAL CENTER, PETACH TIQWA, ISRAEL (2) DEPARTMENT OF OPHTHALMOLOGY, BARZILAI MEDICAL CENTER, ASHKELON , ISRAEL	**63**
AC		
11:10-11:20	**CROSSLINKING TREATMENT OF CYSTIC FILTERING BLEBS IN RABBITS** (1) MATANIS-SUIDAN MILKA (2) MELAMOD ELINA (3) * GEYER ORNA (1) CARMEL MEDICAL CENTER HAIFA (2) CARMEL MEDICAL CENTER HAIFA (3) CARMEL MEDICAL CENTER HAIFA	**64**
11:20-11:30	**HOLOGRAPHIC PATTERNED STIMULATION FOR A RETINAL PROSTHESIS WITH SINGLE CELL RESOLUTION** (1) * FARAH NAIROUZ (1) REUTSKY INNA (1) MATAR SUHAIL (1) GOLAN LIOR (1) MAROM ANAT (1) SHOHAM SHY (1) BIOMEDICAL ENGINEERING TECHNION ISRAEL INT. OF TECHNOLOGY	**65**
11:30-11:40	**GENE THERAPY IN ISRAELI PATIENTS WITH LEBER CONGENITAL AMAUROSIS CAUSED BY A RPE65 FOUNDER MUTATION** (1) * BANIN EYAL (1) BANDAH-ROZENFELD DIKLA (1) OBOLENSKY ALEXEY (2) CIDECIYAN ARTUR V. (2) ALEMAN TOMAS S. (1) MARKS-OHANA DEVORA (1) SELA MALKA (3) BOYE SANFORD (2) SUMAROKA ALEXANDER (2) ROMAN ALEJANDRO J. (2) SCHWARTZ SHARON B. (3) HAUSWIRTH WILLIAM W. (2) JACOBSON SAMUEL G. (1) HEMO ITZHAK (1) SHARON DROR (1) DEPARTMENT OF OPHTHALMOLOGY, HADASSAH-HEBREW UNIVERSITY MEDICAL CENTER, JERUSALEM, ISRAEL (2) SCHEIE EYE INSTITUTE, UNIVERSITY OF	**66**

PENNSYLVANIA, PHILADELPHIA, PA, USA (3) DEPARTMENT OF OPHTHALMOLOGY, UNIVERSITY OF FLORIDA, GAINESVILLE, FL, USA

11:40-11:50 **ANTI-INFLAMMATORY EFFECTS OF ESSENTIAL FATTY ACIDS (EFA) ON CULTURED HUMAN CORNEAL EPITHELIAL CELLS AND CONJUNCTIVAL FIBROBLASTS** **67**

AC

(1) * ERDINEST NIR (2) OVADIA HAIM (1) SHMUELI OR (1) SOLOMON ABRAHAM
(1) DEPARTMENTS OF OPHTHALMOLOGY (2) AND NEUROLOGY, HADASSAH UNIVERSITY HOSPITAL, JERUSALEM, ISRAEL.

11:50-12:00 **CATARACT SURGERY WITH OCT-GUIDED FEMTOSECOND LASER: PRECISION AND EFFICACY** **68**

(1) * PALANKER DANIEL (1) BLUMENKRANZ MARK S. (2) SCHUELE GEORG (1) FRIEDMAN NEIL (3) BATLLE JUAN (3) FELIZ RAFAEL (4) CULBERTSON WILLIAM
(1) DEPARTMENT OF OPHTHALMOLOGY, STANFORD UNIVERSITY, STANFORD, CA (2) OPTIMEDICA CORPORATION, SANTA CLARA, CA (3) LASER CENTRO, SANTO DOMINGO, DOMINICAN REPUBLIC (4) BASCOM PALMER EYE INSTITUTE, MIAMI, FL

12:00-12:10 **THE EFFECTS OF BEVACIZUMAB AND RANIBIZUMAB ON HUMAN VEGF SIGNALING PATHWAYS IN HUMAN ENDOTHELIAL CELL** **69**

(1) * GOLAN SHANI (2) ENTIN-MEER MICHAL (2) MAYSEL-AUSLENDER SOFIA (2) KEREN GAD (1) LOEWENSTEIN ANAT (1) BARAK ADIEL
(1) DEPARTMENT OF OPHTHALMOLOGY (2) DEPARTMENT OF CARDIOLOGY

Session IV – RETINA 1 12:10 - 13:00

Moderators: Michaela Goldstein and Itay Chowers

Time	TITLE	Page
12:10-12:20	**RETINITIS PIGMENTOSA: 9-CIS BETA CAROTENE IMPROVES VISUAL FUNCTIONS IN SOME PATIENTS**	**70**

(1) * ROTENSTREICH YGAL (1) FERMAN-ATAR GILI (2) SADETZKI SIEGAL (3) SHAISH AVIV (3) HARATS DROR (1) BELKIN MICHAEL
(1) GOLDSCHLEGER EYE RESEARCH INSTITUTE, SACKLER SCHOOL OF MEDICINE, TEL AVIV UNIVERSITY, TEL HASHOMER, ISRAEL (2) GERTNER INSTITUTE, SHEBA MEDICAL CENTER, TEL HASHOMER, ISRAEL (3) STRASSBURGER LIPID CENTER, SHEBA MEDICAL CENTER, TEL HASHOMER, ISRAEL

12:20-12:30 **INTRAVITREAL BEVACIZUMAB TREATMENT FOR MACULAR EDEMA DUE TO BRANCH RETINAL VEIN OCCLUSION** **71**
(1) * AXER SIEGEL RUTH (1) DREZNIK AYELET (1) MIMOUNI KARIN (1) BOURLA DAN (1) BOR ELITE (1) WEINBERGER DOV
(1) DEPARTMENT OF OPHTHALMOLOGY, RABIN MEDICAL CENTER, BEILINSON CAMPUS

12:30-12:40 **CHEMOKINE RECEPTOR EXPRESSION IN WHITE BLOOD CELL SUB-POPULATIONS FROM PATIENTS WITH AGE-RELATED MACULAR DEGENERATION** **72**
AC
(1) * GRUNIN MICHELLE (1) BURSTYN-COHEN TAL (2) PELED AMNON (1) CHOWERS ITAY
(1) DEPARTMENT OF OPHTHALMOLOGY, HADASSAH MEDICAL CENTER-HEBREW UNIVERSITY (2) INSTITUTE OF GENE THERAPY, HADASSAH MEDICAL CENTER

12:40-12:50 **BESTROPHIN MODULATES PHAGOCYTOSIS OF PHOTORECEPTORS OUTER SEGMENTS BY RETINAL PIGMENT EPITHELIAL CELLS** **73**
AC
(1) * SAFURI SHADI (1) PERLMAN IDO
(1) RUTH & BRUCE RAPPAPORT FACULTY OF MEDICINE AND RAPPAPORT INSTITUTE, TECHNION-ISRAEL INSTITUTE OF TECHNOLOGY, HAIFA, ISRAEL
.

12:50-13:00 **OPTICAL DENSITY RATIO AS A DIAGNOSTIC TOOL IN THE ASSESSMENT OF RETINAL PATHOLOGIES** **74**
(1) * NEUDORFER MEIRA (1) WEINBERG AMIT (1) GOLDENBERG DAFNA (1) BARAK ADIEL
(1) DEPARTMENT OF OPHTHALMOLOGY, TEL AVIV MEDICAL CENTER, TEL AVIV

Lunch break and Poster viewing 13:00 – 14:00

Guest Lecture 1: 14:00 – 14:30

Prof. Richard A. Stone, MD

William C. Frayer Professor of Ophthalmology
University of Pennsylvania School of Medicine
Scheie Eye Institute & Children's Hospital of Philadelphia

TITLE: **Why Refractive Errors?**

Session V – Poster presentations 2 14:30 – 15:40
Moderators: Dror Sharon and Moti Rosner

(1) DEPARTMENT OF OPHTHALMOLOGY, ASSAF HAROFEH MEDICAL CENTER, SACKLER FACULTY OF MEDICINE, TEL AVIV UNIVERSITY, ISRAEL (2) GOLDSCHLEGER EYE INSTITUTE, SHEBA MEDICAL CENTER, SACKLER FACULTY OF MEDICINE, TEL AVIV UNIVERSITY, TEL-HASHOMER, ISRAEL (3) CELLULAR BIOCHEMISTRY AND HUMAN GENETICS, HEBREW UNIVERSITY-HADASSAH SCHOOLS OF MEDICINE AND DENTAL MEDICINE, JERUSALEM, ISRAEL

31. **RISK FACTORS FOR KERATOCONUS IN PALESTINIAN ARABS: A CASE CONTROL STUDY** **80**

(1) * GORDON-SHAAG ARIELA (2) GARTH JEANNE (1) ESSA MARON (1) GHARA MOHAMMED (1) ABD-EL-KADDER SHATHA (1) SHNEOR EINAT

(1) DEPARTMENT OF OPTOMETRY AND VISION SCIENCE, HADASSAH ACADEMIC COLLEGE, JERUSALEM (2) ST. JOHN OF JERUSALEM EYE HOSPITAL, JERUSALEM

32. **THE ASSOCIATION OF KERATOCONUS WITH BLEPHARITIS.** **81**

(1) * MOSTOVOY DINA (2) VINKER SHLOMO (3) GOLDICH YAKOV (1) LEVARTOVSKY SHMUEL (1) KAISERMAN IGOR

(1) DEPARTMENT OF OPHTHALMOLOGY, BARZILAI MEDICAL CENTER, ASHKELON, ISRAEL (2) DEPARTMENT OF FAMILY MEDICINE, CLALIT HEALTH SERVICES, CENTRAL DISTRICT, REHOVOT, ISRAEL (3) DEPARTMENT OF OPHTHALMOLOGY, ASSAF HAROFEH MEDICAL CENTER, ZERIFIN, ISRAEL

33. **PUPILLOMETER-BASED OBJECTIVE CHROMATIC PERIMETRY IN NORMAL SUBJECTS AND GLAUCOMA PATIENTS** **82**

AC

(1) * SKAAT ALON (1) ELYASHIV SIVAN (2) FERMAN GILI (2) BELKIN MICHAEL (2) ROTENSTREICH YGAL

(1) DEPARTMENT OF OPHTHALMOLOGY, GOLDSCHLEGER EYE INSTITUTE, SHEBA MEDICAL CENTER, TEL HASHOMER, ISRAEL

(2) GOLDSHLEGER EYE RESEARCH INSTITUTE, TEL AVIV UNIVERSITY, TEL HASHOMER, ISRAEL

34. **RETINAL NERVE FIBER LAYER AND OPTIC NERVE HEAD IMAGING: COMPARISON BETWEEN CIRRUS OPTIC COHERENCE TOMOGRAPHY AND HEIDELBERG RETINAL TOMOGRAPH III IN ABILITY TO DISCRIMINATE NORMAL FROM GLAUCOMATOUS EYES** **83**

AC

(1) * KRATZ ASSAF (2) LIM RIDIA (2) GOLDBERG IVAN

(1) DEPARTMENT OF OPHTHALMOLOGY, SOROKA UNIVERSITY MEDICAL CENTER, BEER-SHEVA, ISRAEL AND SYDNEY EYE HOSPITAL, SYDNEY, AUSTRALIA (2) DEPARTMENT OF OPHTHALMOLOGY, SYDNEY EYE HOSPITAL, SYDNEY, AUSTRALIA

35. **DIURNAL INTRAOCULAR PRESSURE CURVES INCLUDING MEASUREMENTS WITH GOLDMANN APPLANATION TONOMETER IN SIDE-LYING POSITION** **84**

(1) * PIVEN ILIA (1) GLOVINSKY YOSEPH

(1) GOLDSCHLEGER EYE RESEARCH INSTITUTE, SHEBA MEDICAL CENTER, OPHTHALMOLOGY DEPARTMENT, TEL AVIV UNIVERSITY, ISRAEL

36. **CHANGES IN ANTERIOR SEGMENT PARAMETERS FOLLOWING INSERTION OF EX-PRESS MINIATURE GLAUCOMA IMPLANT** **85**

AC

(1) * HAMMEL NA'AMA (1) LUSKY MOSHE (2) KAISERMAN IGOR (1) ROBINSON ANAT (1) BAHAR IRIT

(1) OPHTHALMOLOGY DEPARTMENT, RABIN MEDICAL CENTER, BEILINSON CAMPUS, PETACH TIKVA, ISRAEL (2) OPHTHALMOLOGY DEPARTMENT, BARZILAI MEDICAL CENTER, ASHKELON, ISRAEL

37. **OPTIC NERVE HEAD IMAGING: COMPARISON OF CIRRUS OPTIC COHERENCE TOMOGRAPHY AND HEIDELBERG RETINAL TOMOGRAPH III** **86**

AC

(1) * KRATZ ASSAF (2) LIM RIDIA (2) GOLDBERG IVAN

(1) DEPARTMENT OF OPHTHALMOLOGY, SOROKA UNIVERSITY MEDICAL CENTER, BEER-SHEVA, ISRAEL AND SYDNEY EYE HOSPITAL, SYDNEY, AUSTRALIA (2) DEPARTMENT OF OPHTHALMOLOGY, SYDNEY EYE HOSPITAL, SYDNEY, AUSTRALIA

38. **PERIPAPILLARY DISTRIBUTION OF MULLER CELLS WITHIN THE HUMAN RETINAL NERVE FIBER LAYER** **87**

AC

(1) * FRENKEL SHAHAR (2) GOSHEN GAL (3) LEACH LU (1) PE'ER JACOB (1) BLUMENTHAL EYTAN

(1) OPHTHALMOLOGY, HADASSAH-HEBREW UNIVERSITY MEDICAL CENTER, JERUSALEM, ISRAEL (2) MORPHOMETRY LABORATORY, FACULTY OF DENTAL MEDICINE, HEBREW UNIVERSITY, JERUSALEM, ISRAEL (3) OFFICE OF RESEARCH SERVICES, STRITCH SCHOOL OF MED., MAYWOOD, IL, US

39. **IS THERE A CORRELATION BETWEEN INTRACRANIAL PRESSURE AND INTRAOCULAR PRESSURE MEASURED BY HAND-HELD TONOMETRY?** **88**

(1) * GOLAN SHANI (1) KURZ SHIMON (1) MEZAD DAPHNA (1) KESLER ANAT (2) GILADI NIR (3) HALPERIN PINHAS

(1) DEPARTMENT OF OPHTHALMOLOGY (2) DEPARTMENT OF NEUROLOGY (3) DEPARTMENT OF EMERGENCY MEDICINE

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(1) BANDAH-ROZENFELD DIKLA (1) OBOLENSKY ALEXEY (1)

MIZRAHI-MEISSONNIER LILIANA (2) BEN-YOSEF TAMAR (3) SCHWARTZ SHARON B. (3) CIDECIYAN ARTUR V. (1) MERIN SAUL (3) JACOBSON SAMUEL G. (1) BANIN EYAL (1) * SHARON DROR
(1) DEPARTMENT OF OPHTHALMOLOGY, HADASSAH-HEBREW UNIVERSITY MEDICAL CENTER, JERUSALEM (2) GENETICS DEPARTMENT, FACULTY OF MEDICINE, TECHNION, HAIFA (3) SCHEIE EYE INSTITUTE, PHILADELPHIA, PA, USA

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(1) VEKSLIN SHARON (1) NEVET MARIELA JUDITH (1) *BEN-YOSEF TAMAR
(1) DEPARTMENT OF GENETICS AND THE RAPPAPORT FAMILY INSTITUTE FOR RESEARCH IN THE MEDICAL SCIENCES, FACULTY OF MEDICINE, TECHNION, HAIFA

42. **HOMOZYGOSITY MAPPING - A POWERFUL TOOL FOR THE IDENTIFICATION OF MUTATIONS IN KNOWN RETINAL DEGENERATION GENES IN THE ISRAELI AND PALESTINIAN POPULATIONS** **91**
AC
(1) * BANDAH-ROZENFELD DIKLA (1) ZELINGER LINA (1) BERYOZKIN AVIGAIL (1) MIZRAHI-MEISSONNIER LILIANA (1) ELI DALIA (2) SAGI MICHAL (1) ROSENMANN ADA (3) MERIN SAUL (1) CHOWERS ITAY (1) BANIN EYAL (1) SHARON DROR
(1) DEPARTMENT OF OPHTHALMOLOGY, HADASSAH-HEBREW UNIVERSITY MEDICAL CENTER, JERUSALEM
(2) DEPARTMENT OF HUMAN GENETICS AND METABOLIC DISEASES, HADASSAH MEDICAL CENTER, JERUSALEM
(3) ST. JOHN EYE HOSPITAL, JERUSALEM

43. **IDENTIFICATION OF MUTATIONS CAUSING AUTOSOMAL RECESSIVE INHERITED CONE-DOMINATED DISEASES USING HOMOZYGOSITY MAPPING** **92**
AC
(1) * BERYOZKIN AVIGAIL (1) BANDAH-ROZENFELD DIKLA (1) ZELINGER LINA (1) MIZRAHI-MEISSONNIER LILIANA (1) HEMO ITZHAK (1) CHOWERS ITAY (1) MERIN SAUL (1) BANIN EYAL (1) SHARON DROR
(1) DEPARTMENT OF OPHTHALMOLOGY, HADASSAH-HEBREW UNIVERSITY MEDICAL CENTER, JERUSALEM

44. **PHENOTYPE-GENOTYPE CORRELATION IN SPORADIC PATTERN DYSTROPHY** **93**
(1) * JAOUNI TAREQ (2) AVERBUKH EDWARD (3) COHEN TALI (4) SHARON DROR (5) CHOWERS ITAY
(1) OPHTHALMOLOGY DEPARTMENT, HADASSAH MEDICAL CENTER (2) OPHTHALMOLOGY DEPARTMENT, HADASSAH MEDICAL CENTER (3) OPHTHALMOLOGY DEPARTMENT, HADASSAH MEDICAL CENTER (4) OPHTHALMOLOGY

DEPARTMENT, HADASSAH MEDICAL CENTER (5) OPHTHALMOLOGY DEPARTMENT, HADASSAH MEDICAL CENTER

45. **MUTATIONS IN BEST1 AND PERIPHERIN/RDS GENES ARE IMPORTANT CAUSES FOR VITELLIFORM MACULAR LESIONS.** **94**
(1) * PRAS ERAN (2) BIRGER YAEL (3) ABU-HORWITS ALMOGIT (4) ROTENSTREICH YGAL
(1) THE DEPARTMENT OF OPHTHALMOLOGY, ASSAF HAROFEH MEDICAL CENTER, ZERIFIN. (2) THE DEPARTMENT OF OPHTHALMOLOGY, EDITH WOLFSON MEDICAL CENTER, HOLON. (3) THE DANEK GARTNER INSTITUTE OF HUMAN GENETICS, SHEBA MEDICAL CENTER, TEL HASHOMER. (4) THE GOLDSCHLEGER EYE RESEARCH INSTITUTE, SHEBA MEDICAL CENTER, TEL HASHOMER.

46. **FURTHER CHARACTERIZATION OF RISK SNPS FOR AMD IN THE ISRAELI POPULATION** **95**
(1) * ELBAZ SARAH (2) LEDERMAN MICHAL (2) GREINER KATHRIN (1) GRUNIN MICHELLE (1) BURSTYN-COHEN TAL (1) CHOWERS ITAY
(1) OPHTHALMOLOGY. HADASSAH-HEBREW UNIVERSITY MEDI9CAL CENTER (2) ST JOHN EYE HOSPITAL

47 **INSULIN LIKE GROWTH FACTOR-1 FOR PREDICTING METASTATIC UVEAL MELANOMA IN HUMANS** **96**
(1) * BARAK VIVIAN (2) ZLOTO OFIRA (2) PE'ER JACOB (1) KALICKMAN INA (2) FRENKEL SHAHAR
(1) IMMUNOLOGY LABORATORY FOR TUMOR DIAGNOSIS, HADASSAH-HEBREW UNIVERSITY MEDICAL CENTER, JERUSALEM, ISRAEL (2) DEPARTMENT OF OPHTHALMOLOGY, HADASSAH-HEBREW UNIVERSITY MEDICAL CENTER, JERUSALEM, ISRAEL

48 **UVEAL MELANOMA: GENDER DIFFERENCES IN CLINICAL PRESENTATION AND PROGNOSIS** **97**
AC
(1) * ZLOTO OFIRA (1) PE'ER JACOB (1) FRENKEL SHAHAR
(1) DEPARTMENT OF OPHTHALMOLOGY, HADASSAH-HEBREW UNIVERSITY MEDICAL CENTER, JERUSALEM, ISRAEL

49 **FOXP3+ REGULATORY T CELLS IN POSTERIOR UVEAL MELANOMA: CLINICOPATHOLOGIC CORRELATION** **98**
(1) * KHATIB NUR (1) PE'ER JACOB (1) FRENKEL SHAHAR (1) AMER RADGONDE
(1) DEPARTMENT OF OPHTHALMOLOGY, HADASSAH-HEBREW UNIVERSITY MEDICAL CENTER, JERUSALEM, ISRAEL

50 **MUTATION ANALYSIS AND COPY NUMBER VARIATION IN THE BRAF ONCOGENE IN PEDIATRIC LOW-GRADE GLIOMAS** **99**

(1) * LAVIV YOSSEF (2) DRATVIMAN-STOROBINSKY OLGA (1) MICHOWITZ SHALOM (2) BINKOVSKY NATALYA (3) TOLEDANO HELEN (4) GOLDENBERG-COHEN NITZA
(1) NEUROSURGERY DEPARTMENT, RABIN MEDICAL CENTER, PETAH TIQWA; TEL AVIV UNIVERSITY SACKLER SCHOOL OF MEDICINE, TEL AVIV (2) KRIEGER EYE RESEARCH LABORATORY, FELSENSTEIN MEDICAL RESEARCH CENTER PETAH TIQWA (3) PEDIATRICONCOLOGY, SCHNEIDER CHILDREN MEDICAL CENTER OF ISRAEL , PETAH TIQWA, ISRAEL. (4) PEDIATRIC UNIT, OPHTHALMOLOGY DEPARTMENT, SCHNEIDER CHILDREN MEDICAL CENTER OF ISRAEL , PETAH TIQWA, ISRAEL.

51 **LACK OF ONCOGENIC GNAQ MUTATIONS IN MELANOCYTIC LESIONS OF THE CONJUNCTIVA AS COMPARED TO UVEAL MELANOMA.** **100**

(1) * DRATVIMAN-STOROBINSKY OLGA (2) COHEN YORAM (3) FRENKEL SHAHAR (3) PE'ER JACOB (4) GOLDENBERG-COHEN NITZA
(1) THE KRIEGER EYE RESEARCH LABORATORY, FELSENSTEIN MEDICAL RESEARCH CENTER, PETAH TIQWA; (2) SHEBA CANCER RESEARCH CENTER, SHEBA MEDICAL CENTER, TEL HASHOMER (3) DEPARTMENT OF OPHTHALMOLOGY, HADASSAH-HEBREW UNIVERSITY MEDICAL CENTER, JERUSALEM. (4) DEPARTMENT OF OPHTHALMOLOGY, PEDIATRIC UNIT, SCHNEIDER CHILDREN'S MEDICAL CENTER OF ISRAEL, PETAH TIQWA; AND SACKLER FACULTY OF MEDICINE, TEL AVIV UNIVERSITY, TEL AVIV; ISRAEL

52 **BENEFICIAL ASSESSMENT OF VARIOUS TREATMENTS AGAINST MIOSIS AND VISUAL DYSFUNCTION FOLLOWING OCULAR EXPOSURE TO THE NERVE AGENT SARIN** **101**

AC

(1) * GORE ARIEL (1) BLOCH-SHILDERMAN EUGENIA (1) EGOZ INBAL (2) PERI DAVID (1) TURETZ JOSEPH (1) BRANDEIS RACHEL
(1) PHARMACOLOGY (2) ENVIRONMENTAL PHYSICS

53 **THE CORRELATION BETWEEN THE AMOUNT OF MULLER MUSCLE RESECTED DURING MODIFIED MULLERECTOMY SURGERY AND THE CLINICAL RESULT OF PTOSIS REPAIR** **102**

AC

(1) * AVNI-ZAUBERMAN NOA (1) BEN-SIMON GUY (1) KINORI MICKI (1) MORDECHAI ROSNER
(1) GOLDSCHLEGER EYE INSTITUTE, SACKLER FACULTY OF MEDICINE, TEL-AVIV UNIVERSITY, SHEBA MEDICAL CENTER, TEL HASHOMER

54 **THE CORNEAL TRANSPLANT SCORE: AUTOMATIC PRIORITY SCORING SYSTEM FOR KERATOPLASTY RECIPIENT CANDIDATES** **103**

(1) * VARRSANO DAVID (2) ROSENFELD ELDAR
(1) TEL AVIV, SOURASKI MEDICAL CENTER (2) TEL AVIV, SOURASKI MEDICAL CENTER

55 **INCORPORATION OF BONE MARROW CELLS INTO THE OPTIC NERVE IN TWO MOUSE MODELS OF OPTIC NEUROPATHY** **104**

(1) * AVRAHAM-LUBIN BAT-CHEN REVITAL (1) SADIKOV TAMILLA (1) BINKOVSKY NATALYA (2) ASKENASY NADIR (3) GOLDENBERG-COHEN NITZA
(1) THE KRIEGER EYE RESEARCH LABORATORY, FELSENSTEIN MEDICAL RESEARCH CENTER AND SACKLER FACULTY OF MEDICINE, TEL AVIV UNIVERSITY, TEL AVIV; (2) FRANKEL LABORATORY FOR STEM CELL RESEARCH, SCHNEIDER CHILDREN'S MEDICAL CENTER OF ISRAEL, PETACH TIKVA, ISRAEL. (3) PEDIATRIC UNIT, OPHTHALMOLOGY DEPARTMENT, SCHNEIDER CHILDREN'S MEDICAL CENTER OF ISRAEL, PETACH TIKVA, ISRAEL

56 **OCCURRENCE OF DRY EYE SYNDROME AS A MANIFESTATION OF OCULAR GRAFT VS. HOST DISEASE AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION** **105**

(1) * IVANIR YAIR (2) SHIMONI AVICHAI (1) EZRA-NIMNI ORIT (1) S. BAREQUET IRINA
(1) GOLDSCHLEGER EYE INSTITUTE, SHEBA MEDICAL CENTER, SACKLER FACULTY OF MEDICINE TEL AVIV UNIVERSITY, ISRAEL (2) DEPARTMENT OF BONE MARROW TRANSPLANTATION, SHEBA MEDICAL CENTER, SACKLER FACULTY OF MEDICINE TEL AVIV UNIVERSITY, ISRAEL

57 **THE ROLE OF SIX3 IN EARLY EYE DEVELOPMENT** **106**

AC

(1) * SAMUEL ANAT (1) INBAL ADI
(1) DEPARTMENT OF MEDICAL NEUROBIOLOGY, THE INSTITUTE FOR MEDICAL RESEARCH ISRAEL-CANADA, THE HEBREW UNIVERSITY - HADASSAH MEDICAL SCHOOL, JERUSALEM

Session VI – Genetics 15:40 – 16:20

Moderators: Eran Pras and Ruth Ashri-Pedan

Awards and ISVER update 16:20 - 16:50

Poster viewing, wine and cheese 16:50 - 17:20

Session VI – Pediatric Ophthalmology and Visual Function 17:20 – 18:30

Moderators: Ron Ofri and Uri Polat

(1) * LUSTIG AVICHAI (2) KATZIR GADI
(1) DEPT. OF NEUROBIOLOGY AND ETHOLOGY, UNIVERSITY OF HAIFA, HAIFA 31905. (2) DEPT. OF BIOLOGY, UNIVERSITY OF HAIFA AT ORANIM, ORANIM, TIVON 36006

18:00-18:10 AC

THE DEPENDENCY BETWEEN VITREAL DOPAMINE AND DIHYDROXYPHENYLACETIC ACIDS (DOPAC) ON AMBIENT LIGHT INTENSITY. **115**

(1) * COHEN YUVAL (2) PELEG EDNA (1) BELKIN MICHAEL (1) POLAT URI (1) S SOLOMON ARIEH
(1) GOLDSCHLEGER EYE RESEARCH INSTITUTE, TEL AVIV UNIVERSITY, TEL HASHOMER, ISRAEL (2) HYPERTENSION UNIT, DEPARTMENT OF INTERNAL MEDICINE, CHAIM SHEBA MEDICAL CENTER, TEL HASHOMER, ISRAEL

18:10-18:20

VISUAL ACUITY IN CHILDREN OPERATED FOR CONGENITAL CATARACT: COMPARISON OF OUTCOME OF SURGERY WITH AND WITHOUT INTRA-OCULAR LENS IMPLANTATION **116**

(1) BORISOVSKY GILAD (1) WYGNANSKI-JAFFE TAMARA (1) * SPIERER ABRAHAM
(1) GOLDSCHLEGER EYE INSTITUTE, SHEBA MEDICAL CENTER, TEL-HASHOMER; SACKLER FACULTY OF MEDICINE, TEL-AVIV UNIVERSITY, TEL AVIV

18:20-18:30

PERCEPTUAL TRAINING INDUCES VISUAL GAINS THAT OVERCOME THE OPTICAL DEFICITS IN PRESBYOPIA **117**

(1) * STERKIN ANNA (1) POLAT URI (1) YEHEZKEL OREN (1) LEV MARIA (1) ZOMET ATIV (2) SCHOR CLIFTON (2) LEVI DENNIS
(1) FACULTY OF MEDICINE, GOLDSCHLEGER EYE RESEARCH INST, SHEBA MEDICAL CENTER, TEL AVIV UNIVERSITY, ISRAEL (2) SCHOOL OF OPTOMETRY AND HELEN WILLS NEUROSCIENCE INSTITUTE, UC BERKELEY, BERKELEY, CA, USA

Friday, March 25, 2011

Coffee and Posters 08:00 – 08:30

Session VIII – Glaucoma and Cataract 08:30 - 09:30

Moderators: Orna Gayer and Hanna Garzozi

OPHTHALMOLOGY, SYDNEY EYE HOSPITAL, SYDNEY, AUSTRALIA

09:10-09:20 **HEMATOLOGIC BIOMARKERS IN CHILDHOOD CATARACTS** **122**

AC

(1) * WUSSUKU LIOR ORLY (2) PRAS ELON (2) NETZER IRIS (2) ABU-HORVITZ ALMOGIT (1) ALMER ZINA (1) MORAD YAIR (1) GOLDICH YAKOV (3) YAHALOM VERED (1) PRAS ERAN

(1) DEPARTMENT OF OPHTHALMOLOGY, ASSAF HAROFEH MEDICAL CENTER, ZERIFIN (2) SHEBA MEDICAL CENTER, DANEK GARTENER INSTITUTE OF HUMAN GENETICS, TEL HASHOMER (3) NATIONAL BLOOD GROUP REFERENCE LABORATORY (NBGRL), MAGEN DAVID ADOM (MDA) – NATIONAL BLOOD SERVICES, RAMAT GAN

09:20-09:30 **DIFFERENT PHOSPHATASES ARE ACTIVE IN CATARACT AND GLAUCOMA PATIENT AQUEOUS HUMOR AND CORRELATES WITH ITS REDOX STATE** **123**

AC

(1) * LATARIA GALI (2) YULISH MICHAEL (2) EPSTEIN IRENA (2) PIKKEL JOSEPH (1) * BEIT-YANNAI ELIE

(1) 1CLINICAL PHARMACOLOGY DEPARTMENT, THE FACULTY OF HEALTH SCIENCES, BEN-GURION UNIVERSITY OF THE NEGEV (2) OPHTHALMOLOGY DEPARTMENT, REBBECA ZIV HOSPITAL, ZEFAT

Session IX - Retina 2 09:30 - 10:30

Moderators: Joseph Ferentz and Dov Weinberger

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	(1) * OPHIR AVINOAM (2) MARTINEZ MICHAEL (1) OPHTHALMOLOGY, HILLEL-YAFFE MEDICAL CENTER, HADERA (2) OPHTHALMOLOGY, HILLEL-YAFFE MEDICAL CENTER, HADERA	
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	(1) * SEGAL ORI (1) VARON PERRI (1) FERENCZ JOSEPH (1) OPHTHALMOLOGY DEPARTMENT MEIR MEDICAL CENTER	
09:50-10:00	**THE EFFECT OF THROMBIN ON THE STRUCTURE OF TIGHT JUNCTIONS AND THE PERMEABILITY OF RPE AND ENDOTHELIAL CELLS.**	**126**
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(1) 1DEPARTMENT OF OPHTHALMOLOGY, RABIN MEDICAL CENTER, PETAH TIQWA, ISRAEL

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(1) * SOCEA SERGIU (1) MILLER BENJAMIN
(1) "ALBERTO MOSCUNA" OPHTHALMOLOGY DEPARTMENT, RAMBAM MEDICAL CENTER, HAIFA

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(1) * FABIAN IDO DIDI (1) KINORI MICKI (2) ABUDI ANAT (1) SKAAT ALON (1) GLOVINSKY YOSEPH (3) FARKASH INBAL (2) ZOHAR JOSEPH (1) MOISSEIEV JOSEPH
(1) THE GOLDSCHLEGER EYE INSTITUTE, THE SHEBA MEDICAL CENTER AND THE SACKLER FACULTY OF MEDICINE, TEL AVIV UNIVERSITY (2) THE DIVISION OF PSYCHIATRY, THE SHEBA MEDICAL CENTER AND THE SACKLER FACULTY OF MEDICINE, TEL AVIV UNIVERSITY (3) THE FACULTY OF MEDICINE, THE HADASSAH-HEBREW UNIVERSITY

10:20-10:30 **CHARACTERIZING THE RETINAL PHENOTYPE OF CCR2/CX3CL1 DOUBLE KNOCKOUT MICE** **129**
(1) * BURSTYN-COHEN TAL (1) OBOLENSKY ALEX (2) HANHART JOEL (1) TAL DAVID (1) BANIN EYAL (1) CHOWERS ITAY
(1) DEPT. OF OPHTHALMOLOGY, HADASSAH MEDICAL CENTER (2) CURRENT ADDRESS: MEDICAL RETINA SERVICE, MOORFIELDS EYE HOSPITAL, LONDON

Guest Lecture 2: 10:30 – 11:00

Prof. Richard A. Stone, MD

William C. Frayer Professor of Ophthalmology
University of Pennsylvania School of Medicine
Scheie Eye Institute & Children's Hospital of Philadelphia

TITLE: **Rhythms, Light and Refraction**

Coffee and Posters 11:00 – 11:30

Session X – Cornea 2 and Oncology 11:30 - 12:30

Moderators: Irina Barequet and Jacob Pe'er

PE'ER JACOB
(1) SCHOOL OF COMPUTER SCI & ENG, HEBREW UNIVERSITY, JERUSALEM, ISRAEL (2) OPHTHALMOLOGY DEPARTMENT, HADASSAH HEBREW UNIVERSITY MEDICAL CENTER, JERUSALEM, ISRAEL (3) GRADUATE OF CALIFORNIA AT BERKELEY, GRADUATE PROGRAM IN BIOPHYSICS AND DEPARTMENT OF MECHANICAL ENGINEERING. UNIVERSITY OF OF CALIFORNIA AT BERKELEY (4) GOLDSCHLEGER EYE RESEARCH INSTITUTE, TEL AVIV UNIVERSITY

12:20-12:30

AC

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EXPRESSION OF CXCR4 IN PRIMARY AND METASTATIC UVEAL MELANOMA

(1) * LIFSHITS MILLER ARIELA (2) PELED AMNON (1) PE'ER JACOB (1) FRENKEL SHAHAR
(1) DEPARTMENT OF OPHTHALMOLOGY, HADASSAH-HEBREW UNIVERSITY MEDICAL CENTER, JERUSALEM, ISRAEL (2) GENE THEREPY, HADASSAH-HEBREW UNIVERSITY MEDICAL CENTER, JERUSALEM, ISRAEL

Concluding Remarks 12:30 – 12:35

Eyal Banin

ABSTRACTS

Session I – Poster presentations 1

RETINAL TOXICITY OF INTRAVITREAL RITUXIMAB IN A RABBIT MODEL

(1) * HABOT-WILNER ZOHAR (1) SHAHAR JONATHAN (2) ZEMEL ESTER (2) PERLMAN IDO (1) LOEWENSTEIN ANAT
(1) OPHTHALMOLOGY DEPARTMENT, TEL-AVIV SOURASKY MEDICAL CENTER & SACKLER FACULTY OF MEDICINE, TEL AVIV UNIVERSITY,TEL AVIV (2) RAPPAPORT INSTITUTE, RUTH & BRUCE RAPPAPORT FACULTY OF MEDICINE, TECHNION, HAIFA

Introduction: Rituximab is a chimeric mouse/human monoclonal antibody that acts against the B cell antigen CD20. This antigen is expressed by all B cells until they differentiate into mature plasma cells. Treatment with rituximab results in a marked, sustained reduction in the number of both normal and malignant B cells . Recently, few studies published on the use of 1 mg/0.1 ml intravitreal rituximab for vitreoretinal lymphoma and demonstrated its effective treatment. Although clinical observations from a small number of patients do not point to retinal toxicity, no study has yet been published addressing this fundamental aspect. Our aim was to evaluate retinal toxicity of intravitreal rituximab in a rabbit model.
Patients / Methods: Seven New Zealand white rabbits were used. The Right eye of each rabbit was injected with 1 mg/0.1 ml rituximab solution (Experimental eye) and the left eye was injected with 0.1 ml saline (control eye). Electroretinogram (ERG) and Visual Evoked Potential (VEP) were recorded at 3 hr, 3 days, 1, 2 and 4 weeks. Histological preparations and GFAP immunostaining were made throughout the follow-up period. In addition, slit lamp examination was performed in all time points.
Results: No differences in the b-wave maximal (saturating) amplitude (Vmax), the luminance for reaching 50% of Vmax (σ) or the light-adapted amplitude ERG were found between experimental and control rabbit eyes. Similar flash VEP responses were found in experimental and control rabbit eyes. Morphology and GFAP expression of retinas in eyes exposed to the rituximab solution was normal. No abnormal findings were noticed on slit lamp examinations.
Conclusions: A dose of 1 mg/0.1 ml of rituximab, the clinically used dose, did not cause measurable or morphological toxic effects to the rabbit retina. These findings may lay the ground for its safety intraocular use.

FUNCTIONAL AND MORPHOLOGICAL CHANGES IN THE RETINAS OF CCR2 AND CX3CR1 KNOCKOUT MICE

(1) * EZRA-ELIA RAAYA (1) SHPIGEL Y NAHUM (1) BARISHAK Y ROBERT (1) OFRI RON
(1) KORET SCHOOL OF VETERINARY MEDICINE, HEBREW UNIVERSITY OF JERUSALEM, REHOVOT, ISRAEL

Introduction: Accumulation of microglial cells (MC) and macrophages in the subretinal space is suspected to be a key step in the pathogenesis of age-related macular degeneration (AMD). The chemokine Cx3cl1 and its receptor, Cx3cr1, are constitutively expressed in the retina, and are considered to have a role in retinal homeostasis of MC. Ccl2 and its receptor, ccr2, are also expressed in the retina under certain conditions, and might play a role in monocyte and MC recruitment and accumulation in AMD. Our aim was to evaluate functional and morphological changes in the retinas of Cx3cr1 knockout (KO) and Ccr2 KO mice, as a first step towards our major objective of developing a new Cx3cr1/Ccr2 double KO mice model.
Patients / Methods: Scotopic and photopic electroretinograms (ERGs) were recorded from seven Ccr2 KO, five Cx3cr1 KO and five control (C57BL) mice. Retinas of both Ccr2 and Cx3cr1 KO mice were studied histologically.
Results: Scotopic and photopic b-waves implicit times of Cx3cr1 KO mice were significantly prolonged compared to controls. Photopic b-wave and flicker amplitudes were significantly lower. ERGs of Ccr2 KO mice were not significantly different from those of control animals; though scotopic a-wave amplitudes tended to be lower than those of C57BL. In both groups we observed indications of degenerative changes in the RPE, and proliferation with “lacy-like” atrophy. Undulation of the outer and inner nuclear layers, associated with accumulation of debris between the RPE and photoreceptors, was also observed.
Conclusions: This is the first report of changes in retinal function in Cx3cr1 KO's. ERG deficits observed are compatible with those reported in other AMD mice models. Our histological findings confirm typical lesions in both KOs and together with ERG findings in Cx3cr1 KO reinforce our selection of Ccr2 KO and Cx3cr1 KO as founders of a Ccr2/Cx3cr1 DKO mouse.

INCIDENCE AND RISK FACTORS OF DIABETIC RETINOPATHY IN DIABETES TYPE 2 IN JEWISH AND BEDOUIN POPULATION IN SOUTHERN ISRAEL.

(1) CHORNY ALEX (2) LIFSHITZ TOVA (2) LEVY JAIME (3) GOLDFARB DANIEL (2) * KNYAZER BORIS
(1) FACULTY OF MEDICAL SCIENCES, BEN-GURION UNIVERSITY IN THE NEGEV, BEER SHEVA, ISRAEL (2) OPHTHALMOLOGY DEPARTMENT, SOROKA UNIVERSITY MEDICAL CENTER, BEN-GURION UNIVERSITY IN THE NEGEV, BEER SHEVA, ISRAEL (3) CLALIT HEALTH SERVICES, SOUTHERN DISTRICT, BEER SHEVA, ISRAEL

Background: Diabetic retinopathy is the most common microvascular complication of diabetes and accounts for 14.4% of cases of legal blindness in Israel. In recent years, there is a dramatic increase in the number of diabetic patients in the Bedouin population in the Negev region.
Purpose: The purposes of this study were to analyze the demographic and clinical features of diabetes type 2 patients in the Jewish and Bedouin populations, and to find out the incidence of diabetic retinopathy and its risk factors within these populations.
Methods: Data was collected from 523 diabetes type 2 patients (350 Jews and 173 Bedouins), which were examined by ophthalmologists at different clinics in Southern Israel, and which weren't diagnosed with diabetic retinopathy until that examination. All the data was analyzed by univariate analysis, and a multivariate model was built to predict the risk to develop diabetic retinopathy, separately for Jewish and Bedouin population in the Negev.
Results: The average age of the Jewish diabetics was 64±10.3 years, and the average age of the Bedouin diabetics was 58.6±12 years ($P<0.001$). The average duration of the diabetes was approximately 7.7 years and was same in both populations. Treatment with insulin was administered to 14.5 % of Bedouins, compared to 5.7% of Jewish population ($P<0.001$). Eye complications (diabetic retinopathy and/ or maculopathy) were found in 13.4% of Jews, compared to 22% of Bedouins ($P<0.01$). Compliance to treatment in Jewish population was high compared to Bedouins. In the multivariate analysis we found 6 predicting factors for the development of diabetic retinopathy in the Jewish population - long duration of diabetes, older age, high HbA1C, insulin treatment, high levels of LDL and creatinine; and 4 predicting factors in the Bedouin population – long duration of diabetes, high HbA1C, insulin treatment and smoking.
Conclusions: The Bedouin diabetic patients in the Negev region suffer more from retinal diabetic damage compared to Jewish patients. Common risk factors for both populations are long duration of diabetes, high HbA1C and insulin treatment. Compliance to treatment in Jewish population was high compared to Bedouins. The findings of this study have shown that educational and screening program in both populations should be proposed to reduce the burden and to improve the clinical outcome of this devastating diabetes complication.

THE DIAGNOSTIC SIGNIFICANCE OF THE ERG A/B RATIO IN RETINAL DISORDERS

(1) * FERMAN-ATTAR GILI (1) ROTENSTREICH YGAL
(1) GOLDSCHLEGER EYE INSTITUTE, SHEBA MEDICAL CENTER, TEL-HASHOMER, ISRAEL

Introduction: Purpose: to investigate the electroretinogram (ERG) a-wave to b-wave (a/b) ratio in retinal disorders including retinitis pigmentosa (RP), cone-rod dystrophy (CRD) and congenital stationary night blindness (CSNB) in comparison to ocularly healthy individuals.
Patients / Methods: In a retrospective study the ERG records of both eyes of 128 subjects, including 53 RP patients, 12 CRD patients, 9 CSNB patients and 50 normal subjects were examined. All ERG testing were performed according to ISCEV standards protocol. ERG a-wave to b-wave ratio was calculated for scotopic condition in three incremental light intensities stimuli (2.44cd-s/m², 23.5cd-s/m², and 252cd-s/m²) and for photopic condition in two incremental light intensities (2.44cd-s/m² and 7.8cd-s/m²). The averages of the a/b ratios were compared between each group of subjects under each illumination.
Results: The average ERG a/b ratios for 2.44cd-s/m² stimulus under scotopic and photopic conditions were found to be in RP 0.69±0.05, 0.57±0.07,in CSNB 1.20±0.12,0.46±0.05, in CRD 0.47±0.06, 0.67±0.18 and in normal subjects 0.49±0.01, 0.29±0.01 respectivly . The average photopic and scotopic ERG a/b ratios in the RP and CSNB groups were significantly higher than that of normal subjects for all light intensities stimuli ($P<0.001$ for RP and CSNB patients). Only scotopic dimmer light intensities a/b ratios of the CSNB group was higher than the RP group. The scotopic and photopic a/b ratios of the CRD group were statistically higher from normal subjects in response to the brighter light intensities only ($P<0.05$). The scotopic a/b ratio in RP patients was significantly higher than in CRD patients only under the dimmer light intensity ($P<0.05$).
Conclusions: There is significantly higher a/b ratios in RP, CRD and CSNB as compared to normals for stimuli of different light intensities. In CSNB the inner compared to outer retina was found to be more affected than the RP and CRD patients in the scotopic condition. In the RP patients the inner retina was found to be more affected than the outer retina compared to CRD patients in the scotopic condition. These measures can help to elucidate the amount of pathology in the inner versus the outer retina in different types of retinal dystrophies.

INTRAVITREAL BEVACIZUMAB TREATMENT FOR MACULAR EDEMA DUE TO CENTRAL RETINAL VEIN OCCLUSION

(1) AXER SIEGEL RUTH (1) * DOTAN ASSAF (1) BOURLA DAN (1) MIMOUNI KARIN (1) BOR ELITE (1) WEINBERGER DOV
(1) DEPARTMENT OF OPHTHALMOLOGY, RABIN MEDICAL CENTER, BEILINSON CAMPUS

Introduction: We report the visual acuity (VA) and anatomical outcome of a cohort of 35 patients who received intravitreal bevacizumab (IVB) as a treatment for central vein occlusion (CRVO) induced macular edema.
Patients / Methods: Retrospective analysis of the medical records of all consecutive patients who received IVB due to CRVO induced macular edema from 2/07 till 8/10 and were followed for at least 6 months in Rabin medical center, Beilinson campus, was performed. The patients received 3 to 4 loading doses of IVB (1.25 mg), and were followed every 6 to 8 weeks. IVB was repeated when macular edema was present.
Results: The cohort included 35 eyes of 35 patients, with a mean age of 65.5 (SD 13.5) years, and a mean follow up time of 17.7(SD 10.8) months. The mean number of injections was 9.3 (SD 5). Systemic diseases included: Hypertension in 74.3%, hyperlipidemia in 34.3% hypercholesterolemia in 28.6%, NIDDM in 57.1%, and atherosclerotic cardiovascular disease in 37.1%. Glaucoma occurred in 28.6%. The mean initial logMAR visual acuity (VA) was 0.9 (SD 0.49), and the mean initial Snellen VA was 6/98, which improved to logMAR VA of 0.7 (SD 0.5), and Snellen VA of 6/65 at the final visit ($p= 0.009$). The Snellen VA was preserved or improved in 83% of the eyes, and 60% of the eyes gained 2 or more lines. Positive correlation was found between the initial and final VA ($p<0.0005$). The mean initial central maculr thickness (CMT) was 489.5 (SD 175) microns, and the final CMT was 395 (SD 223) microns. This difference was not statistically significant ($p=0.24$). However, positive correlation was found between the gain in VA and the reduction in CMT ($p<0.0001$). No correlation was found between the VA and the number of injections.The mean initial and final IOPs were 13.9 (SD 2.9) and 15.1 (SD 3.5) mm Hg respecively. This difference was not statistically significant. There was no statistically significant difference in VA and CMT between pseudophakic and phakic patients.
Conclusions: IVB for the management of CRVO, improved visual acuity and .reduced CMT. Patients presenting with better initial VA had better final VA.

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

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(1) TEL-AVIV UNIVERSITY, TEL-HASHOMER, ISRAEL , GOLDSCHLEGER EYE RESEARCH INSTITUTE (2)TEL-HASHOMER, ISRAEL, CANCER RESERCH CENTER (3)TEL-HASHOMER, ISRAEL, HEMATOLOGY DEVISION

Introduction: To investigate the effect of subretinal injection of allogeneic human derived bone marrow mesenchymal stem cell population (hBM-MSCs) on the retinal functional electroretinographic activity and retinal structure of the Royal College of Surgeons (RCS) rats.
Patients / Methods: hBM-MSCs from healthy donors exvivo expended (CD73+; CD90+, CD105+, CD45-), up to for four passages were transplanted into the sub-retinal space of one eye of 20 RCS rats 4 weeks of age. Ten RSC rats were subretinal injected with saline as control. The ERG responses of both eyes of all the animals was tested before the injections and after the injection during twenty four weeks. Animals were dark-adapted for a minimum of six hours prior to the ERG measurements. ERGs were recorded from both eyes simultaneously using golden wire loops on the corneas. The eyes were enucleated and processed for histology.
Results: Four weeks after injection, the b-wave amplitude responses of the scotopic and photopic ERG showed 77% deterioration from baseline compared to 94% deterioration (P=0.005) in the control groups (not injected eyes and saline injected eyes). These significant diferences ($p<0.05$) were found up week ten. However post week 10 only 5 animals were left. A cryo-sections obtained at 2-weeks post hBM-MSCs injection, showed a uniform spread of thin red layer (DiI stained cells) over the entire sub-retinal space.
Conclusions: Using a new administration technique that allows homogenous sub-retinal distribution of stem cells we showed for the first time that a hBM-MSCs is capable of preserving significant retinal function

THE ROLE OF LIM-DOMAIN BINDING PROTEINS IN RETINAL DEVELOPMENT

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Introduction: LIM-domain binding (Ldb) proteins are essential cofactors to the LIM proteins including the LIM only (LMO) and LIM-homeodomain (LIM-HD) factors. The binding of the Ldbs to the LIM proteins results in different consequences depending on the promoter involved and can activate or repress gene expression in a dosage dependent manner. Functional studies revealed roles for LIM-proteins in early stages of optic cup formation as well as neurogenesis of retinal neurons (e.g: Lim1, Lhx2, Islet). Interestingly, complete loss of Ldb1 results in embryonic lethality at E9.5-10.0 due to the truncation of head structures, thus preventing studies on Ldb1 function in the retina. In contrast the Ldb2-/- mice do not exhibit a retinal phenotype and thus Ldb2 seems dispensable for retinogenesis. The aim of this study is to investigate the roles of the two mammalian Ldb proteins (Ldb1 and Ldb2) in retinogenesis.
Patients / Methods: To this end we established the Ldb1loxP/loxP;Ldb2-/-;a-Cre mice in which the Ldbs were deleted exclusively in the retinal progenitors of the optic cup prior to onset of cell differentiation. The phenotype of Ldb1 f/f Ldb2-/-;αCre was compared to that of controls. Embryos and post-natal mice were examined with Immunoflorescence on paraffin sections.
Results: During embryogenesis, Ldb1 expression is detected throughout the optic cup including the neuroblastic layer (NBL) and in precursors populating the inner nuclear layer (INL). In the adult retina Ldb1 expression is maintained in neurons of the inner nuclear layer and ganglion cells but is lost from photoreceptors. The inactivation of Ldb1 in the Ldb1loxP/loxP; Ldb2-/-;α-Cre mutants was evident at E12. The loss of Ldbs resulted in depletion of the retinal progenitors based on reduction in the number of cells expressing ki67, Sox2 and Chx10. This elimination of RPCs probably is due to premature onset of neurogenesis following Ldb1 loss. The loss of Ldb1 further abrogates the formation of specific retinal lineages including the ganglion cells and photoreceptor cells.
Conclusions: Our initial analysis revealed a role for Ldb in maintaining the pool of RPCs and in acquisition of distinct retinal lineages.

ERECTILE DYSFUNCTION IS ASSOCIATED WITH RETINOPATHY IN DIABETIC MEN: TWO MANIFESTATIONS OF A SYSTEMIC MICRO-VASCULAR DISEASE

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Introduction: Erectile dysfunction (ED) and diabetic retinopathy are prevalent manifestations of systemic vascular disease in diabetic men. However, to the best of our knowledge, the association between ED and diabetic retinopathy has never been studied.
Patients / Methods: A prospective study conducted between October 2008 and April 2010 in the Retina clinic of a tertiary medical center. The study group included men with proliferative diabetic retinopathy (PDR) or with severe non-proliferative diabetic retinopathy (NPDR). The control group included diabetic men without retinopathy or with mild NPDR. All men filled in the Sexual Health Inventory for Males questionnaire (SHIM) in order to detect ED and assess its severity. Significant ED was defined as SHIM questionnaire score lower than 18.
Results: The cohort included 103 diabetic men: 65 (63.2%) men in the study group and 38 (36.8%) men in the control group. Mean age for the entire cohort was 63.7±8.7 years, and mean diabetes duration was 14.6±8.9 years. Mean SHIM score for the entire cohort was 11.5±6.5, and 76 (73.8%) men had significant ED. Men in the study group had higher prevalence of significant ED compared with men in the control group [87.7% vs. 50.0%; OR 7.1 (95%CI 2.7-18.9); $p<0.0001$], as well as lower mean SHIM score (9.5±5.3 vs. 14.7±6.9; $p<0.0001$). Binary logistic regression analysis and linear regression analysis showed that significant ED and SHIM scores, respectively, were associated with diabetic retinopathy ($p<0.0001$ for both) independent of age, diabetes duration, ischemic heart disease, cerebrovascular disease, hypertension, hyperlipidemia and smoking.
Conclusions: ED is associated with diabetic retinopathy independent of age, diabetes duration, macro-vascular co-morbidities and cardiovascular risk factors. We believe diabetic men with retinopathy should be screened for ED, and vice versa.

POLY-LACTIC-CO-GLYCOLIC ACID (PLGA) - IS IT TOXIC TO THE RETINA?

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Introduction: Recently controlled and slow release devices for the posterior segment (ozurdex, experimental antibody release devices) increasingly make use of Poly lactic co glycolic acid (PLGA) as the biodegradable component in the device. The purpose of this study is to evaluate retinal toxicity of PLGA.
Patients / Methods: Empty PLGA beads (a ratio of 50:50 of lactic and glycolic acid, average diameter of 50 µm) were prepared and sterilized. The beads were dissolved in saline and injected intravitreally in two doses (10, 20 mg/0.1ml) to the right (experimental) eye of each rabbit, the left (control) eye was treated with 0/1ml of sterile saline. Five rabbits were included in each group. Electroretinogram (ERG) and visual evoked potentials (VEP) was recorded at 3 hours, 3 days, 1, 2 and 4 weeks post injection. A wave to b wave amplitude analysis was done. Histology examination and immunostaining for glial fibrillary acidic protein (GFAP) was done.
Results: The average Vmax ratio and amplitude ratio (dark and light adapted state respectively) of the ERG recordings were ~1. Average log sigma difference for the dark adapted state at 0. A wave to b wave amplitude graphs revealed no~all the time points was significant difference between control and experimental eyes in both groups. The retinas of experimental and control eyes from both dose groups' rabbits showed normal histology but positive GFAP staining only in experimental eyes.
Conclusions: Intravitreally injected empty PLGA did not cause changes in retinal function or structure. GFAP positive staining of eyes that were treated with both doses indicate Muller cells activation and therefore possibly a small degree of retinal damage. Although it is hard to extrapolate from an animal model to human eye these data indicate the safe use of PLGA intraocularly.

IMMUNE INTERACTIONS OF HUMAN EMBRYONIC STEM CELL-DERIVED RPE CELLS IN DYSTROPHIC RCS RATS

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Introduction: Regenerative cell therapy holds promise in restoring vision in eyes affected by degenerative disease. We have previously shown survival and function of retinal pigment epithelium cells(RPE) derived from human embryonic stem cells(hESCs) in the RCS-rat model of retinal degeneration caused by RPE dysfunction. Key to the successful application of such technology in humans are the immune interactions of the transplanted cells with the host. In the present study we examined the immunologic consequences of transplanting hESC-derived frozen/thawed (F/T) RPE-cells in dystrophic RCS-rats with and without systemic immunosuppressive cyclosporin treatment.
Patients / Methods: RPE cells were derived in-vitro from hESCs according to our published protocol, and frozen for long-term preservation. Subsequently, thawed cells were transplanted into the subretinal space of one RCS rat eye at 3weeks of age. Fellow control-eyes were either non-treated or medium-injected. Survival and effect of the transplanted cells on retinal function were assessed using in-vivo fundus imaging and ERG recordings 4-5weeks after transplantation. At this timepoint, serum levels of three major cytokines, IL-10, TNF-α, and INF-γ, were determined by Elisa. Histology and immunohistochemistry were used to identify the transplanted cells and the presence of CD4,CD8, CD25 and CD172a-positive cells in vicinity to the grafts.
Results: ERG-recordings revealed that retinal function was better preserved in hESC-RPE transplanted eyes as compared to control non-transplanted fellow-eyes. Interestingly, a more prominent rescue effect was present in non-immunesuppressed animals than in cyclosporine-treated. In transplanted, non-suppressed animals, serum IL-10 levels were elevated; this increase did not occur in cyclosporine-treated transplanted animals, and TNF- α levels were also suppressed in this group. Serum levels of INF-γ did not significantly differ. At 4-5weeks post-transplant, we did not observe a prominent local inflammatory response or presence of immune cells in proximity to the grafts.
Conclusions: F/T-RPE-like cells can survive for at least 4-5weeks after transplantation into RCS-rat eyes, and confer functional and structural rescue. Interestingly, this protective effect was more pronounced in non-immunesuppressed animals. The lack of a significant local retinal inflammatory response supports the concept that the subretinal space functions as an "immune privileged" site. The serum cytokine profile may suggest that transplanted cells can confer an immune-tolerant state.

ROLE OF SIRT6 IN RETINAL AGING

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Introduction: Sirtuins, also known as Silent Information Regulator Two (Sir2) proteins, are a family of proteins with histone deacetylase and/or mono-ribosyltransferase activity. SIRT6 is one of the seven mammalian homologs of Sir2, and possesses histone H3K9 and H3K56 deacetylase activity that modulates telomeric chromatin and cellular senescence. Overexpression of sirtuins in many organisms promotes longevity, while their absence may cause early senescence. In the present study we used sirt6 knockout mice (Sirt6-/-) to assess the role of Sirt6 in retinal aging.
Patients / Methods: Retinal function and structure were compared over the span of 10 months between three groups of mice: homozygous Sirt6-/- knockouts, heterozygous Sirt6+/- (hz), and normal wild type (wt) mice. At 1,6 and 10 months of age, retinal function was evaluated by electroretinography (ERG) and quantitative histologic techniques were used to assess retinal structure.
Results: Sirt6-/- mice demonstrated a high rate of early postnatal lethality and were characterized by developmental retardation, low body weight and a short lifespan. At 1 month of age Sirt6-/- mice demonstrated a trend toward lower dark-adapted b-wave amplitudes as compared with wt animals. At this time, no changes in outer nuclear layer (ONL) thickness were found between wt and Sirt6-/- mice. However, at 6 months, dark-adapted ERG responses were significantly (by 45% at highest stimulus intensity) reduced in Sirt6-/- animals compared with wt control. Cone function was also markedly affected, being 2.5-3-fold lower in Sirt6-/- mice. ONL thickness was significantly reduced in the central retina of Sirt6-/- mice ($p<0.02$) at this time point. At 10 months of age severe impairment of retinal function was observed in Sirt6-/- mice, with dark-adapted b-wave amplitudes reduced by 39% and cone-flicker ERG amplitudes reduced by 75% as compared with wt. Further thinning of the ONL not only in the central but also in the mid-peripheral and peripheral retina was evident, accompanied by thinning of other retinal layers. There were no significant differences in ERG amplitudes between wt and hz mice.
Conclusions: Sirt6-/- mice demonstrate age-dependent impairment of retinal function accompanied by thinning of the ONL. The results suggest a role for Sirt6 in maintaining survival and function of retinal cells over time.

DIFFERENTIATION OF PAX6- RPCS IS PROLONGED AND SKEWED TOWARDS EARLY AMACRINE TYPES

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Introduction: Amacrine cells are a diverse group of interneurons with over 30 distinguishable morphological subtypes that modulates the information flow from bipolar to ganglion cells. Studies have shown that the subtype identity of amacrine cells depends on their day of birth. The transcription factor Pax6 was previously implicated in multiple functions during retinogenesis, and was found to be required for the multipotency of RPCs as Pax6- RPCs generate exclusively Amacrine cells.
Patients / Methods: Using conditional Pax6 knockout models we characterized the various attributes of Amacrine cells development.
Results: We found that Pax6- RPCs generate almost exclusively the earliest amacrine subtypes and that amacrine maturation was grossly delayed. In addition, while expression of amacrine specification factors remained largely unperturbed, we noticed that the Pax6- RPCs generated a reduced number of differentiating amacrine cells during embryonic stages. Further more, while we noticed a clear reduction in BrdU uptake by mutant RPCs, a cell cycle exit analysis did not indicate increased cell cycle exit. We also noticed that amacrines differentiation which normally occurs between E13.5 and P0 extended from E15.5 to P15 in the mutant. Finally, we describe an abnormal expression pattern of several key factors involved in cells cycle regulation.
Conclusions: This study indicates that Pax6 is required for regulating both differentiation timing and cell fate acquisition. We suggest that without Pax6 RPCs receive conflicting cues for both differentiation and proliferation and spend a longer time in early G1 phase of the cell cycle.

HYPERGLYCEMIA INDUCES MICROPARTICLES FORMATION AND AFFECTS THEIR ANTIGENIC EXPRESSION AND THROMBOGENICITY

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Introduction: Diabetic retinopathy (DR) can result in severe visual loss that occurs due to ischemia- induced proliferation of new vessels and increased vascular permeability.

Diabetic patients demonstrate increased production of microparticles (MPs) and increased MPs of platelet origin and demonstrate a variety of thrombogenic and angiogenic profiles correlating to different diabetic vascular complications.

We hypothesize that systemic MPs reflect and affect the balance between thrombogenicity, angiogenesis and inflammation. We also believe that the local release of MPs from disrupted microvascular cells may play a role in the pathogenesis of DR.

The study objective was to isolate and characterize MPs derived from primary human retinal endothelial cells (HREC) in hyperglycemic conditions.

Methods: MPs were isolated from HREC cultured in hyperglycemic conditions for 24 hours. Hyperosmolar conditions were used as controls.

MPs were characterized and compared to their parent cells by flow cytometry. Several parameters were analyzed including endothelial markers (CD144, CD31), content of negatively charged phospholipids (NC-PL), tissue factor (TF), the main initiator of blood coagulation, its inhibitor tissue factor pathway inhibitor (TFPI), endothelial protein C receptor (EPCR), thrombomodulin (TM) and vascular endothelial growth factor (VEGF) receptors KDR and Flt-1.

Results: HREC stimulation resulted in increased levels of cell apoptosis and release of MPs. Isolated MPs from HREC stimulated by hyperglycemia expressed a much higher content of NC-PL compared to their cellular origin, 71.16% in MPs and 15.21% in cells. Stimulated HREC expressed low levels of TF 2.6% with a slight increase in TF expression on MPs (~7.5%). MPs of HREC stimulated by hyperglycemia expressed lower levels of natural anticoagulants including EPCR (2.425%) and TFPI (25.22%) compared to cellular EPCR (82%) and cellular TFPI (74.2%). Similar results were demonstrated in the hyperosmolar group. Stimulated HREC MPs are procoagulant, regardless of stimulation conditions hyperglycemia or hyperosmolarity.

Conclusions: Retinal endothelial cells MPs released during hyperglycemia are procoagulant and express increased TF and NC-PL, which are essential for coagulation, and decreased natural anticoagulants. This may contribute to the

microvascular damage in the retina by enhancing local ischemia through micro-occlusions.
Further investigation is needed to establish their role as local affecters in the pathogenesis of diabetic retinopathy.

PROGRESSION OF LOW MYOPIA AND ASTIGMATISM IN AIRCREW

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Introduction: Ametropia can be a debilitating problem in aircrew. In spite of meticulous initial screening, some pilots do suffer a progression of myopia and astigmatism during their active service. The purpose of this study was to evaluate the progression and stabilization of myopia and astigmatism in air crew.
Patients / Methods: In a retrospective cross sectional study, 100 myopic/astigmatic aircrew (200 eyes) in the Israel Air Force (age> 30y) were randomly selected and their medical records were reviewed for progression of myopia and astigmatism since recruitment. All underwent annual refraction and ocular exams. We calculated changes in SEQ and astigmatism and the time of stabilization of refraction.
Results: On average, spherical equivalent progressed from -0.46±0.51D at age 18 to -1.2±1.19D (max seq -2.75D) stabilizing around 40 years of age. Cylinder progressed from 0.42±0.35D at age 18 to 0.60±0.53 D (max cyl 3.0D) stabilizing around 35-40 years of age. The maximal progression rate was noted between age 20-25 for cylinder (0.04D/year) and age 25-30 for spherical equivalent (0.1D/year).
Conclusions: Astigmatism progression reaches a peak earlier than myopia progression (20-24 years vs 25-30 years) Both tend to stabilize around the age of 40.

REDUCTION IN ASTIGMATISM USING PROPRANOLOL AS FIRST-LINE THERAPY FOR PERIOCULAR CAPILLARY HEMANGIOMA

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Introduction: Monocular astigmatism causing amblyopia is a vision-threatening complication of a periocular capillary hemangioma. The aim of this study was to examine the shift in astigmatic error following the use of oral propranolol as first-line treatment for periocular capillary hemangioma.
Patients / Methods: Study population: Three healthy infants (2 males) clinically diagnosed with periocular capillary hemangioma. Cycloplegic refraction measurements were obtained at presentation. After a comprehensive clinical evaluation, oral propranolol therapy was starting with a loading dose and titrated up to 2 mg/kg/day under monitoring of heart rate, blood pressure and blood glucose alterations. Clinical follow-up and repeating cycloplegic refraction measurements were undertaken at the 1-week, and 1- and 3-month follow-up visits. Intervention: Oral propranolol therapy for infants diagnosed with periocular capillary hemangioma. Main outcome measures: Astigmatic refractive errors before and after propranolol treatment.
Results: The infants' mean age at the initiation of propranolol therapy was 6.7 months (range: 3-9.0 months). A rapid therapeutic effect was noticed in all cases, including a major change in lesion size and color. No complications were recorded during or following treatment. The mean astigmatic error decreased from 2.83 diopter before propranolol treatment to 1.33 diopter after one month of treatment. The drug was well tolerated by all 3 patients and no side effects were noted.
Conclusions: Infants can benefit from a rapid meaningful reduction in periocular capillary hemangioma induced astigmatism following oral propranolol treatment. Propranolol seems to be an effective and safe drug, which can be used as a steroidal-sparing first-line treatment modality in this patient population.

AN EVALUATION OF THE L-80 AUTOREFRACTOMETER

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Introduction: Purpose: A clinical evaluation of the L80 wave+ autorefractometer (AOR) (Visionix) was performed to evaluate validity and repeatability compared with non-cycloplegic subjective refraction. The L80 wave+ AOR is a new device which can measure auto-refraction, keratometry, topography of the cornea and high order ocular aberrations. It is the first Hartmann Shack technique based machine that has a specific autorefractor function that is designed to be used as an AOR and not a wavefront device.
Patients / Methods: Refractive error measurements were obtained from 100 eyes of 50 subjects (aged 25 ± 2.71 years), subjectively by a masked optometrist, and objectively with the L80 wave+ AOR. Intra-test and inter-test variability was assessed on 28 new subjects (58 eyes).
Results: The refractive error determined by the L80 wave+ AOR was slightly over-minus as compared to subjective refraction (-0.47 ± 0.47D for the spherical component, -0.20 ± 0.27 D for the cylinder component). An offset of 0.5 D sphere and 0.25 D cylinder on the L-80 AOR results in no statistically significant difference between the subjective and objective measurements ($p = 0.49$, $p = 0.06$, $p = 0.199$, $p = 0.37$ and $p = 0.69$, for sphere, cylinder, spherical equivalent, J0 and J45, respectively). The instrument was valid and reliable over a wide range of refractive errors (-11.25 to +3.50 D sphere equivalent). High Intra-test and inter-test repeatability was demonstrated for all parameters measured.
Conclusions: The L80 wave+ AOR represents a reliable and valid objective refraction tool for general optometric practice

UNDERSTANDING THE VISUAL WORLD AS A CHAMELEON

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Introduction: The common chameleon (Chamaeleo chameleon; Chamaeleonidea, Reptilia) is an arboreal lizard that forages visually for insect prey, using "sit/slow move and wait" tactics. Their eyes are highly mobile and perform large amplitude, independent, saccadic movements while scanning the environment. At any given time only one eye is accommodated, while the other is in a hyperopic, resting, refractive state. Attention switches between the eyes (Ott et al. 1998) while they scan regions opposite one another (Avni et al., 2006a, 2006b). Once prey is detected, the eyes converge, the tongue is loaded onto the hyoid ("initial protrusion"), distance is estimated using accommodation effort, and the tongue is shot at the prey. Chameleons' optic nerves are fully decussated and visual information from one eye is transmitted only to the contra-lateral optic tectum. While visually guided behavior in chameleons is well studied, the visual parameters eliciting their actual prey capture are unknown. Aims: To determine: (I) If chameleons respond to computerized "prey", (II) The visual parameters that affect prey detection, categorization and orientation.
Patients / Methods: Methods: The chameleons were tested on (a) images of real prey, (b) computerized a "prey" model (black rectangle with mobile "legs" on a white background), projected on a computer screen while controlling for linear/angular velocity, distance, motion amplitude and size.
Results: Results: (I) The chameleons responded to the computer images with full predatory responses. (II) (1) Latencies to respond to computerized prey were shorter than to images of real prey, (2) Optimal prey size (0.8x1.5 deg – 3.2x6 deg) was similar to chameleons of all size groups, (3) Marked individual differences were observed in the response to different prey size.
Conclusions: Conclusions: This is the first evidence for chameleons' predatory response to computerized "prey". Once a chameleon responds naturally to computerized stimuli an array of visual cues can be tested within or outside range of natural variation, e.g. contrast, focus, color, brightness, motion, moving background, etc. Visual acuity in relation to body and eye size will be considered in the results discussion.

A NOVEL VIDEO TOOL FOR THE ASSESSMENT OF INFANTS VISUAL ACUITY

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Introduction: Preferential visual acuity cards allow for the quantification of an infant's visual acuity. Their use in clinics is limited however, due to the equipment costs, skills and time required to administer the test. Visual acuity can be assessed by testing for optokinetic nystagmus (OKN). We have developed a computer-screen OKN-movie for infants that determines visual acuity by presenting variously sized OKN stimuli.
Patients / Methods: In this pilot study, forty-six children, ranging between 4 months and 12 years, were assessed both with our tool and a conventional near-vision test (Teller, Lea symbols, or Jaeger). Both normal and diseased eyes were assessed. The study was approved by the local Helsinki ethics review board.
Results: Conventional vision assessment could not be performed on 4 children due to lack of cooperation. In all 4 cases however, the children demonstrated interest in the OKN-video and an OKN-vision-score could be obtained. A favorable association was found between the scores of the OKN-tool and the distance-equivalent scores of the conventional tests for the 42 remaining children (Spearman rank correlation -0.3602, p-value 0.0044).
Conclusions: These preliminary results suggest that our OKN-video tool is a promising, cost-effective and user-friendly option for assessing infant's and toddler's visual acuity. It appears to be particularly useful in cases resistant to conventional testing.

FIXATIONAL EYE MOVEMENTS FOLLOWING STIMULUS ONSET REVEAL TWO TYPES OF SACCADIC INTRUSIONS

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Introduction: During attending a stationary visual target, our fixation is interrupted by involuntary low-amplitude saccadic eye movements, termed saccadic intrusions. Recently, several studies have suggested that saccadic intrusions execution, formerly referred as "microsaccades", is not random in time but rather is correlated with the stimuli onset. It was also found that saccadic intrusion suppression (intervals without saccadic intrusions) is correlated with specific stimuli features, such as contrast.
Patients / Methods: We performed several experiments, with and without fixation point in the center of the display, and with varying stimulus onset intervals. Subjects were instructed to report whether or not they have detected the target or discriminated between target orientations. Eye movements of the subjects were tracked during the experiments and analyzed off-line for detection and categorization of saccadic intrusions.
Results: We found two groups of saccadic intrusions divided by their latencies following stimulus onset. The first group is at about 200 milliseconds and the second group is above 300 milliseconds.
Conclusions: We show that the latency of the latter type of saccadic intrusions is task-dependent and delayed to at least 300 msec after stimulus onset. We also show that, on a trial by trial basis, the latency of saccadic intrusions is significantly correlated with the reaction time of the subject.
This supports the suggestion that this type of saccadic intrusions marks the end of processing and the "readiness" for attending new stimuli.

CLINICAL FINDINGS IN PATIENTS WITH HIGH HYPERMETROPIA

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Introduction: Hypermetropia is a refractive error affecting about 5% of the young population. In this condition, the ocular structure is usually normal, although macular abnormalities are rarely reported in patients with high hypermetropia. We analyzed clinical findings in patients with high hypermetropia.
Patients / Methods: 9 patients with high hypermetropia underwent a full ophthalmic examination, including refraction, orthoptic evaluation, slit-lamp examination, and funduscopy. Ocular coherence tomography (OCT) was performed in a subset of 3
Results: 9 children between the age of 6 and 18 years were included. All patients were of Bedouin origin and two were products of consanguineous marriages. Two patients had family history of eye problems. Visual acuity ranged from 6/7.5-6/60 , refractive errors (spherical equivalent) ranged from +5.75 to +15.75 diopters. All patients had astigmatism and five had anisometropia of at least 1.5 diopters. Six patients developed amblyopia. Spectacles were prescribed to all patients, but half of them had difficulty wearing them. An ophthalmic examination showed a reduced foveal light reflex in two cases and in one case retinal folds were observed. In the two first cases the OCT showed a normal retinal structure. In the third case, a girl with refractive errors of 13+ D, the OCT confirmed multiple macular folds
Conclusions: High hypermetropia, similar to high myopia, can be associated with disruption of normal ocular structure and ocular morbidity, causing impaired vision. Early diagnosis and close follow up are needed to prevent an additional visual loss due to reduced compliance with glasses and amblyopia, which is very common in this condition. A presence of macular folds in a patient with high hypermetropia should raise a possibility of posterior microphthalmos (a rare hereditary condition in which the eye anterior segment is normal in size and configuration, but the posterior segment is reduced in size)

CAN POSTERIOR CORNEAL ASTIGMATISM EXPLAIN RESIDUAL INTERNAL ASTIGMATISM IN PSEUDOPHAKIC EYES?

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Introduction: When implanting a toric intraocular lens the power and axis of the lens is intended to correct anterior corneal astigmatism. Residual internal astigmatism is not taken into account and might affect the results of cataract surgery with toric IOL. The purpose of this study was to determine whether posterior corneal astigmatism can account for the internal astigmatism in pseudophakic eyes.
Patients / Methods: 82 eyes (41 patients) that had uncomplicated phacoemulsification with spherical intraocular lens implantation during 2008 were evaluated at least one year post operatively. They underwent refraction, keratometry, posterior cornea keratometry with the GALILEI™ Dual Scheimpflug Analyzer (Ziemer Group; Port, Switzerland) and a full dilated ocular examination. Patients with astigmatism >2D were excluded. The internal residual astigmatism was calculated by vectorically subtracting the anterior keratometric astigmatism from the refractive astigmatism at the corneal plane and correlated with the posterior corneal astigmatism.
Results: Mean postoperative keratometric astigmatism was 0.83 D±0.50 [SD]) and mean postoperative refractive astigmatism was 0.70±0.52 D (P = 0.10). Regression analysis found a significant correlation between the refractive and keratometric errors of the J0 component (P<.001, r2 = 0.56) and between the refractive and keratometric errors of the J45 component (P<.001, r2 = 0.29). Internal residual astigmatism was 0.53±0.52 on J0 and -0.22±0.45 on J45. Mean posterior corneal astigmatism was 0.34±0.21D (0.21±0.24 on J0 and 0±0.24 on J45) and could explain about 10% (r2=0.1, P<0.001) of the residual internal astigmatism both on J0 and J45.
Conclusions: Keratometric astigmatism was responsible for about only 29%-56% of the refractive astigmatism. Posterior corneal astigmatism could explain about 10% of the residual internal astigmatism.

SYSTEMIC RISK FACTORS FOR BLEPHARITIS

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Introduction: Blepharitis is a very common under-diagnosed condition whose etiology is still unclear. Although it has been shown to associated with other conditions such as chalazia its systemic associations have not been investigated. The purpose of this study was to evaluate the prevalence of systemic medical conditions among patients with blepharitis.
Patients / Methods: In a retrospective case control study, all the members which were diagnosed with blepharitis in the Central District of Clalit Health Services in Israel, (years 2000-2009; n=16706) and 16706 age and gender matched controls randomly selected from the district members were included. We analyzed of the prevalence of various ocular and systemic risk factors as well as age, gender, marriage status, country of origin, place of residency and socioeconomic status.
Results: Demographically, a significantly higher tendency to develop blepharitis was found in populations of lower socioeconomic class, in population living in non urban areas and in Ashkenazi Jews. A significant association of $P< 0.001$ was found with some inflammatory diseases (gastritis, peptic ulcer, asthma, arthropathy, and ulcerative colitis), psychological associated conditions (anxiety, irritable bowel syndrome, neuroses and depression), hormonal conditions (hypothyroidism and prostatic hypertrophy), cardiovascular diseases (carotid artery disease, hyperlipidemia, hypertension and ischemic heart disease), and other eye conditions (chalazion, pterygium). The strongest associations found were between blepharitis and: chalazia (Odds ratio {OR} 4.7 ; confidence interval { CI } 3.8 - 5.7); rosacea (OR 3; CI 2.1 - 4.3); pterygia (OR 2.0; CI 1.5 – 2.6); ulcerative colitis (OR 2.3; CI 1.2 - 4.2) irritable bowel syndrome (OR 1.8 ;CI 1.3 - 2.5), anxiety (OR 1.6; CI 1.4 - 1.9), and gastritis (OR 1.6; CI 1.4 - 1.7).
Conclusions: Some ocular and systemic conditions are more prevalent among patients with blepharitis. Better understanding of the patho-physiological association between those diseases and blepharitis may help in its treatment and prevention.

COMPARISON OF ADVERSE SENSATIONS FOLLOWING INSTILLATION OF PRESERVED AND PRESERVATIVE-FREE DICLOFENAC SODIUM 0.1% EYE DROPS

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Introduction: Topical Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are widely used in ophthalmology. Diclofenac sodium 0.1% is often prescribed for the treatment of postoperative inflammation and pain relief. Its use has been associated with local adverse effects, which most commonly include transient discomfort, burning and hyperemia. These adverse effects have been linked to preservatives, and there is a constant industrial effort to create more tolerable preparations. The purpose of this study is to compare the early adverse sensations following instillation of preserved and preservative-free diclofenac sodium 0.1% (Voltaren Ophtha and Dicloftil, respectively).
Patients / Methods: One drop of each compound was instilled in a masked manner in either eye of healthy volunteers. The volunteers rated the amount of discomfort, itching sensation, burning sensation and pain in each eye using Visual Analogue Scale (VAS). Each parameter was rated before instillation, at 15 seconds, and 1, 5, 15 and 30 minutes after instillation. Values were tabulated and compared using paired t-test.
Results: Thirty volunteers participated in the study. Subject age was 33.17±10.94 years, range 29 to 64. Ten were female and 20 male. Mean adverse sensation before instillation was 2% or less for all parameters in both preparations. After instillation, Mean maximal value for discomfort, itching sensation, burning sensation and pain was higher in the eyes receiving preserved drops ($p<=0.01$ in each comparison).
Conclusions: These results indicate that the preservative-free diclofenac sodium preparation tested is better tolerated than the preserved preparation. Further research is needed to identify the factor (acidity, osmolarity, preservative or other) causing this difference.

FREQUENCY OF INVOLVEMENT OF THE DIFFERENT EXTRA-OCULAR MUSCLES IN MYASTHENIA GRAVIS

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Introduction: Each extra-ocular muscle may be involved in myasthenia gravis masquerading any type of ocular motor pathology. The frequency of involvement of each muscle is not well established in the medical literature. This study was designed to determine if there is any tendency for a specific muscle or muscles combination to be predominantly affected.
Patients / Methods: Retrospective chart review of myasthenic patients with extra-ocular muscles involvement. Included were 30 patients that had a clinical diagnosis of myasthenia gravis confirmed by at least one additional positive test: Tensilon test, acetylcholine receptor antibodies, thymoma on chest CT or suggestive EMG. Only patients in whom the neuro-ophthalmological examination documented involvement of a specific extra-ocular muscle (or muscles) were included.
Results: Frequency of involvement of each muscle in this cohort was as follows: inferior oblique 63%, lateral rectus 30%, superior rectus 23%, inferior rectus 20%, medial rectus 13%, and the superior oblique was involved in 6% of the patients.
Conclusions: The inferior oblique was the most frequently affected muscle. Diplopia caused by paresis this muscle is rarely encountered (other than as a part of oculomotor nerve palsy); hence, when a patient presents with vertical diplopia that results from an isolated inferior oblique palsy, myasthenic etiology should be highly suspected

ANALYSIS OF CELLULAR AND MOLECULAR EVENTS ASSOCIATED WITH OPTIC NERVE DEGENERATION AND REGENERATION

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Introduction: To elucidate the regenerative potential of injured optic nerve (ON). Results are presented of a study on the regenerative potential of CNS mammalian axons using our unique rat optic nerve model. The purpose was to analyze the cellular and molecular events that control the degenerative and regenerative processes in lower vertebrate such as goldfish, and mammals, following trauma to optic nerve. Understanding these events may lead to treatments for diseases and trauma that end in blindness.
Patients / Methods: The right optic nerve of adult rats was completely transected while sparing the vasculature and the meninges. Hyaluronic acid (HA)-based hydrogel containing supportive factors or self-assembling peptides (SAP) were implanted in the gap generated by the surgery. Two weeks and one month after the surgical procedure the animals underwent MRI evaluation of the visual pathway. Non-injured optic nerve served as positive control and axotomized optic nerve not implanted with HA or SAPs served as negative control. In a parallel set of experiments, the right optic nerve of adult goldfish was crushed or cut (equal number of fish in each group) under deep anesthesia. Two weeks and one month after the injury, markers associated with degenerative and regenerative processes were studied in the optic nerve and retina.
Results: The regenerative process was traced in vivo using Mn2+ enhancing signal. The signal in non-injured optic nerve was detected in the retina, optic nerve, optic tract, lateral jeniculate body, and visual cortex. The signal in axotomized axons was detected only in the vicinity of the retina and not in the optic nerve. These results reflect the degenerative process that destroys the ON axons in response to ON injury. Axotomized ONs that were treated with either HA or self-assembling peptides exhibited marked regeneration of the ON. Wefound out that administration of Semaphorins to ijured goldfish optic nerve markedly disrupted the regenerative process .
Conclusions: Conclusion: The optic nerve of lower vertebrates, such as goldfish, is capable of regeneration and regain of function while higher mammals, such as rat, require special modulations of the neuronal environment to enable partial regeneration.

Session II – Cornea 1

DELAYED LOSS OF CORNEAL EPITHELIAL STEM CELLS IN A CHEMICAL INJURY MODEL, ASSOCIATED WITH LIMBAL STEM CELL DEFICIENCY IN RABBITS

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Introduction: Ocular injuries following exposure to the chemical agent sulfur mustard (SM) are characterized by an acute phase, expressed by corneal erosions and inflammation of the anterior segment, followed by delayed corneal neovascularization and epithelial defects. Using impression cytology and histology, we defined the late injury, as Partial Limbal Stem Cell Deficiency (PLSCD). LSCD may derive from direct destruction of corneal epithelial stem cells (SC) and/or from altered stromal niche. The present study aimed to investigate the mechanism underlying LSCD in SM injuries, focusing on the primary effects of SM on corneal epithelial SC, compared to central corneal epithelium.
Patients / Methods: The chemical injury was induced by ocular exposure of rabbit eyes to SM vapor. Clinical follow-up was conducted including pachymetry. Eyes were taken for histology and molecular biology at different time points up to one week (complete healing of corneal erosions). SC were identified by morphology, immunohistochemistry and RT-PCR of ABCG2 and p63 and by in vivo Bromo-deoxy Uridine (BrdU) labeling.
Results: The slow cycling corneal epithelial SC were not damaged during the acute phase, in contrast to the severe loss of the highly proliferating epithelial cells in the central cornea. Furthermore, the SC in the limbus divided and migrated towards the injured central cornea as in a normal healing process, shown by increase in limbal epithelium thickness, elevation of ABCG2 mRNA and protein and pattern of BrdU labeling. The number of BrdU label retaining cells in the limbus was not decreased and the xyz phenomenon of corneal epithelial proliferation and regeneration was shown. Yet, while the limbal epithelium was not damaged, the limbal stroma displayed cellular infiltration and nerve damage.
Conclusions: LSCD associated with SM toxicity is not derived from a direct cytotoxic effect of SM, but indirectly from pathological processes in the SC niche. The absence of a primary damage of the epithelial SC, supports the notion that slow mitotic cells are more resistant to SM, a potent alkylating agent, than the proliferating cells and indicates the presence of a therapeutic window for intervention to avoid the development of LSCD associated with the SM long-term injuries.

SHORT TERM CLINICAL EVALUATION OF A NOVEL 23.5 DIAMETER GAS PERMEABLE SCLERAL CONTACT LENS

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Introduction: Gas-Permeable Scleral contact lenses are supported by the sclera and vault the cornea, thus allowing fitting of highly irregular corneas, many of which have failed with conventional contact lenses. These lenses can be used therapeutically for people suffering from chronic dry eye syndromes and offer protective functions for conditions such as trichiasis. The purpose of this research was short term clinical evaluation of a novel 23.5 diameter sclera contact lens produced by Soflex, Israel.
Patients / Methods: This scleral lens has a unique aspheric back optical surface with eccentricity of 0.40 to minimize higher order wavefront aberrations. It is made of Boston XO material with a DK off 100, center thickness of 0.4 mm at a power of 6 Diopters. Eleven patients (17 eyes) with highly irregular corneas participated in the study. Patients included keratoconus and corneal irregularities after penetrating keratoplasty. All were unable to successfully wear or achieve good visual acuity with other types of contact lenses. Lenses were fitted using preformed technique and were non-fenestrated.
Results: In this short term study, all the patients and all but one eye were successfully fitted with the scleral lenses. Many patients have reported long wearing time of >10 hours. The median best ±corrected visual acuity (Snellen Fraction) with the scleral lenses was 0.80 2.3, in compared with the Best Corrected Visual Acuity (BCVA) prior to the 0.30 (p±lenses of 0.32<0.001, t-test). Four patients went from counting fingers in one or both eyes to better that 0.67 with the scleral lenses.
Conclusions: Scleral lenses expand the management of various corneal abnormalities. The main indication for scleral lenses is optical correction of an irregular corneal surface, especially KC and corneal transplant.

THE EFFECT OF RIBOFLAVIN-UVA INDUCED COLLAGEN CROSSLINKING ON INTRAOCULAR PRESSURE MEASUREMENT

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Introduction: Corneal collagen cross-linking (CXL) using riboflavin (vitamin B2) and UVA irradiation has recently been introduced as a novel therapeutic option for the treatment of corneal ectasia, such as keratoconus. An increase in overall stiffness and rigidity in human corneas of up to 330% has been reported following this treatment.
Purpose: to investigate whether CXL affects the Tonopen measurements of intraocular pressure (IOP)
Patients / Methods: CXL with 0.1% riboflavin solution and 30 minutes of UVA radiation was performed on the right eye of 16 New Zealand albino adult rabbits (1.8 to 2.4 kg) (30 eyes). The left eye served as a control. IOP was measured by a pressure transducer system (True IOP) and by the Tonopen hand held device (corneal applanation tonometer) before treatment, at 1 week, 1 months and 3 months following CXL. Reference pressure in the globe was increased by increments of 10 mm Hg from 10 to 40 mm Hg, using an anterior chamber infusion on a stand with variable height, and tonopen IOP measurements were recorded for each reference pressure, in both eyes.
Results: Before CXL, tonopen readings were similar between the two eyes. Tonopen underestimated the true IOP in all cases. Following CXL treatment, IOP measurements were significantly higher in the treated eye, at all time interval. The most significant difference between true and measured IOP was noticed at 20 mmHg
Conclusions: IOP measurements following CXL are overestimated by the Tonopen, probably due to increased stiffness of the treated cornea

TOPICAL TREATMENT WITH TACROLIMUS 0.03% OINTMENT FOR SUBEPITHELIAL INFILTRATES SECONDARY TO ADENOVIRAL KERATOCONJUNCTIVITIS

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Introduction: To evaluate the treatment with topical tacrolimus 0.03% ointment (Protopic; Fujisawa Health, Deerfield, IL) in patients with subepithelial corneal infiltrates (SEIs).
Patients / Methods: We prospectively reviewed the records of 9 patients (11 eyes) before and after the treatment with tacrolimus 0.03% ointment twice daily. All patients had been treated with topical corticosteroids previously without improvement or had to stop the medication secondary to intraocular pressure elevation. The objective data recorded included best-corrected Snellen visual acuity, intraocular pressure and contrast sensitivity. Shirmer test, severity of conjunctival injection, conjunctival chemosis,punctate epithelial keratitis during the course of treatment, presence and severity of corneal subepithelial infiltrates were evaluated by a clinical score.
Results: Seven males (77%) and 2 females (22%), mean age of 52 +/- 10 years and. mean follow-up on tacrolimus was 6 +/- 2 months were included. The mean best-corrected Snellen visual acuity (Decimal) before and after treatment was 0.67+/- 0.29 and 0.98 +/- 0.20, respectively, with statistically significant improvement. Contrast sensitivity improved significantly at high spatial frequencies. Patients reported statistically significant reduction in the severity of symptoms before and after the treatment. Most of the patients reported no foreign body sensation, glare, or other side effects with topical tacrolimus treatment. Overall, patients noted an improvement in vision and satisfaction with tacrolimus treatment.
Conclusions: Topical tacrolimus 0.03% ointment is good alternative treatment in patients with SEIs who do not respond to other treatment modalities or have unwanted side effects from topical steroids

FLAP THICKNESS USING THE MORIA ONE USE-PLUS AND THE MORIA M2 MICROKERATOMES

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Introduction: Creating a flap of desirable size, thickness, and smoothness is a crucial step in LASIK. The Moria M2 Single Use 90-µm microkeratome (Moria, Antony, France) is a rotating, mechanical microkeratome with a mostly superior hinge position, which has been used for years in conventional LASIK. The Moria One Use-Plus microkeratome was recently introduced for thin-flap LASIK. The One Use-Plus is a linear mechanical microkeratome with a nasal hinge position.
Patients / Methods: In 1047 consecutive eyes that underwent LASIK we analyzed the accuracy and consistency of corneal flap thickness created using the Moria One Use-Plus -90 (OUP-90, n=415) microkeratome compared with the Moria M2 Single Use 90-microm microkeratome (M2-SU-90, n=632). Both groups were operated between January 2010 and August 2010 at Care-Vision Center, Tel-Aviv, Israel by the same 3 surgeons (each surgeon used both devices equally). In all cases, flap thickness was measured intra-operatively by ultrasonic pachymetry using the subtraction method.
Results: We did not find a significant difference in central flap thickness between the microkeratomes (113±15 microm vs. 111±22 microm in the OUP-90 and M2-SU-90 groups respectively, P = 0.1 t-test). We noticed a significant tighter distribution of flap thicknesses in the OUP-90 group. This resulted in a significantly lower standard deviation in the OUP-90 group (15 micron vs 22 micron, P < 0.001, F test). Similarly, the range of flap thicknesses in the OUP-90 group was tighter (73-152 micron) than in the M2-SU-90 group (52-174 micron). We noted a slightly increase rate of buttonholes in the M2-SU-90 group (0.47%, n=3 vs. 0.24%, n=1, p=0.9) and one incomplete flap and one free flap in the OUP-90 group while none in the M2-SU-90 group. We also noted a similar proportion of postoperative microstriae (2.7% vs. 2.1% respectively, p = 0.67) and DLK (1.2% vs. 2.4% respectively, p = 0.24).
Conclusions: The new Moria One Use-Plus is a safe and effective mechanical microkeratome which has a better predictability and accuracy than the Moria M2.

Session III – Highlights in Ophthalmology

THE USE OF BIOLON DURING DONOR'S CORNEAL HARVESTING FOR PRESERVATION OF THE ENDOTHELIUM

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Introduction: The use of viscoelastic substances has been proven to decrease damage to the corneal endothelium when applied during intraocular surgeries. Our purpose was to evaluate the protective effect of Biolon use on corneal endothelium, during donor's corneal harvesting.
Patients / Methods: A prospective, randomized, double blind, comparative trial was held. One cornea from each donor was harvested using intracameral injection of Biolon, and the other cornea, from the fellow eye, was harvested without Biolon (control). Endothelial images were acquired at the center of each cornea with a specular microscope 1 day after harvesting, and endothelium cell counts (ECC) were measured.
Results: 120 corneas were harvested from 60 donors, 28 men and 32 women. The mean age of the donors was 61.4+/-17.0 (median 68, range 17-86). ECC in the Biolon group was 2839+/- 412.5 (range 1950-4198), and in the control group 2748+/- 429.7 (range 1722-3620). (p=0.03, paired t-test), (p=0.02, Wilcoxon test for paired sample).
Conclusions: Intracameral Biolon injection while harvesting corneas seems to protect the endothelium from the mechanical damage induced during the procedure. Routine use of intracameral Biolon should be considered in this setting.

CROSSLINKING TREATMENT OF CYSTIC FILTERING BLEBS IN RABBITS

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Introduction: The use of MMC increased the frequency of hypotony maculopathy after trabeculectomy. Hypotony maculopathy is reported even without a detectable bleb leak. The bleb leaks subclinically and appears Seidel-negative, while it is seeping aqueous through microscopic areas of attenuated epithelium with lack of underlying sufficient fibrovascular or collagen support. Thus, alternative treatment to reinforce the bleb wall should be considered to decrease the risk of MMC-related bleb leaks. Collagen crosslinking induced by the photosensitizer riboflavin and ultraviolet A (UVA) irradiation has been found to be successful in stabilizing the cornea in keratoconus. We therefore presumed that collagen crosslinking might be useful in reinforcing the filtering bleb. This study evaluated the effect of collagen crosslinking on the cystic filtering blebs in rabbits.
Patients / Methods: 12 New Zealand white rabbits underwent trabeculectomy with MMC in both eyes. Thirty days following surgery and when a cystic bleb was present , one eye of each rabbit underwent a single UV irradiation with the photosensitizer riboflavin for 30 minutes on the bleb, the fellow eyes were not treated and served as control. Eyes were followed for 6 months and then enucleated and sent for histology.
Results: At the end of 6 months of follow-up 10 of the cross linking treated blebs and 9 of the control blebs survived. The functioning blebs looked avascular white in the cross linking treated group while the control blebs were avascular cystic. There was no difference in the extent and height of the functioning blebs in both groups, likewise there was no significant difference in the intraocular pressure among groups. The cross linking treated blebs domes contained formed epithelium overlying fibrovascular tissue. The control blebs domes showed attenuated epithelium, fragmented basement membrane, and acellular stroma.
Conclusions: : Collagen crosslinking by the photosensitzer riboflavin and ultraviolet light is an effective mean for reinforcing the cystic filtering bleb while achieving the desired outcomes of low intraocular pressure.

HOLOGRAPHIC PATTERNED STIMULATION FOR A RETINAL PROSTHESIS WITH SINGLE CELL RESOLUTION

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Introduction: Retinal prostheses for patients with outer-retinal degenerative diseases could interface directly with surviving retinal neurons using electrode array implants. Direct optogenetic stimulation has recently been introduced as an alternative method for spatially and temporally precise, minimally-intrusive control of neurons. However, to generate activity patterns that will be translated into a meaningful perception in the brain requires methods that can selectively excite a large population.
Patients / Methods: Here, we describe novel projection/excitation strategies that can be used to selectively control large retinal neuronal populations, with high temporal precision (msec) and efficient use of light power. Of existing display technologies, digital holographic projection ideally meets these constraints, because the use of phase-modulating spatial light modulators (SLMs) and light diffraction allows an efficient use of input light. Our system directs light from Blue, Green and Red DPSS Lasers onto a Ferroelectric liquid crystal SLM that displays binary holograms. Light patterns were coupled into the camera port of an inverted microscope and projected onto retinas, whose responses were measured using a Multi-Electrode Array (MEA)
Results: We demonstrate responses of a population of retinal ganglion cells to patterns of light holographically projected unto optogenetically transfected retinas, and following the dispersion of light absorbers. Using our methods, the neurons exhibit spatially-selective responses with a single cell resolution. In addition, we demonstrate sub-millisecond timescale control over the projected light patterns, multi-wavelength excitation, and computational strategies that eliminate the effect of speckle.
Conclusions: High-rate holographic projection was demonstrated as an enabling photo-stimulation modality towards the development of a retina neuro-prosthetic with single cell resolution and millisecond timing precision. We also show how focused illumination pulses absorbed by photo-absorbers led to rapid (milliseconds timescale) thermal transients with a well- defined and highly-localized dynamics, laying the foundation to a new strategy: photo-absorber induced neural-thermal stimulation (PAINTS).

GENE THERAPY IN ISRAELI PATIENTS WITH LEBER CONGENITAL AMAUROSIS CAUSED BY A RPE65 FOUNDER MUTATION

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Introduction: Gene therapy of human patients with Leber congenital amaurosis (LCA) due to mutations in the RPE65 gene became a reality following demonstration of safety and efficacy in RPE65-mutant dog and mouse models, and over the last three years has been successfully applied by three groups worldwide. Our goal was to identify and offer similar treatment to RPE65 LCA patients in the Israeli population.
Patients / Methods: A long-term program to characterize phenotype and genotype of Israeli patients with hereditary retinal degenerations was launched at our center a decade ago. Visual function and structure are evaluated using electrophysiological techniques, light- and dark-adapted perimetry, and non-invasive color, infrared, OCT and autofluorescence imaging. Molecular genetic techniques including homozygosity mapping and direct sequencing are used to identify disease-causing mutations. Gene therapy was performed in two RPE65 LCA patients by subretinal injection of the AAV2-CB-hRPE65 viral vector carrying the normal human RPE65 gene (Phase I clinical trial NCT00821340).
Results: A homozygous splicing mutation (c.95-2A>T; IVS2-2A>T) in the RPE65 gene was identified in 33 LCA patients from 10 unrelated families, all of North-African Jewish ancestry. Haplotype analysis revealed a shared homozygous region, indicating a population-specific founder mutation estimated to have emerged 100-230 (mean, 153) generations ago. Photoreceptor layer thickness was mapped by OCT in two of the LCA patients, and following vitrectomy, viral vector was delivered into the subretinal space at sites showing residual ONL. No toxicity or complications were observed to date. Post-operative follow-up indicates up to 100-fold increased sensitivity to light in the treated regions, persisting in the first patient for at least 9 months (the last timepoint thus far evaluated).
Conclusions: Sub-populations of defined ethnic origin who were historically isolated often manifest autosomal recessive disease due to highly prevalent founder mutations, and this can assist in obtaining a rapid molecular genetic diagnosis. Among North African Jews, the IVS2-2A>T RPE65 mutation causes over 50% of LCA cases, and gene therapy can now be offered to such patients. Previous studies by others as well as the present study attest to the safety and efficacy of such treatment.

ANTI-INFLAMMATORY EFFECTS OF ESSENTIAL FATTY ACIDS (EFA) ON CULTURED HUMAN CORNEAL EPITHELIAL CELLS AND CONJUNCTIVAL FIBROBLASTS

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Introduction: Recent studies showed that systemic Essential Fatty Acids (EFAs) may improve the symptoms of dry eye syndrome due to their anti-inflammatory effects. We have established an in-vitro model system to evaluate the anti-inflammatory effects of EFAs and mechanism of action on corneal epithelial cells and conjunctival fibroblasts in vitro.
Patients / Methods: Cell were incubated for 3 hours with different doses of three EFAs: Alpha-linolenic acid (ALA), Gamma-linolenic acid (GLA) and Linolenic acid (LA). Oleic acid (OA) and Dexamethasone (DM) served as negative and positive controls, respectively. Cells were stimulated with Polyinosinic:polycytidylic acid (poly I:C), or Lipopolysaccharide (LPS), combined with CD14 and LPS binding protein (LBP). Seven hours post exposure to EFAs, cells and supernatants were collected and tested for Prostaglandin (PGE2) secretion (Radio-immuno assay) and for pro-inflammatory protein levels with Cytometric bead array (CBA) and Western blot analysis. The mRNA levels of the inflammatory cytokines Interleukin (IL)-6, IL-8, IL-1β, and Tumor necrosis factor-α (TNFα) were tested by real time PCR. Viability of cells was tested with FITC-Annexin V/PI and MTT assays at the end of each treatment.
Results: The viability in the corneal epithelial cells and conjunctival fibroblasts was 95.5±1 and 97±0.8% respectively as compared to the negative control. The protein secretion of IL-6, IL-8, IL-1β, TNFα and PGE2 after stimulation with LPS and poly I:C was dramatically decreased after treatment with ALA as compared to OA, LA, GLA and DM ($p < 0.05$). In addition, ALA inhibited the LPS and Poly I:C-induction of inhibitory factor-κBα (I-κBα).
Conclusions: Our results demonstrate that ALA may serve a potent anti-inflammatory agent in ocular surface inflammation. The anti-inflammatory effect of ALA was more pronounced when compare to corticosteroids, and was mediated through NF-κB signal transduction.

CATARACT SURGERY WITH OCT-GUIDED FEMTOSECOND LASER: PRECISION AND EFFICACY

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Purpose:
We report on the precision, reproducibility and efficacy of an OCT-guided femtosecond laser cataract system to facilitate and automate the capsulorhexis and lens fragmentation.
Methods:
In a randomized clinical trial 29 patients underwent cataract surgery of both eyes. One randomly assigned eye received capsulotomy and lens fragmentation with a femtosecond laser (Catalys, Optimedica) while the other acted as a control eye with standard manual cataract surgery. The excised capsulotomy disc was removed, followed by phacoemulsification and placement of an intraocular lens. Calibrated high definition video microscopy was used to measure the excised capsulotomy disc. The shape of the anterior capsular disc and centration of the resulting opening was also assessed. Cumulative Dispersed Energy (CDE) was recorded and analyzed with respect to study arm and cataract grade (LOCS).
Results:
The average deviation of the capsulotomy disk diameter from intended was 29μm ± 25μm with laser and 329μm ± 250μm with manual CCC. With 1 defining a perfect circle, the average circularity for laser capsulotomies was 0.94 ± 0.04, while for manual CCC it was 0.77 ± 0.15. Cataracts with LOCs grade 1 to 4 were treated in both groups with 50% of cataracts being grade 3. On average the CDE was reduced by 40% from 18.9 (manual) to 11.6 (laser). All results were statistically significant with $P < 0.05$.
Conclusion:
Deviation of the diameter of the anterior capsulotomies produced by femtosecond laser from intended was 12 times smaller and deviation from round shape 4 times lower than those with manual CCC. Pre-conditioning of the cataract with the femtosecond laser reduced the CDE by 40%, which might lead to reduction of surgical side-effects like endothelial cell loss. Future studies will evaluate how the improved precision and reproducibility of OCT-guided femtosecond cataract surgery translates into refractive outcomes with various types of IOLs.

THE EFFECTS OF BEVACIZUMAB AND RANIBIZUMAB ON HUMAN VEGF SIGNALING PATHWAYS IN HUMAN ENDOTHELIAL CELL

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Introduction: We conducted an experiment exploring the effects of Bevacizumab and Ranibizumab on genes involved in signal transduction and cell signaling downstream of vascular endothelial growth factors. We analyzed the expression of genes directly mediating VEGF signaling.
Patients / Methods: Human umbilical vein cell lines were seeded and then incubated for 12 hours in hypoxic chamber. VEGF was added to the cell cultures, and few hours later either Bevacizumab, Ranibizumab or nothing were added to different cell samples for 24 hours. RNA was produced from the cells and converted to cDNA. Real Time PCR, SABiosciences' RT² Profiler PCR Array assay was performed according to manufacturer's instructions.
Results: 1. Comparing the gene expression after exposure to Bevacizumab as compared to control: several genes were upregulated (KDR, NFATC2) and others were down regulated (PLA2G12A, RAC2, HGDC, PRKCG) as compared to control. 2. Comparing the gene expression after exposure to Ranibizumab as compared to control: fewer genes were upregulated (PTGS2) and downregulated (NOS3) 3. When comparing the gene expression after exposure to Ranibizumab as compared to Bevacizumab - we demonstrated several genes up regulated in Bevacizumab as compared to Ranbizumab (Nfatc2 and KDR) and others down regulated (Pla2g12a, Pla2g1b, Ppp3r2, Rac2)
Conclusions: We hereby describe preliminary results of altered gene expression down stream the VEGF signal pathway when comparing Ranibizumab treatment to Bevacizumab. The genes mostly affected: -KDR- a type III receptor tyrosine kinase- It functions as the main mediator of VEGF-induced endothelial proliferation, survival, migration, tubular morphogenesis and sprouting. - PLA2G12A- Selectively expressed in type 2 helper T (Th2) clones. -RAC2- a GTPase which belongs to the RAS superfamily of small GTP-binding proteins. It regulate the control of cell growth, cytoskeletal reorganization, and the activation of protein kinases - PTGS2- the key enzyme in prostaglandin biosynthesis, responsible for the prostanoid biosynthesis involved in inflammation and mitogenesis. -NOS3- a reactive free radical which acts as a biologic mediator in several processes -NFATC2- This complex plays a central role in inducing gene transcription during the immune response. Our results suggest different gene expression after exposure to Ranibizumab and Bevacizumab and may indicate a somewhat different biological activity of the two compounds.

Session IV – RETINA 1

RETINITIS PIGMENTOSA: 9-CIS BETA CAROTENE IMPROVES VISUAL FUNCTIONS IN SOME PATIENTS

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Introduction: High oral doses of 9-cis beta carotene were shown to improve retinal functions as measured by electroretinography (ERG) and perimetry in patients with congenital stationary night blindness and in rodent models of retinitis pigmentosa (RP). The purpose of this study was to determine whether this therapy is efficacious for RP.
Patients / Methods: In a double-masked, placebo-control, cross-over trial, patients with RP (not genetically diagnosed) were given daily 4 commercially available 15mg capsules containing powder containing 7.5 mg 9-cis beta carotene for 90 days. This was followed by a washout and a cross-over period, each of 90 days. Before and after each period, the patients were tested for best corrected visual acuity and underwent ERG using the ISCEV compliant protocol and Goldmann perimetry. Maximal scotopic b-wave ERG responses were used as the primary end point. Z-test was used to evaluate the average differences between treatment and from baseline.
Results: Twenty nine patients completed the study, the visual functions of 34.5% of them showed marked improvement. The dark adapted b-wave improved significantly by an average of 56% in average ($p=0.002$) and the light adapted b-wave by 21% ($p=0.01$).The visual field showed significant improvement after treatment as compare to baseline ($p=0.01$) but not to placebo treatment which caused some improvement, probably due to the subjective nature of perimetry.
Conclusions: The ERG response and visual field of over a third of the RP patients improved significantly by the 9-cis beta carotene treatment compare to placebo. This treatment is probably beneficial only to patients with relevant to pathogenetic mechanisms. The results presented here have to be evaluated in patients with genetically selected forms of retinitis pigmentosa and the optimal dose has yet to be determined.

INTRAVITREAL BEVACIZUMAB TREATMENT FOR MACULAR EDEMA DUE TO BRANCH RETINAL VEIN OCCLUSION

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Introduction: We report the functional and anatomical outcome of a cohort of 45 patients who received intravitreal bevacizumab (IVB) as a treatment for BRVO induced macular edema.
Patients / Methods: Retrospective analysis of the medical records of 45 consecutive patients who received intravitreal bevacizumab (Avastin) due to BRVO induced macular edema from 2/07 till 8/10 in Rabin medical center, Beilinson campus, was performed. The patients received 3 to 4 loading doses of IVB (1.25 mg), and were followed every 6 to 8 weeks. IVB was repeated when macular edema was present. Grid laser photocoagulation was performed as well when macular edema persisted after 4 to 6 avastin injections.
Results: The cohort included 45 eyes of 45 patients, with a mean age of 70.7 (SD8.5) years.The mean follow up time was 18.8 (SD 8.3) months, and the mean number of injections was 8.8 (SD 3.8). Systemic diseases included: Hypertension in 73.3% of the patients, hyperlipidemia in 35.6%, hypercholesterolemia in 31.1%, NIDDM in 40%, and atherosclerotic cardiovascular disease in 31.1%. 11 patients (24.4%) had glaucoma. 14 patients (33%) received grid laser treatment before the IVB, while 23 patients (51%) received grid laser treatment during the study period. The visual acuity (VA) was preserved or improved in 80% of the eyes. The mean initial logMAR VA was 0.63 (SD 0.43) (mean snellen VA, 6/43); the mean final logMAR VA was 0.4 (SD 0.33), (mean snellen VA 6/21). This difference was statistically significant ($p<0.0005$). The mean initial central macularl thickness (CMT) was 382.2 (SD 155.6) microns, and the mean final CMT was 320.5 (SD 172.8) microns. This difference was statistically significant ($p=0.028$). Positive correlations were found between the initial VA and the initial and final CMT ($p=0.004$), between initial and final VA ($p<0.0005$), as well as between the gain in VA and the reduction in the CMT ($p=0.03$). No correlations were found between the initial or final VA and the length of follow up, with laser treatment before or during the study, or between VA and the number of injections.
Conclusions: IVB for the management of macular edema due to BRVO, with and without laser treatment, reduced CMT and improved visual function.

CHEMOKINE RECEPTOR EXPRESSION IN WHITE BLOOD CELL SUB-POPULATIONS FROM PATIENTS WITH AGE-RELATED MACULAR DEGENERATION

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Introduction: Data from both Age- related Macular Degeneration (AMD) patients and rodent models of the disease suggest that both chemokine receptor signaling and macrophages are involved in the pathogenesis of AMD. We aim to test the association between expression of chemokine receptors in sub-populations of white blood cells and AMD.
Patients / Methods: Peripheral blood was drawn from treatment-naïve neovascular AMD (NV-AMD) patients (n=17; 9 females, 8 males) and age-matched control subjects (n=15; 8 females, 7 males). Immunophenotyping was performed on whole blood using antibodies recognizing various white blood cell types (T, B, and NK lymphocytes, CD14+CD16- and CD14+CD16+ monocytes). Expression of CCR1, CCR2, CCR5, CX3CR1, and CXCR4 chemokine receptors was assayed on each cell type using FACS.
Results: The number of cells belonging to each of the white blood cell sub-populations tested was similar between NV-AMD patients and controls. Average percentage (±SEM) of cells expressing CCR2 was increased in the sub-population of CD14+CD16+ monocytes from AMD patients (15.9%±3.6) compared with controls (6.1%±1.6; P=0.02; T-test). A trend towards increased CCR1 expression on CD14+CD16+ monocytes from AMD patients (7.4%±2.5) vs. controls (2.5%±0.8; P= 0.09; T-test) was also observed. CCR2 and CCR1 expression on T cells, B cells, NK cells, and CD14+CD16- sub-population of monocytes were similar between patients and controls. Similarly, percentage of cells expressing CCR5, CX3CR1, and CXCR4 was similar in patients and controls on every cell type tested.
Conclusions: Expression of the CCR2 chemokine receptor is up-regulated by the CD14+CD16+ subset of monocytes in NV-AMD patients. Previous studies demonstrated increased CCL2 (CCR2 ligand) levels in AMD eyes, accumulation of macrophages in vicinity of AMD lesions, and modulation of CNV by macrophages. Our findings further implicate CCR2 and macrophages in the pathogenesis of NV-AMD. Additional investigation is required to elucidate whether CCR2 signaling is crucial for monocyte recruitment in AMD and if it may serve as a therapeutic target for the disease.

BESTROPHIN MODULATES PHAGOCYTOSIS OF PHOTORECEPTORS OUTER SEGMENTS BY RETINAL PIGMENT EPITHELIAL CELLS

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Introduction: Best vitelliform macular dystrophy (Best Disease) result from specific mutations in the bestrophin gene, which is localized to the retinal pigment epithelium (RPE) cells. Despite established molecular functions, the physiological role played by the bestrophin protein (Best1) in RPE cells and the mechanism of Best Disease are yet unknown. Lipofuscin accumulation suggests involvement of photoreceptors outer segments (POS) in disease pathogenesis. Accordingly, we tested the effects of Best1 mutations on the phagocytosis process of POS by RPE cells.
Patients / Methods: Different Best1 mutations associated with distinct phenotypes were generated using site-directed mutagenesis. Verified vectors were cloned into pBABE-puro retroviral vectors and subsequently used to transduce ARPE19 cells, thus generating RPE cell lines stably expressing different variants of Best1. Monolayers of these lines were challenged with FITC labeled POS according to different protocols. Trypan blue was used to discriminate between bound and engulfed POS.
Results: Phagocytosis of POS by RPE lines displayed saturation characteristics. Following a saturating pulse of POS, RPE lines expressing Best disease associated mutants (R218S or E300D) displayed enhanced binding and engulfment compared to wild-type (wt). In contrast, V86M, associated with autosomal dominant vitreoretinochoroidopathy (ADVIRC), resulted in reduction in these processes. To better characterize this modulation, curves were fitted to a Michaelis-Menten model. Vmax and Km were increased in Best, but both were decreased in ADVIRC, compared to wt. Interestingly, the line expressing R47H mutant associated with adult-onset vitelliform dystrophy (AVMD) had Vmax and Km values intermediate between Best and wt variants.
Conclusions: Best1 mutations modulate phagocytosis in a phenotype-dependent manner. The decreased affinity for POS observed in Best Disease and AVMD, and decreased maximal phagocytosis capability observed in ADVIRC, may underlie the mechanism of lipofuscin accumulation in RPE cells, characteristic of these phenotypes.

OPTICAL DENSITY RATIO AS A DIAGNOSTIC TOOL IN THE ASSESSMENT OF RETINAL PATHOLOGIES

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Introduction: Purpose To test the hypothesis that hyporeflective spaces have different optical reflectivities according to the pathology of the eye. OCT optical density ratio (ODR) values of subretinal fluid (SRF) in eyes with rhegmatogenous retinal detachment (RRD) and retinoschisis (RS) were compared with values of neovascular age-related macular degeneration (nAMD), diabetic macular edema (DME), central serous chorioretinopathy (CSC), and pseudophakic cystoid macular edema (PCME).
Patients / Methods: SD OCT (Spectralis), was used to evaluate subretinal fluid in eyes with RRD (n=18), RS (n=10), nAMD (n=17), DME (n=7), CSC (n=17) and PCME (n=4). Images were generated using horizontal scans within subretinal fluid areas. Raw scan data were exported and used to calculate light reflectivity profiles using image J software. Reflectivity data were acquired by projecting two identical rectangular boxes onto the subretinal spaces and the corresponding vitreous. Light reflectivity in the vitreous and subretinal spaces for the various pathologies were measured. ODRs were calculated by dividing the mean pixel intensity of the SRF by the mean pixel intensity of the vitreous
Results: Measured ODR values: RRD (0.67:0.19), RS (O.7:0.16), nAMD (1.47:0.73), DME (1.48:0.51), CSC (1.43:0.48), and PCME (1.36:0.52). Post-hoc Tukey B yielded significant differences in ODR values between nAMD/DME/CSC/PCME and RRD/RS ($p<0.05$). Confounders (age, image quality, vertical distance between measurements) were accounted for by multiple linear regression (adjusted $R2=0.507$; $p<0.001$) without affecting the significance of the difference.
Conclusions: Although OCT reveals neither origin nor composition of the subretinal spaces, the lower reflectivity of the SRF in RRD/RS compared to nAMD/CSC/DME/PCME may be due to the presence of proteins (e.g., albumin) and acute-phase serum reactants in the fluid. These pathologies are caused by a breakdown of the blood–retinal barrier, unlike SRF found in RRD/RS which has no exudative or inflammatory components. ODR profile analysis may be an adjunctive tool to differentiate between uncertain retinal pathologies in subretinal fluid.

Session V – Poster Presentation 2

COMPARISON OF CENTRAL CORNEAL THICKNESS MEASUREMENT USING GALILEI™ DUAL SCHEIMPFLUG ANALYZER TO ULTRASOUND PACHYMETRY

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Introduction: The GALILEI™ Dual Scheimpflug Analyzer (Ziemer Group; Port, Switzerland) is a new device for corneal and anterior segment analysis that combines Placido-based corneal topography and dual Scheimpflug anterior segment imaging. The integrated system exploits the advantages of both technologies in a single exam, along a common reference axis.The purpose of this study was to compare the accuracy and agreement of central corneal thickness (CCT) measurements by the GALILEI™ with those obtained with ultrasonic pachymetery (UP).
Patients / Methods: The GALILEI™ Dual Scheimpflug Analyzer and ultrasonic pachymetry (ALCON OcuScan RxP) were used to measure CCT in 132 eyes of 66 participants under topical anesthesia. The subjects did not have any ocular pathology except for cataract, myopia/hyperopia and/or astigmatic ametropia.
Results: Mean CCT was 559+29 µm when measured by the GALILEI™ system and 526+30 µm when measured by US pachymetry. The mean CCT values difference (Galilie-UP) was 33.2+16.2 µm and statistically significant ($P<0.0001$, paired t-test). There was high correlation between the CCT readings by the two methods. ($r = 0.85$, $P<0.0001$, Pearson's correlation coefficient). Multivariate regression analysis found that age ($p=0.01$) and mean K value ($p=0.01$) had a significant effect on the CCT difference while mean CCT ($p=0.21$) and mean astigmatism ($p=0.06$) did not have a significant effect on the measured CCT difference (GALILEI -UP).
Conclusions: Mean CCT values measured by the GALILEI™ Dual Scheimpflug Analyzer were significantly higher than those measured by the ultrasonic device. GALILEI - UP difference was affected by age and astigmatism.

INTRAOCULAR PRESSURE MEASUREMENTS AND BIOMECHANICAL PROPERTIES OF THE CORNEA IN EYES AFTER PENETRATING KERATOPLASTY

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Introduction: The aims of this study were to compare intraocular pressure (IOP) measurements obtained using the Goldmann applanation tonometer (GAT), the TonoPen XL (TonoPen) and the Ocular response analyzer (ORA), and to determine the influence of corneal factors on IOP measurements, in eyes that had undergone penetrating keratoplasty (PK).
Patients / Methods: Study population: Sixty one post-PK eyes were enrolled in this study. Intervention: IOP was measured using the GAT, DCT, TonoPen and ORA. Corneal hysteresis (CH) and corneal resistance factor (CRF) as provided by the ORA were recorded. Central corneal thickness (CCT) was measured using an ultrasound pachymeter. Main outcome measures: IOP and corneal biomechanical factors.
Results: IOP measurements were obtained in an average of 65 months (6-209 months) after PK surgery. ORA derived IOP measurements (corneal-compensated IOP (IOPcc) and Goldmann-correlated IOP (IOPg)) and TonoPen XL IOP all correlated in a significant manner to GAT IOP measurements. IOPcc and TonoPen XL IOP values were higher than GAT IOP ($P<0.001$ and $P=0.001$, respectively), while IOPg readings did not differ from GAT IOP ($P=0.054$). CCT did not correlate to any tonometry technique. In a regression analysis, CH and CRF were found to play a role in IOP prediction.
Conclusions: CCT may be of less importance than CH and CRF in IOP determination in post-PK eyes, perhaps due to lower modulus of elasticity in these eyes. GAT IOP seems to be lower than other tonometry techniques in post-PK eyes.

DOES CROSS LINKING TREATMENT INFLUENCE THE PENETRATION OF MOXIFLOXACIN?

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Introduction: Corneal cross linking procedure results in compaction of the cornea. the purpose of this study was to evaluate the penetration of moxifloxacin into the rabbit eye after cross linking treatment.
Patients / Methods: One eye of 10 NZW rabbits underwent cross linking treatment. One month following the treatment one drop of 5 mg/ml moxifloxacin (Vigamox, Alcon) was applied to both eyes of each rabbit, every 15 minutesX4 one hour prior to anterior chamber sample. The samples were sent to HPLC for antibiotic concentration analysis. The eyes were enucleated and sent for histology analysis.
Results: The average level of moxifloxacin in the treated eye group was 2.264µg/ml (SD=0.884 1.09-4.20). The average level in the non treated eye group was 2.428 (SD=1.165 0.89-4.72). One tailed paired T-Test was preformed resulting in a p=0.205. Out of the 10 specimen tested 6 treated eyes had lower moxifloxacin aqueous humor concentrations and 4 had higher concentrations.
Conclusions: Penetration of moxifloxacin to the anterior chamber of rabbits is not influenced by their prior treatment with corneal crosslinking.

PREVALENCE AND ASSOCIATED FACTORS OF KERATOCONUS IN JERUSALEM; A CROSS-SECTIONAL POPULATION-BASED STUDY

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Introduction: Purpose: To determine prevalence and associated risk factors of keratoconus in a population sample in Jerusalem.
Patients / Methods: Volunteers participated in this population-based study. Videokeratography was performed on both eyes of each subject who also completed an anonymous questionnaire. Keratoconus was defined by cone apex ≥ 50D, inferior-superior dioptric difference ≥ 3D, as well as positive results from the software indices KISA, KCI and KSI. The association between independent predictors and keratoconus was analyzed using multivariate logistic regression analysis.
Results: Of a total of 987 volunteers, 981 (mean age 24.4) were included. The prevalence of definite keratoconus among all subjects was 2.34 % (95% CI 1.4 – 3.3). It was significantly higher in men (4.91%, CI 2.6 -7.3) than women (1.07%, CI 0.3 -1.9) but not between Israeli Arabs (3.0%, CI 0.6 -5.4) and Israeli Jews (2.2%, CI 1.2 – 3.3). Keratoconus was significantly associated with positive family history of the disease (adjusted OR 17.1, CI 5.0-57.8, P = 0.000), male gender (adjusted OR 5.4, CI 2.1-14.3, P = 0.001) and allergies (OR 3.0, CI 1.2-7.6, P = 0.02), but not with eye rubbing or dry eye.
Conclusions: The prevalence of keratoconus in Jerusalem was found to be much higher than that seen in other parts of the world, except India. This may be related to a combination of genetic and environmental factors. Positive family history, male gender and allergies were shown to be significant predictors. The results of this study signals a need for public health outreach and intervention for keratoconus.

Session VI – Cornea 1

USE OF AMPHOTERIC RISING SOLUTION FOR TREATMENT OF OCULAR TISSUES EXPOSED TO NITROGEN MUSTARD.

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Introduction: Ocular exposure to mustard agents may cause severe acute and prolonged injury to the anterior segment tissues. Considering absence of known antidote to mustard gas, the effective decontamination of external eye surface after exposure is of paramount importance. The purpose of the present study was to assess the effectiveness of Diphoterine rising solution (DRS) in reducing ocular damage after exposure to nitrogen mustard (NM) and to assess whether it would yield better eye protection than would saline solution.
Patients / Methods: One eye of sixteen New Zealand Albino rabbits was exposed to 2% NM. Immediate thorough irrigation was performed with either 500cc of DRS (treated group) or with 500cc of normal saline (control group). Magnitude of ocular injury and response to treatment were assessed by examiners masked to the treatment groups during 22 days following the exposure.
Results: Immediate ocular irrigation with DRS was significantly more effective than immediate irrigation with saline in terms of corneal, iris and anterior chamber injury and systemic oxidative stress reaction. In the DRS treated group the corneal opacity and corneal neovascularization were less severe, development of iris atrophy was delayed and intraocular pressure was better maintained when compared to the control group. In addition, systemic oxidative stress associated with exposure to NM was significantly higher in saline treated group than in DRS treated group.
Conclusions: The findings of this study indicate the effectiveness of DRS in reducing of NM induced ocular injuries. Its use should be considered as an immediate treatment modality of ocular injuries caused by mustard agents.

RISK FACTORS FOR KERATOCONUS IN PALESTINIAN ARABS: A CASE CONTROL STUDY

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Introduction: Keratoconus is a progressive non-inflammatory corneal thinning disorder. Several studies suggest that both environmental and genetic factors play a role in the etiology of KC, but a definite etiology has not been established. Our aim was to elucidate the risk factors forf keratoconus in a population sample Palestinian Arabs.
Patients / Methods: This case-control study included keratoconus patients who were diagnosed by ophthalmologists at the St. John Eye Hospital in Jerusalem. The control group included age and sex matched individuals (1:2 ratio) who were randomly selected from patients at the hospital without KC, but with other ophthalmic diseases. Study subjects were asked to fill out a self- administered questionnaire that included demographic and geographic details on the sampled person and questions on ocular and general health status. We compared exposures in the KC cases and unaffected controls in order to assess risk factors associated with KC.
Results: Overall, 171 patients (57 cases and 114 controls) with a mean age of 25.16 ±7.59 were studied. The following risk factors were found to be associated with KC: dry eye (36.8% vs. 14.0%; $p<0.002$, Chi-square), eye rubbing (59.7% vs. 1.8%; $p<0.0001$, Fisher exact test), allergies (10.5% vs. 1.8%; $p<0.02$. Fisher exact test), consanguinity (42.1% vs. 26.3%; $p<0.04$, Chi-square) and family history of KC (38.8% vs. 5.3%; $p<0.0001$, Chi-square).
Conclusions: Our results suggest both genetic and environmental influences on the etiology of KC. Dry eye, eye rubbing and allergies may increase the risk for developing KC. Positive family history of KC and consanguinity were both shown to be significant predictors. The results of this study signal a need for public health outreach and intervention for keratoconus

THE ASSOCIATION OF KERATOCONUS WITH BLEPHARITIS.

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Introduction: Keratoconus (KC) is a non-inflammatory progressive thinning disorder of the cornea, which leads to progressive mixed myopic and irregular astigmatism. Previously an association has been reported with eye rubbing. Since blepharitis is a common conditions that can cause eye itching and rubbing we wanted to assess the prevalence of blepharitis among patients with keratoconus.
Patients / Methods: A prospective comparative observational study. 50 patients aged 18 - 45 years old with keratoconus and 72 control patients of similar ages and gender were included. Patients with keratoconus were chosen from a list of keratoconic patients of Central District of Clalit Health Services in Israel and were invited over the telephone to undergo examination. 72 control subjects were chosen from the medical personnel stuff of the Clalit District. All subjects underwent full ophthalmologic examination including uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA) with refractive error measurement using autorefractometer, slit-lamp biomicroscopy, IOP measurement , indirect ophthalmoscopy . Assessment of blepharitis included survey of eyelids and detection of missing eyelashes. The eyelids were checked for presence of scales and foam on the eyelashes. Additionally a meibomian gland dysfunction (MGD) test was performed and the results were graded according to scheme of Mathers et al. The participants underwent corneal topography examination and central corneal thickness (CCT) measurement. All patients were asked to answer two questionnaires: the OSDI questionnaire for dry eyes and a questionnaire regarding symptoms, signs and risk factors of blepharitis.
Results: The study and control groups had similar age and gender distribution. Statistically significant more patients with keratoconus reported suffering from blepharitis compared with control's subjects ((24% vs.2.8%, p=0.0009) and reported eye rubbing more than once a day ((36% vs. 11.1%, p=0.002), red and tired eyes (12% vs 0%,p= 0.009). On ocular examination we noticed significantly more signs of blepharitis in the keratoconus group compared with controls (Scales: 48% vs. 8.2%, $p<0.0001$; Foam: 54% vs. 2.7%, $p<0.0001$; MGD Grade 3: 40% vs. 6.3%, $p<0.0001$; Missing eyelashes: 40% vs. 1.4%, $p<0.0001$).
Conclusions: Signs and symptoms of blepharitis are more prevalent among keratoconus patients.

PUPILLOMETER-BASED OBJECTIVE CHROMATIC PERIMETRY IN NORMAL SUBJECTS AND GLAUCOMA PATIENTS

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Introduction: Recently we have demonstrated significant results using Pupillary Light Reflex (PLR) as an objective chromatic perimetry in retinitis pigmentosa patients. In the current study we evaluated this novel system in glaucoma patients.
Patients / Methods: We used a pupillometer [Ronald Consult, Germany] and standard automated perimetry in eight normal individuals and four Glaucoma patients. PLR were measured for three different stimuli: short wavelength stimuli (SWS) (peak 480nm) in two incremental light intensities (40cd/m2,100 cd/m2) in each of eleven different visual field points. In each point in the visual field the PLR amplitudes were calculated for each stimulus. The PLR ratio between the different stimuli was also calculated.
Results: The averages of the PLR amplitudes for the normal subjects in response to low intensity SWS of the 11 points ranged between 0.89mm to 1.4mm and for the glaucoma patients ranged between 0.44mm to 1.04mm ($P<0.001$). The averages PLR amplitude for the high intensity SWS of the 11 points ranged between 1.19mm to 1.71mm in the normal subjects and between 0.5mm to 1.01mm for the glaucoma patients ($P<0.001$). The averages of the PLR ratio between the low and high intensity SWS was significantly higher in the glaucoma patients then in the normal subjects ($P=0.02$).
Conclusions: Reduced pupil response to full field stimuli in high intensity SWS was previously found to be correlated with gangelion cell damage in glaucoma patient. This study demonstrated that high intensity SWS PLR in glaucoma patients was more reduced compare to normal subjects in different locations of the visual field. Pupillometer-based chromatic perimetry may possibly be used as an objective measure for visual field defects in gangelion cell damage.

RETINAL NERVE FIBER LAYER AND OPTIC NERVE HEAD IMAGING: COMPARISON BETWEEN CIRRUS OPTIC COHERENCE TOMOGRAPHY AND HEIDELBERG RETINAL TOMOGRAPH III IN ABILITY TO DISCRIMINATE NORMAL FROM GLAUCOMATOUS EYES

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Introduction: Purpose: To evaluate and compare the diagnostic performance for glaucoma detection between a spectral-domain optical coherence tomograph (OCT) and confocal scanning laser ophthalmoscope.
Patients / Methods: One eye from each individual was selected randomly for ONH imaging by the spectral domain Cirrus HD-OCT (OCT; Carl Zeiss Meditec, Inc., Dublin, CA) and Heidelberg Retinal Tomograph (HRT; Heidelberg Engineering, GmbH, Dossenheim, Germany), respectively. Glaucoma was defined based on the presence of visual field defects with the Humphrey visual field analyzer (HVF; Carl Zeiss Meditec, Dublin, CA). The diagnostic sensitivity, specificity and area under the receiver operating characteristic curve (AUC) were computed of all retinal nerve fiber layer (RNFL) and optic nerve head (ONH) parameters.
Results: Results: One hundred seventy-three subjects (88 glaucoma and 85 normal subjects) were included in this study. RNFL measurements- The pairwise AUC's of superior RNFL thickness was significantly greater for Cirrus OCT compared to HRT3 (0.815 and 0.693, respectively, P=0.005). Other pairwise sectoral and mean RNFL thickness AUC's were not statistically different (P≥0.095). ONH measurements- The AUC's of pairwise measurements of average cup to disc ratio (CDR), cup volume, disk area and rim area were not statistically different (P≥0.238). The best 3 of Cirrus OCT were inferior quadrant RNFL, mean RNFL and superior quadrant RNFL (AUC's of 0.826, 0.822 and 0.815, respectively). The best 3 discriminative parameters for HRT3 were rim volume, inferior quadrant RNFL and rim area (AUC's of 0.788, 0.769 and 0.761, respectively). The difference between these AUC's was not statistically significant (P≤0.132). When defining glaucoma as having "outside normal limits" in ≥1 of any RNFL or ONH parameters (most specific criteria) or as having "outside normal limits" or "borderline" in ≥1 of any RNFL or ONH parameters (least specific criteria), The AUC's of Cirrus OCT were significantly greater than HRT3 (0.779 and 0.644, respectively, P<0.001, and 0.758 and 0.687, respectively, P=0.015).
Conclusions: Conclusions: When using the superior quadrant RNFL measurement or the categorical classification of both technologies, Cirrus OCT have a better ability than HRT3 to detect glaucoma.

DIURNAL INTRAOCULAR PRESSURE CURVES INCLUDING MEASUREMENTS WITH GOLDMANN APPLANATION TONOMETER IN SIDE-LYING POSITION

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Introduction: The intraocular pressure (IOP) fluctuates during the day and is also affected by postural position. Supine position causes substantial increase in IOP. This may be harmful in glaucoma patients. Goldmann applanation tonometry (GAT) is the "golden-standard" and has been used only in sitting position. New system for IOP measurement by GAT in side-lying position was developed (patent pending) and used during diurnal IOP measurement in a clinical set-up. Purpose: Evaluation of clinical data obtained during diurnal IOP measurements in the sitting and side-lying positions.
Patients / Methods: The IOP (N=26) was measured by GAT in sitting position at 4 time points: 9am, 12am, 3pm, and 6pm and after 15 minutes supine, in side lying position at 12:30am. Central corneal thickness was also measured.
Results: The average sitting IOP diurnal fluctuation (maximum diurnal IOP – minimum diurnal IOP) was 3.3 ± 2.0 mmHg, range 0 to 10 mmHg. It negatively correlated to the central corneal thickness (R=0.54, p=0.014, Pearson correlation). Sitting IOP was higher in the morning than in the afternoon (paired t test, p=0.08). Side lying IOP was higher (3.3 ± 2.0 mmHg) than peak diurnal sitting IOP (paired t test, p=0.000). In the side-lying position the increase in IOP was equal in both eyes (4.25 ± 2.8 and 4.9 ± 2.9, paired t test, p=0.54).
Conclusions: Side-lying IOP is substantially higher than peak diurnal sitting IOP and may be more harmful in glaucoma patients. IOP fluctuations tend to be higher in eyes with thinner corneas and may contribute to their increased risk of glaucoma progression. The increase in IOP in the side-lying position is probably dependant on the level of the eyes relative to the heart therefore which eye is above which is of negligible importance.

CHANGES IN ANTERIOR SEGMENT PARAMETERS FOLLOWING INSERTION OF EX-PRESS MINIATURE GLAUCOMA IMPLANT

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Introduction: The aim of this study was to evaluate the effect of Ex-PRESS Miniature Glaucoma Implant surgery on corneal curvature and anterior segment parameters obtained with the Pentacam rotating Scheimpflug camera (Oculus inc.).
Patients / Methods: A total of 13 eyes of 13 consecutive patients (8 men, 5 women) were evaluated pre-operatively, on the first postoperative day and 3 months postoperatively with the Pentacam. We compared measurements of anterior and posterior corneal curvature, anterior and posterior corneal astigmatism, anterior chamber depth (ACD), anterior chamber volume (ACV) and anterior chamber angle (ACA) before and after surgery. All study eyes were pseudophakic
Results: IOP decreased significantly from 33.2±11.2 mmHg pre-operatively to 5.9±5.1 mmHg on the first postoperative day ($p<0.0001$) and 18±6 mmHg at 3 months following surgery ($p=0.0002$). On the first post-operative day the anterior corneal astigmatism increased from 2.3±1.3 D to 3.7±2 D ($p=0.04$); the posterior corneal astigmatism increased from 0.5±0.2 D to 0.9±0.6 D ($p=0.03$); the ACD decreased from 4.3±0.9 mm to 3.5±1.1 mm ($p=0.05$) and the ACV decreased from 197.9±40.5 to 166.8±50 mm3 ($p=0.09$). All of these changes in anterior segment parameters were not statistically significant at 3 months after surgery
Conclusions: Ex-PRESS Miniature Glaucoma Implant surgery significantly decreased IOP, and had a transient effect on anterior segment parameters. Corneal curvatures, ACD, ACV, and ACA were not affected at 3 months follow up

OPTIC NERVE HEAD IMAGING: COMPARISON OF CIRRUS OPTIC COHERENCE TOMOGRAPHY AND HEIDELBERG RETINAL TOMOGRAPH III

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Introduction: Purpose: To study the relationship between optic nerve head (ONH) parameters measured by spectral domain optical coherence tomography (OCT) and confocal scanning laser ophthalmoscope.
Patients / Methods: One eye from each individual was selected randomly for ONH imaging by the spectral domain Cirrus HD-OCT (Carl Zeiss Meditec, Inc., Dublin, CA) and Heidelberg Retinal Tomograph (HRT; Heidelberg Engineering, GmbH, Dossenheim, Germany). Glaucoma was defined based on the presence of visual field defects with the Humphrey visual field analyzer (Carl Zeiss Meditec, Dublin, CA). Only the ONH parameters that are measured by both technologies were compared: average cup to disc ratio (CDR), rim area, disc area and cup volume (paired t test). The relationship between the measurements was evaluated using a Pearson correlation analysis. Differences were analysed using Bland-Altman method. The agreement of the categorical classification was evaluated (κ statistics). The diagnostic sensitivities, specificities and the area under the receiver operating characteristic curves (AUC) were examined.
Results: One hundred seventy-three subjects (88 glaucoma and 85 normal subjects) were included in this study. ONH parameters, as determined by the Cirrus OCT and HRT3 were strongly correlated. All measurements were significantly different, but for disk area the difference was marginal ($P<0.0001$ and 0.031, respectively). Proportional bias for all measurements was demonstrated by Bland- Altman plots except for disk area. The agreement of categorical classification was excellent for CDR ($\kappa=0.944$) and good for rim area and cup volume ($\kappa=0.631$ and 0.713, respectively). The highest sensitivities at fixed specificities were achieved by Cirrus OCT for rim area (38.82% at 98% specificity and 68.24% at 80% specificity). AUC's of CDR, rim area, disk area and cup volume were not significantly different between the 2 technologies.
Conclusions: ONH measurements by Cirrus OCT and HRT3 are correlated but different. The difference for CDR, cup volume and rim area is proportional to these parameters' value (proportional bias). The highest AUC's, sensitivities and specificities were achieved by Cirrus OCT. The results suggest that in clinical practice, interchangeable use of the categorical classification of CDR, can be considered.

PERIPAPILLARY DISTRIBUTION OF MULLER CELLS WITHIN THE HUMAN RETINAL NERVE FIBER LAYER

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Introduction: To purpose of this study is to describe the distribution of Muller cells within the peripapillary human retinal nerve fiber layer (RNFL).
Patients / Methods: Eleven unpaired normal postmortem eyes were recruited into this study. Each eye was sectioned using the “umbrella technique” to obtain a concentric peripapillary ring centered on the optic disc, with a diameter of 3.0mm. Immunohistochemistry with anti- CRALBP antibodies (Santa Cruz Biotechnology, Santa Cruz, CA) stained Muller cells within each ring. Slides were scanned with a ScanScope scanner (Aperio Technologies, Vista, CA) and analyzed with Matlab (MathWorks, Natick, MA). Statistical analysis was performed with JMP statistical discovery 7.0 (SAS, Cary, NC).
Results: RNFL thickness measurements measured with the MatLab code were more accurate than the previously published ones, but with the same distribution around the peripapillary ring (262.5, 339.4, 285.4 and 347.5 microns for the temporal, superior, nasal and inferior quadrants, respectively). Muller cells were found to be unevenly distributed in the peripapillary retinas. The relative Muller cells staining to the thickness of each measured segment (16.6%, 15.2%, 21.3%, and 17.9% for the temporal, superior, nasal and inferior quadrants, respectively) showed a marked increase in the nasal quadrant.
Conclusions: RNFL thickness measurements by imaging techniques should compensate for the lower relative content of Muller cells superiorly and the higher content nasally. Further study should compare the distribution of Muller cells in normal versus glaucomatous eyes.

IS THERE A CORRELATION BETWEEN INTRACRANIAL PRESSURE AND INTRAOCULAR PRESSURE MEASURED BY HAND-HELD TONOMETRY?

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Introduction: The aim of this study is to provide data on the controversial issue of whether handheld measurements of intraocular pressure (IOP) are capable of accurately predicting elevated intracranial pressure (ICP) in patients undergoing lumbar puncture (LP).
Patients / Methods: All patients over the age of 18 years who underwent an LP in the emergency or neurological departments for any reason between October 2007 and July 2010 were eligible to participate in this prospective observational pilot study. IOP was measured with the Tono-Pen XL while they were in the supine position before undergoing LP. ICP was measured in the lateral recumbent position. ICP and bilateral IOP were measured, and the mean and maximum values of IOP were calculated. The association between ICP and each one of the four IOP measures was evaluated by the Pearson correlation coefficient.
Results: Twenty-four patients (mean age 37.8 ± 15.8 years, 10 males and 14 females) were enrolled. The reasons for their requiring an LP were headache (19/24 patients), evaluation for hemiparesis (2/24), cognitive deterioration (1/24) seizures (2/24). Nine had elevated mean opening pressure (>20 cm H2O). Six had an elevated mean IOP (>20 mmHg), and four of these six also had an elevated opening pressure. There was no significant correlation between the ICP measurements and any of the IOP measurements.
Conclusions: Handheld ocular tonometry has poor sensitivity and specificity for the prediction of increased ICP and is not an effective tool for screening ICP in the ED or neurology department.

MUTATIONS IN FAM161A ARE CURRENTLY THE MOST COMMON CAUSE OF AUTOSOMAL RECESSIVE RETINITIS PIGMENTOSA IN THE JEWISH POPULATION

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Introduction: We recently reported the identification of FAM161A as a major cause of autosomal recessive retinitis pigmentosa (arRP) due to null mutations in the Israeli population. The current study extends the mutation analysis of FAM161A in the Jewish population and explores localization of the protein in the human retina.
Patients / Methods: Clinical and molecular analyses included family history, ocular examination, full-field electroretinography (ERG), perimetry, homozygosity mapping and mutation analysis. Immunohistochemistry was performed on retinal sections using antibodies raised against different parts of the protein.
Results: We previously reported that the most common FAM161A mutations in the Jewish population are c.1355_6delCA (p.T452SerfsX3) and c.1567C>T (p.R523X). Genotyping of these mutations in a large cohort of Jewish RP patients from Israel and USA revealed a prevalence of 11% (21/193) and 3% (5/193), respectively, in this population. Due to the high carrier frequency of the c.1355_6delCA mutation in the North African Jewish sub-population (carrier frequency of 1 out of 32 individuals), homozygosity for this mutation was also identified in families with an autosomal pseudo-dominant pattern of inheritance. The majority of patients with FAM161A mutations had an RP phenotype; one patient manifested an atypical retinal degeneration. The FAM161A protein was studied in the human retina by immunohistochemistry, using the HPA032119 antibody. The analysis revealed a positive and intense signal in photoreceptor inner segments as well as weaker staining in the outer plexiform layer. No expression was evident in photoreceptor outer segments. To gain further understanding of FAM161A expression, we raised antibodies against the C-terminal, N-terminal, and the alternatively-spliced and highly conserved exon 4 of FAM161A. The data of protein localization experiments using these antibodies will be presented at the meeting.
Conclusions: FAM161A mutations are currently the most common cause of arRP in the Jewish population (14%). The data we provide here bring to 30 the number of arRP families with FAM161A mutations originating from Europe, India, and Israel.

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

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Introduction: CERKL mutations are associated with severe retinal degeneration. CERKL encodes for a novel ceramide kinase (CERK)-like protein. Both CERK and CERKL harbor a kinase domain related to the diacylglycerol kinases, a Pleckstrin Homology domain, and a CERK-specific region, bearing a putative calcium/calmodulin binding motif. Several studies have been conducted to prove a biochemical similarity between CERK and CERKL enzymatic activities. However, so far there has been no evidence that CERKL phosphorylates ceramide or any other lipid substrate in vitro or in vivo. CERKL's function in the retina is unknown. The purpose of this work is to characterize CERKL's retinal expression pattern and function.
Patients / Methods: A specific anti-CERKL antibody was used to study the localization of the endogenous CERKL protein in the mouse retina. A calcium-overlay assay was used to determine whether CERKL actually binds calcium. GST pull-down assay will be used to investigate a possible interaction between CERKL and calmodulin. To identify CERKL-binding proteins we used the Ras-Recruitment system.
Results: In the mouse retina CERKL is located in the ganglion cell layer, in amacrine cells of the inner nuclear layer, and in cone photoreceptors. Based on a calcium-overlay assay, CERKL does not appear to bind calcium directly. One of the identified CERKL-binding proteins is a ubiquitously expressed calcium-binding protein. Interaction between CERKL and this protein was confirmed by a co-immunoprecipitation assay. Serial deletion constructs are being used to map the specific interaction sites in both proteins.
Conclusions: The severe retinal phenotype associated with human CERKL mutations indicates that this gene plays a crucial role in retinal activity. The high expression level of CERKL in cones correlates with the CERKL-associated phenotype in humans, which involves severe cone degeneration. CERKL's localization in the retina as well as the identified calcium-binding partner indicate that CERKL may require an interaction with one or several calcium-binding proteins, in order to sense changes in calcium concentration as part of the phototransduction cascade.

HOMOZYGOSITY MAPPING - A POWERFUL TOOL FOR THE IDENTIFICATION OF MUTATIONS IN KNOWN RETINAL DEGENERATION GENES IN THE ISRAELI AND PALESTINIAN POPULATIONS

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Introduction: The rate of consanguinity in the Israeli and Palestinian populations is relatively high, leading to homozygosity in disease-causing genes. This enables us to use the homozygosity mapping technique in our populations. The aim of the current study was to use single nucleotide polymorphism (SNP) microarrays in order to identify mutations causing autosomal recessive (AR) retinitis pigmentosa (RP) and Leber congenital amaurosis (LCA) in the Israeli and Palestinian populations.
Patients / Methods: We recruited for the study 108 families (most of which are consanguineous) with the diagnosis of ARRP or AR-LCA. We excluded from this analysis 21 families in which we previously reported the identification of mutations in novel (e.g. IMPG2, FAM161A, and DHDDS) or known (EYS) RP genes. Blood samples were drawn from family members and genomic DNA was extracted and analyzed by whole genome SNP microarray. Bioinformatic analyses were made and homozygous regions harboring known RP and LCA causing genes were found, followed by sequencing of genes of interest.
Results: We analyzed whole genome SNP array data of patients from 108 families for homozygosity and identified in most patients large homozygous regions (>20Mb) harboring known retinal degeneration genes. Subsequent sequence analysis revealed the identification of disease-causing mutations (in the RDH12, TULP1, NR2E3, USH2A, CRB1, CERKL, RPE65, and AIPL1 genes) in 13 of the families (~12%). Only two families shared the same mutation and 3 of the mutations were novel. In 7 of the 13 families, the mutation was identified in the largest or second largest homozygous region in the genome.
Conclusions: Our results demonstrate that homozygosity mapping using SNP microarrays is an efficient method for searching of disease causing genes in consanguineous families with the diagnosis of ARRP or AR-LCA. Analysis of the remaining families in which no mutations could be detected in known retinal degeneration genes could lead to the identification of novel disease genes.

IDENTIFICATION OF MUTATIONS CAUSING AUTOSOMAL RECESSIVE INHERITED CONE-DOMINATED DISEASES USING HOMOZYGOSITY MAPPING

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Introduction: The Israeli population is known to have a relatively high degree of consanguineous marriages, leading to a relatively high frequency of autosomal recessive diseases. Our purpose was to use homozygosity mapping as a tool for identification of genes causing cone-dominated diseases in the Israeli population.
Patients / Methods: Clinical analysis included family history, ocular examination, full-field electroretinography (ERG), and funduscopy. Molecular analysis included homozygosity mapping and mutation analysis of candidate genes.
Results: We recruited 240 families with cone-dominated retinal diseases, including cone-rod degeneration, cone dystrophy, achromatopsia, and maculopathies. The inheritance pattern in most of the families (55%) was autosomal recessive, mainly due to a relatively high level of consanguinity. Aiming to identify the causative genes in these families we performed homozygosity mapping using whole genome genotyping in 69 of the families. The analysis revealed the identification of 14 mutations, 9 of which are novel, in 18 of the families. The mutations were identified in 7 genes, including ABCA4, CNGA3, KCNV2, and PROM1. Interestingly, the identification of the causative gene led to a revised diagnosis in patients from 7 families.
Conclusions: Accurate clinical diagnosis of cone-dominated diseases may be difficult to obtain, mainly because of the young age in which patients are diagnosed. Identifying the disease-causing gene in these patients might result in a more reliable diagnosis. We have shown here that homozygosity mapping is an efficient tool for identification of disease-causing genes in the Israeli population.

PHENOTYPE-GENOTYPE CORRELATION IN SPORADIC PATTERN DYSTROPHY

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Introduction: Sporadic pattern dystrophy (PD) is often suggested in the differential diagnosis of age related macular degeneration (AMD). Mutations in the Peripherin/RDS gene were described in familial PD but their involvement in sporadic PD is unclear. We aim to characterize the phenotype and genotype of patients diagnosed with sporadic PD in the Israeli population.
Patients / Methods: Sequential groups of patients diagnosed with PD based on clinical findings in a tertiary referral center between July 2010 and Dec 2010 were included in the study. Charts and retinal imaging (color fundus photographs, autofluorescence, OCT) were reviewed. The four exons of the Peripherin/RDS gene were sequenced and genotyped. Further genotyping for the common risk alleles for AMD in the CFH, C3 and HTRA1 genes was performed.
Results: Twenty patients were recruited (12 female; 8 male), mean age was 75.4 years (range 59-90, SD 9.0). Patients showed either the Butterfly form or the adult onset vetilliform form of PD. Autofluorescence imaging showed central focal, linear or multifocal hyperflourescent patterns. OCT showed subretinal dome shaped deposits and RPE atrophic changes. Choroidal neovascularization in at least one eye was diagnosed in 6 patients. Genotyping of the Peripherin/RDS gene showed no mutations, but several known single nucleotide polymorphisms (SNPs) in the gene were detected. The risk SNP in HTRA1, CFH, and C3 were identified in 42%, 52.6%, and 40% of the patients, respectively.
Conclusions: Sporadic PD is a relatively common diagnosis in the retina clinic. It is genetically distinct from familial PD in that Peripherin/RDS gene mutations are not associated with sporadic PD, yet, it is phenotypically indistinguishable from familial PD. The prevalence of risk SNPs for AMD in sporadic PD cases which we have evaluated is similar to the general population except for the C3 SNP which shows similar prevalence in sporadic PD and AMD patients.

MUTATIONS IN BEST1 AND PERIPHERIN/RDS GENES ARE IMPORTANT CAUSES FOR VITELLIFORM MACULAR LESIONS.

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Introduction: Purpose: To describe the phenotypes and analyze the BEST1 and peripherin/RDS genes in 3 unrelated families and 6 sporadic patients with vitelliform macular degeneration.
Patients / Methods: The probands of 3 families and 6 sporadic patients underwent an ophthalmic examination including dilated fundus examination, fundus autoflouresence imaging and optical coherence tomography (OCT). In all probands and in selected family members, flourescein angiography and electrophysiological testing were performed. Blood samples were obtained from affected family members for analysis of the BEST1 and peripherin/RDS genes.
Results: We observed three clinical phenotypes; classic Best disease, vitelliform pattern dystrophy and sporadic patients manifesting adult vitelliform macular degeneration. Three BEST1 missense mutations (W93R, E98D, and N296S) were identified in affected members of Best macular dystrophy families, while a truncating peripherin/RDS gene mutation (c.441delT) was identified in a family manifesting vitelliform pattern dystrophy. Sporadic patients with vitelliform macular lesions did not carry identifiable mutations in the coding regions of these genes.
Conclusions: Vitelliform macular lesions may accompany clinical different disorders. Some elderly patients with probands showing pattern dystrophies may be misdiagnosed with age related macular degeneration owing to the phenotypic similarities between these conditions in the advanced state. Two novel BEST1 gene mutations (W93R and E98D) were identified in Best vitelliform macular dystrophy families and a previously not described phenotype was associated with a peripherin/RDS gene mutation.

FURTHER CHARACTERIZATION OF RISK SNPS FOR AMD IN THE ISRAELI POPULATION

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Introduction: To gain additional insight into the association among risk SNPs in the CFH, HTRA1, and C3 genes and age-related macular degeneration (AMD) in the Israeli population, and to evaluate the usefulness of using genotyping for these genes as diagnostic tests for the disease.
Patients / Methods: Genotyping for the rs11200638 SNP in HTRA1, Tyr402His variant in complement factor H (CFH), and rs2231099 SNP in complement component 3 (C3) was performed in 379 AMD patients and 196 controls. Association of risk alleles and genotypes with the diseases was evaluated. The usefulness of genotyping as diagnostic test for AMD was assessed at several stringency levels.
Results: Each of the three tested SNPs showed a strong association with AMD in the entire Israeli population ($P<0.0001$ for each of the SNPs). Interestingly, the HTRA1 SNP was strongly associated with AMD among Arabs ($P=0.0022$) while the SNPs in CFH and C3 were not associated with AMD in the Arab population which was tested (17 patients; 16 controls). Evaluation of genotyping as a diagnostic test yielded specificity, sensitivity, and positive- and negative predictive values which were not sufficiently informative for the application of the test in clinical use.
Conclusions: Risk SNPs in CFH, HTRA1, and C3 are strongly associated with AMD in the Israeli population. Among Arabs, the HTRA1 SNP appears to have a major role in AMD. Genotyping for these SNPs is not useful for clinical application as a marker for the disease.

INSULIN LIKE GROWTH FACTOR-1 FOR PREDICTING METASTATIC UVEAL MELANOMA IN HUMANS

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Introduction: A number of studies have shown associations between high levels of Insulin like growth factor-1 receptor (IGF-1R) and metastatic Uveal Melanoma (UM). The purpose of this study was to examine the potential of IGF-1 in early detection of liver metastasis in patients with UM.
Patients / Methods: IGF-1 serum levels were analyzed by ELISA (R&D Systems, Minneapolis, MN, USA) for 118 subjects in 3 different groups: 55 UM patients who did not develop metastasis within 10 years from diagnosis (DF), 22 metastatic patients, and 41 healthy subjects. Matched pairs univariate analysis was performed for the following 22 metastatic patients' serums: 12 and 6 months before the diagnosis of metastasis and at the day of diagnosis. The levels of the biomarker were compared between the control group, DF group and metastatic UM patients' group by using ANOVA and student t-test.
Results: The mean±SD levels for the control, 10yDF, and metastatic groups were: 152.47±15.91, 115.18±13.78, and 96.31±21.59 ng/ml, respectively (p=0.0006). IGF-1 serum levels have been statistically significantly higher in the control group compared to both DF patients (p= 0.006) and metastatic UM patients (p=0.0003). In the matched pairs analysis the mean IGF-1 level increased from 12 months prior to diagnosis of liver metastasis to 6 months prior to diagnosis by 28.4% (p= 0.0193), and decreased from 6 months prior to diagnosis to the day of diagnosis by 10.7% (p=0.2435).
Conclusions: IGF-1 levels in UM patients were significantly lower compared to healthy subjects. Therefore, there is an association between low levels of serum IGF-1 and UM. During the year prior to the metastatic diagnosis, IGF-1 levels did not change along a clear trend. Consequently, IGF-1 failed as a predictive marker for metastatic UM.

UVEAL MELANOMA: GENDER DIFFERENCES IN CLINICAL PRESENTATION AND PROGNOSIS

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Introduction: The purpose of this study was to examine the clinical differences in development and manifestation of uveal melanoma (UM) between men and women.
Patients / Methods: The study included 723 patients (325 men and 398 women) with UM, who were treated between 1988 and 2010 at a single center (Hadassah-Hebrew University Medical Center, Jerusalem, Israel). Men and women were compared regarding differences in annual incidence, age at diagnosis, size and intraocular location of the tumor, symptoms leading to diagnosis, recurrence, metastases development and mortality. Statistical analysis included: student t-test, ANOVA, Pearson correlations and Kaplan-Meier survival analysis.
Results: Annual incidence was not associated with gender. No significant gender difference in diagnosis age was observed (men: 60.96 years vs. women: 60.16 years). No significant gender differences in tumors' diameter or height were observed. Tumors were more frequently located posterior to the equator in men than in women (42.28% vs. 33.99%; p=0.03). However, men were less likely than women to complain of symptoms prior to the diagnosis (77.10% vs. 84.65%; p=0.04). Men developed metastases more than women (15% vs. 10%; p=0.05). In the subgroup of patients who developed metastases, the time until development of metastases was shorter in men compared with women (metastases 1 and 5 year after diagnosis of UM: 24% vs. 12.96%; 84% vs. 50%, respectively; p=0.01). Men had a worse survival rate than women (5, 10 and 15 years: 83.09% vs. 92.09%; 76.68% vs. 85.12%; 71.63% vs. 77.37%, respectively; p=0.002). No gender difference was observed in the disease's recurrence rate.
Conclusions: No gender differences in UM were observed regarding annual incidence, age, size or recurrence of the tumor. However, men were more likely to develop UM posterior to the equator, though they surprisingly tended to complain less. The prognosis of UM in men was worse than in women. Men developed more metastases and the time from the diagnosis of UM until development of metastases was shorter. Finally, the overall mortality from UM was higher in men compared with women.

FOXP3+ REGULATORY T CELLS IN POSTERIOR UVEAL MELANOMA: CLINICOPATHOLOGIC CORRELATION

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Introduction: Regulatory T cells (Tregs) have potent immunosuppressive abilities contributing to tumor evasion from the immune system. Increased numbers of Tregs were detected in malignant lesions and peripheral blood from cancer patients in a variety of malignant diseases and were associated with poor survival in various malignancies. The aim of this study was to examine the expression of Foxp3 in uveal melanoma and to correlate it with clinicopathologic parameters.
Patients / Methods: Foxp3 expression was immunohistochemically evaluated in primary tumors of 77 patients who underwent enucleation at Hadassah-Hebrew University Hospital between the years (1986-2006). Nineteen metastatic liver sections were also stained.
Results: Forty-five tumors were from females; age range was between 19 and 86 years (mean 60.7 y). Fifty-nine tumors were Foxp3 positive. Of the epithelioid/mixed-type tumors (n=59), 45 were Foxp3 positive (76.3%) whereas of the spindle-type tumors (n=16), 13 were Foxp3 positive (81.3%). Of the tumors located in the choroid (n=41), 30 were Foxp3 positive (73%), whereas of the tumors located in the ciliary body (n=35), 29 were Foxp3 positive (82.9%). With regard to the extracellular matrix pattern; of the silent/normal pattern (n=24), 12 were Foxp3 positive (50%) whereas of the network/loops/parallel with cross-link patterns (n= 30), 27 were Foxp3 positive (90%) (p=0.001); there was an increased odds of developing a higher vascular pattern in Foxp3-positive tumors (OR=9.0, 95% CI=2.14-38.46). Mean tumor diameter was 13.68 mm ±SD 3.45 for Foxp3-negative tumors, whereas it was 14.56 mm ± SD 4.25 for Foxp3-positive tumors. In patients who developed liver metastasis (n=32), 27 were Foxp3 positive (84.4%) whereas in patients without metastasis (n=24), 16 were Foxp3 positive (66.7%) (p=0.12). No information was available on the remaining 21 patients. Nineteen liver metastatic sections were also studied; 16 were found to positively express Foxp3.
Conclusions: We were able to detect Foxp3-positive Tregs in approximately 77% of posterior uveal melanoma samples. No correlation was demonstrated between the expression of Foxp3 and tumor size, location, cell type and metastasis. However, a significant correlation was shown with the higher vascular patterns. To develop novel therapeutic strategies, we must gain insight into the mechanisms of Treg control and regulation in uveal melanomas.

MUTATION ANALYSIS AND COPY NUMBER VARIATION IN THE BRAF ONCOGENE IN PEDIATRIC LOW-GRADE GLIOMAS

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Introduction: Low grade gliomas (LGG) are the most common primary central nervous system tumors in children and frequently involve the optic pathway. The molecular mechanisms that underlie the development and progression of these tumors are not yet understood. The deregulation of MAPK signaling, especially of the RAF genes, emerges as a common finding in pilocytic astrocytoma (PA). In particular, it has been demonstrated that tandem duplications at chromosome 7q34 targeting the BRAF locus, define a hallmark genetic lesion in PA development. It has also been found that a single mutation in the V600E locus can result in activation of the BRAF protooncogene. The purpose of this study is to investigate the occurence of BRAF mutations and to analyze copy number variation of the BRAF oncogene.
Patients / Methods: Following IRB approval, 36 samples of low grade gliomas from children were analyzed using chip-based matrix assisted laser desorption-time-of-flight (MALDI-TOF) mass spectrometer for the point mutation V600E. Direct sequencing was used to validate the results for several samples. Copy number variation of the BRAF gene was analyzed by Digital PCR Analysis software (copy number, applied biosystems).
Results: 10 of the 36 samples were from the optic pathway. Only 1 was positive for the V600E BRAF mutation (10%), whereas no mutations were found in the remaining 26 samples, taken from the posterior fossa (15), temporal lobe (6), and other (5) areas. An increase in the BRAF copy number was found in 50% (5/10, 13/26), in the optic pathway and the non optic pathway LGG tumors.
Conclusions: An increase in the copy number variations of the BRAF gene, and activating mutations, may play a role in the development of LGG. The findings are similar in optic pathway gliomas and other LGG. It is hoped that a better understanding of the molecular changes that drive the initiation and growth of LGG will lead to the development of more effective therapies to preserve vision in these young children.

LACK OF ONCOGENIC GNAQ MUTATIONS IN MELANOCYTIC LESIONS OF THE CONJUNCTIVA AS COMPARED TO UVEAL MELANOMA.

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Introduction: PURPOSE: Somatic mutations in codon 209 of the GNAQ gene are the first initiating events to be identified in uveal melanoma. The purpose of this study was to search for GNAQ209 mutations in conjunctival melanocytic lesions.
Patients / Methods: Forty archival samples of conjunctival melanocytic lesions (conjunctival nevi, primary acquired melanosis, and conjunctival melanoma), 27 samples of uveal melanoma, and 11 samples of uveal melanoma metastases to the liver (3 of which matched primary uveal melanoma samples)-a total of 78 samples from 75 patients- were examined for the presence of GNAQ209 mutations by using chip-based, matrix-assisted laser-desorption time-of-flight (MALDI-TOF) mass spectrometry. Direct sequencing was also performed.
Results: The GNAQ209 mutation was identified in 12 (44.5%) uveal melanoma samples and 4 (36.5%) of the 11 metastases of uveal melanoma. It was not detected in any of the other melanocytic lesions.
Conclusions: The GNAQ209 mutation rate in uveal melanoma in this study is in line with the rate in other reports. The finding of the same genotype in the primary tumors and their metastases suggests that mutation in GNAQ is an early event in uveal melanoma tumorigenesis. The lack of GNAQ mutations in conjunctival melanocytic lesions suggests the involvement of a different tumorigenic pathway from that of uveal melanoma.

BENEFICIAL ASSESSMENT OF VARIOUS TREATMENTS AGAINST MIOSIS AND VISUAL DYSFUNCTION FOLLOWING OCULAR EXPOSURE TO THE NERVE AGENT SARIN

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Introduction: Eye exposure to the organophosphorus irreversible acetylcholinesterase inhibitor sarin results in long-term miosis (a reduction of at least 50% of pupil width) and reduction in visual function. Anti-cholinergic drugs, such as atropine, are used topically in order to counter these effects and obtain symptomatic relief. Unfortunately, such compounds attenuate ocular discomfort at the expense of producing mydriasis and partial cycloplegia symptoms, which may worsen visual performance. This study was aimed to test the efficacy role of various drugs in contradicting the sarin-induced miosis and visual impairment, which will minimally affect vision.
Patients / Methods: Male Pigmented Long-Evans rats were topically exposed to sarin (0.2-1 μg), and 20 min later were topically treated. Pupils were illuminated with an infrared spotlight and images were digitally recorded with a computerized infrared-capable video camera, thus measuring pupil width. Pupil width was determined 15 min -8 h following exposure and treatment. Visual function assessment was performed using the Cued Morris Water Maze task, 15-35 min following sarin exposure and treatment. In this version, cued navigation involves finding a goal location by approaching a single cue that marks the visible goal. The cue was a circular green rod (5 cm high) attached to the visible escape platform (1 cm above the surface of the water).
Results: Rats exposed topically to various sarin doses showed a dose-dependent miosis, which partially recovered within 4-8 h. Treatments differentially improved the sarin induced miosis and the resulting impairment in visual performance.
Conclusions: The miotic as well as the visual defects observed, following topical sarin exposure are contradicted to various extent by the treatments used.

THE CORRELATION BETWEEN THE AMOUNT OF MULLER MUSCLE RESECTED DURING MODIFIED MULLERECTOMY SURGERY AND THE CLINICAL RESULT OF PTOSIS REPAIR

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Introduction: The modified mullerectomy procedure is useful for patients with minimal ptosis and good levator function. This procedure is similar to Fasanella-Servat tarsomyectomy except that the resection is only of the conjunctiva and Muller muscle, sparing the tarsus. The aim of this work was to test if there is a correlation between the amount of muller muscle resected during the surgical procedure and the clinical ptosis repair as measured by the MRD.
Patients / Methods: Fourteen patients (22 eyes) with involutional ptosis were included in this study. The mean age was 62 (range 49-81). All underwent modified mullerectomy procedures performed by one surgeon (Guy Ben-Simon). All the resected specimens were sent for pathologic examination and stained with Masson-Trichrom. The amount of Muller muscle was evaluated and graded (1 - few muscle fibers, 2 - medium amount of muscle, and 3 - many muscle bundles).
Results: Before the operation 10 eyes had severe ptosis (MRD: 0-1 mm), and 12 had mild-moderate ptosis (MRD: 2-3 mm). All eyes had clinical improvement after the operation. The eyes with the severe ptosis had more significant improvement. In the severe ptosis group the MRD was improved by mean of 2.55 mm, as compared with 1 mm in the mild-moderate ptosis group. The pathological evaluation demonstrated that more Muller muscle was resected in the severe ptosis group as compared to the mild-moderate group (mean grade of the amount of resected Muller muscle of 2 vs 1.8, respectively). However, the difference was not statistically significant ($p=0.548$).
Conclusions: The modified mullerectomy procedure was found to be effective. The clinical improvement as measured by MRD was correlated to the amount of Muller muscle resected at surgery but the differences were not statistically significant. The research is planned to be continued to enlarge the number of participants in order to receive more conclusive results.

THE CORNEAL TRANSPLANT SCORE: AUTOMATIC PRIORITY SCORING SYSTEM FOR KERATOPLASTY RECIPIENT CANDIDATES

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Introduction: The need accompanied by the extreme lack of various human organs including corneas for transplantation has created long waiting lists in most countries. Transplant calculators specific for each organ have long become a gold standard. We describe an automatic scoring system for keratoplasty recipient candidates in a situation of tissue shortage; and to evaluate system accuracy in predicting decisions made by a cornea specialist.
Patients / Methods: A system was created on an electronic spreadsheet. Candidate input data include best achieved vision in the operated and in the fellow eye, potential vision in the operated eye, discomfort level, risk of infection, waiting time and estimated success rate. A single priority score was computed for each candidate. Evaluation: Forty sets of candidate data were randomly created and divided to 20 pairs. A cornea surgeon decided which candidate in each pair should have surgery if only a single cornea was available. The same decision was then made through the scoring system. Results were compared.
Results: The scoring system produces values between 0 (lowest priority) and 18 (highest priority) for each candidate. Average score value in our randomly created cohort was 6.35±2.38 (mean±S.D.), range 1.28 to 10.76. Average score difference between the candidates in each pair was 3.12±2.10 (mean±S.D.), range 0.08 to 8.45. The manual scoring process, although theoretical, was mentally and emotionally demanding for the surgeon. Agreement was achieved between the human decision and the calculated value in 19 of 20 pairs. Disagreement was reached in the pair with the lowest score difference (0.08).
Conclusions: With worldwide donor cornea shortage, waiting for transplantation can be long. Repeated periodic manual sorting of priority for transplantation in a long waiting list is difficult, time consuming and prone to error. The suggested system may help achieve just distribution of available tissue.

INCORPORATION OF BONE MARROW CELLS INTO THE OPTIC NERVE IN TWO MOUSE MODELS OF OPTIC NEUROPATHY

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Introduction: Purpose: To evaluate the incorporation and differentiation of BMSC into the injured optic nerve, following rAION or optic nerve crush induction, with and without intraocular injection of growth factors.
Patients / Methods: rAION (n=62) was induced by the activation of a photosensitive dye, injected intravenously, over the optic nerve head. Optic nerve crush (n=15) was induced to the globe by forceps. The small cells population isolated from the bone marrow of transgenic GFP+ mice, were lineage depleted after selection by counterflow elutriation. The BMC were injected intravitreally (IVT; n=10 rAION, n=10 crush) or intravenously (IV; n=16 rAION, n=5 crush). Optic nerve analysis for incorporation and differentiation was performed 1 month post transplantation using immunohistochemistry for GFP, GFAP, Vimentin, NeuN, CNPase, O4 and CD45. Another group of rAION underwent intraocular injection of growth factor [3 mice for each growth factor: vascular endothelial growth factor (VEGF), ciliary neurotrophic factor (CNTF) or brain derived neurotrophic factor (BDNF)] one day post rAION induction, immediately with cell transplantation (total 36 mice, IV; n=9, IVT;n=9) and analyzed 1 and 6 months after the transplantation.
Results: In both models, GFP+ donor cells were detected only in the injured optic nerve, 1 and 6 months post injury induction. Most of the cells were localized immediately behind the globe. There were no differences regarding the route of transplantation. When evaluated 6 months post transplantation, the GFP+ donor cells were also detected along the nerve. The incorporated cells stained with glial markers (vimentin and GFAP), were concentrated in the area of the injury, where glial scarring occurred. Intraocular growth factor administration did not shift the differentiation pattern of engrafted cells to either oligodendrocyte or myeloid lineages.
Conclusions: BMC donor cells can be detected in the injured optic nerve for up to 6 months post injury and transplantation. Both models of injury and routes of injection led to a similar rate of incorporation. Most of the cells adopted the glial phenotype and differentiation, regardless the presence of intraocular injection of growth factors.

OCCURRENCE OF DRY EYE SYNDROME AS A MANIFESTATION OF OCULAR GRAFT VS. HOST DISEASE AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Introduction: Allogeneic hematopoietic stem cell transplantation (HSCT) is performed for a variety of hematologic diseases and malignancies can cause graft versus host disease (GVHD). An immune response is mounted by the transplanted cells against host target organs (skin, liver, mucous membranes and eyes). Ocular GVHD manifested as dry eye syndrome can cause severe and sight threatening complications. We evaluated the incidence, severity and influence of ocular GVHD on HSCT patients in Sheba medical center.
Patients / Methods: In this cross sectional study, 111 consecutive patients treated at a HSCT center after allogeneic HSCT in the past 3 years had a full ophthalmic examination including tear breakup time (BUT), Schirmer test, corneal staining and filled the ocular surface disease index (OSDI) questionnaire.
Results: 111 patients were evaluated: 37% had past/present ocular GVHD 60% had past/present non-ocular GVHD. No association was found between the occurrence of ocular GVHD and non-ocular GVHD (p=0.37). No association was found between the indication for HSCT and occurrence of ocular GVHD (p=0.3). Statistically significant correlations were found between the subjective (OSDI score) and the objective (tear BUT, Schirmer test and corneal staining) parameters for dry eye disease and between visual acuity. Schirmer test was < 5mm in 49% of all patients and in 30% of patients undiagnosed with ocular GVHD. The mean OSDI score was 13, and in 29% it was >20. Of all subjects 47% had no previous ocular exanimation.
Conclusions: Severe dry eye is a common finding after HSCT, although many patients are either asymptomatic or had no previous ocular examination. This manifestation of Ocular GVHD is an important complication of HSCT and can cause objective and subjective disturbances in patients. GVHD involving other organs or the indication for HSCT were not predictive for ocular GVHD. Routine ophthalmological follow-up and patients and stuff education on the sign symptoms and complications of ocular GVHD is mandatory.

THE ROLE OF SIX3 IN EARLY EYE DEVELOPMENT

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Introduction: Six3 is a highly conserved transcription factor essential for eye formation. In zebrafish there are three Six3 homologues - six3a, six3b and six7. Combined six3b and six7 loss of function results in microphthalmia or anophthalmia. In six3b;six7-deficient embryos, eye progenitors are present in the eye field, yet eye tissues fail to develop later on. We aim to identify the cellular and molecular events that underlie failure of eye progenitors to develop into eyes when Six3 function is abrogated.
Patients / Methods: 1. We will label eye progenitor cells in six3b;six7-deficient embryos and follow them in live embryos to find whether they die, fail to proliferate or fail to migrate to their proper location. 2. We are taking two approaches to identify the molecular mechanisms of Six3 function. First, in an unbiased approach we will isolate eye progenitors from normal and six3b;six7-deficient embryos and perform gene expression profiling, looking for downstream targets of Six3. Our second approach is to examine the effect of Six3 loss of function on candidate targets, such as components of signaling pathways known to be required in eye development.
Results: We have generated transgenic fish lines in which the chimeric protein CD8-GFP is expressed in eye progenitors under the regulation of the eye-specific rx3 promoter. These transgenic lines afford isolation of eye progenitors from embryos. Subsequently isolated progenitors will be used for gene expression profiling by microarrays. As for the second approach, we chose one of the candidate targets of Six3 - the Wnt/β-catenin pathway, which was shown to inhibit eye specification. We have interfered with Wnt/β-catenin pathway activity in six3b;six7-deficient embryos by misexpressing the Wnt antagonist dickkopf-1. This resulted in partial rescue of the anophthalmic phenotype.
Conclusions: Upregulation of Wnt/β-catenin pathway activity does not appear to be the major cause for lack of eyes in six3b;six7-deficient zebrafish embryos.

Session VI – Genetics

ELUCIDATING THE TRANSCRIPTIONAL TARGETS OF PAX6 IN MAMMALIAN RETINOGENESIS

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Introduction: The Pax6 transcription factor is essential and sufficient for eye formation in vertebrates and invertebrates species. Previously, Pax6 was documented to be essential for the multipotency of retinal progenitor cells (RPCs), as Pax6 loss from RPCs resulted in their exclusive differentiation to subtype of amacrine ineterneuorns, while other retinal cell types did not form. The aim of the current study is to reveal genes that are directly regulated by Pax6 in the RPCs and thus mediate its role during retinal neurogenesis.
Patients / Methods: Two high-throughput experiments were conducted in our lab; including comparison of gene-expression profiles of mutant and control RPC's using the mouse Affymetrix Gene Chip microarray and ChIP-Chip using Pax6 specific antibodies and mouse Affymetrix Promoter Array. The intersection of the two lists produced 215 genes, which are putative direct transcriptional targets of Pax6 in the developing retina. Using this novel data, I have selected factors implicated in mediating the differentiation of amacrine, ganglion and horizontal cells, early born cell types that do not develop following Pax6 loss. The reduced expression of the selected targets was validated by in-situ hybridization and immuno-labeling. The binding of the promoter by Pax6 in vitro was validated by electromoblity shift assay (EMSA).
Results: Using these approaches three novel direct targets of Pax6 were identified Pou4f2, Fgf15 and Sip1.
Conclusions: Together, this study reveals novel components of the gene network regulated by Pax6 in the generation of early born retinal cell types.

REVEALING THE FUNCTION OF CERAMIDE KINASE-LIKE (CERKL), A PROTEIN INVOLVED IN HUMAN RETINAL DEGENERATION, BY STUDYING ITS INTERACTIONS WITH OTHER RETINAL PROTEINS

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Introduction: CERKL is a novel gene encoding for a ceramide kinase-like protein. CERKL mutations lead to severe retinal degeneration with early macular involvement. CERKL's function in the retina is currently unknown despite vast research. Our goal is to characterize CERKL by identifying its protein-protein interactions in the mammalian retina.
Patients / Methods: CERKL-interacting proteins were identified implementing the Ras Rrecruitment System (RRS) on a bovine retina cDNA library. Co-immunoprecipitation in COS-7 cells was used to verify the identified interactions. Serial deletion constructs were used to map the interacting sites. We are also examining the influence of known disease-causing mutations on these interactions. The effect of calcium on these interactions is tested using a GST pull-down assay.
Results: Nine candidate proteins were identified in the library screen, three of which are calcium-binding proteins. Two of them belong to a family of calcium-binding retinal proteins involved in the recovery mechanism of the photo-transduction cascade. Previously described mutations in one of these proteins cause human retinal degeneration with similar clinical presentation to CERKL mutations. The interaction between the proteins was verified using co-immunoprecipitation. The interaction between CERKL and at least one of these proteins appears to be calcium-dependent.
Conclusions: CERKL's function is currently unknown. Our findings link CERKL to the recovery mechanism of the photo-transduction cascade. This research has important implications for understanding of CERKL's retinal function and the pathophisiology associated with CERKL mutations in humans.

IDENTIFICATION OF NEW GENES REQUIRED FOR NORMAL EYE DEVELOPMENT

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Introduction: Eye development is a complex process that requires the coordinated function of many genes. Our laboratory is focused on identifying new genes that are required for normal eye development and understanding how these genes regulate eye formation.
Patients / Methods: We use zebrafish as a model organism. Zebrafish embryos develop externally, are transparent and are amenable to genetic manipulations. Therefore, zebrafish embryos are particularly suitable for molecular genetic studies of eye morphogenesis. To identify new genes required for eye development a chemical mutagenesis was performed and mutant embryos were screened for eye phenotypes.
Results: We identified two lines carrying mutations that affect eye development. In one line mutant embryos had coloboma. Positional cloning identified the mutant gene as Lmo2. Lmo2 function is specifically required for hematopoiesis and vasculature development. We found that the hyaloid artery of mutant embryos was significantly enlarged and we hypothesize that the abnormally large blood vessel interfered with optic fissure closure. Consistent with this hypothesis, stopping the circulation in these embryos resulted in collapsed vessels and rescue of the coloboma phenotype. In the second line, mutant embryos initially show normal development of the lens, which subsequently detaches from the retina or appears to degenerate. Histological analyses identified abnormal changes of the lens epithelium. We are currently carrying out positional cloning to identify the mutant gene.
Conclusions: Two new zebrafish mutants with abnormal eye development will add to our understanding of eye morphogenesis and lens development. By analyzing Lmo2 mutants we identified a role for normal hyaloid artery development in optic fissure closure. Through identification of a second mutant, we will gain knowledge on regulation of lens development.

A MISSENSE MUTATION IN THE DEHYDRODOLICHYL DIPHOSPHATE SYNTHASE (DHDDS) GENE IS ASSOCIATED WITH AUTOSOMAL RECESSIVE RETINITIS PIGMENTOSA IN ASHKENAZI JEWS

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Introduction: Retinitis pigmentosa (RP) is the most common inherited retinal degeneration with a prevalence of 1:4,000. The disease is heterogeneous and 35 loci are currently linked to autosomal recessive RP (arRP). Several newly identified genes were not a priori considered candidates for RP and were identified by whole genome linkage analysis. Our aim is to identify new arRP-associated genes using homozygosity mapping.
Patients / Methods: All patients were evaluated clinically and with visual function studies. Genomic DNA was tested for mutations in the DHDDS gene by sequencing and enzymatic restriction and for homozygosity using the Affymetrix whole genome 250K and 6.0 single nucleotide polymorphism (SNP) arrays.
Results: Using homozygosity mapping we identified a shared 3.7Mb homozygous region on chromosome 1p35.3-p36.11 in Ashkenazi Jewish (AJ) patients with arRP who belong to 2 unrelated families. Sequence analysis revealed a homozygous missense mutation, c.124A>G (p.K42E), in the DHDDS gene encoding the dehydrodolichyl diphosphate synthase in 5 affected individuals of the 2 above-mentioned families, as well as in 14 other AJ patients with RP of 12 unrelated families. The haplotype in these 2 families was found to be identical, suggesting a founder effect. The mutation was not identified in an additional set of 107 AJ patients with RP, 20 AJ patients with other inherited retinal diseases, or in 70 patients with retinal degeneration of other origins. The mutation was found heterozygously in 1/322 ethnically-matched normal controls. The statistical difference between the cohort of patients and controls was highly significant ($p<0.0001$). The affected amino acid (K42) is located immediately after the diphosphate binding site of the enzyme. Clinical phenotype of patients homozygous for the c.124A>G mutation was within the spectrum associated with arRP.
Conclusions: DHDDS is a key enzyme in the pathway of dolichol which plays an important role in N-glycosylation of many glycoproteins, including rhodopsin. Previous studies showed that distruption of this pathway in the frog eye results in an RP-like phenotype. Our results support a pivotal role of DHDDS in retinal function and might allow for new therapeutic interventions for RP.

OCT MACULAR CHANGES AFTER STRABISMUS SURGERY

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Introduction: Variations in macular optical coherence tomography (OCT) measurements before and after cataract surgery and retinal detachment surgery are known to occur. Possible changes of macular thickness after strabismus surgery were not reported. We examined macular thickness changes before and after uncomplicated extraocular muscle surgery.
Patients / Methods: We prospectively evaluated 60 eyes of 30 healthy patients undergoing elective unilateral extraocular muscle surgery. The recti muscles were operated in 23 eyes and the oblique muscles in seven. Their fellow eyes served as controls. OCT (Staratus, OCT 3) measurements were performed preoperatively and one day after surgery. The retinal map was divided into minimal foveal thickness, a central 1-mm disk area, and two peripheral ring areas with diameters of 3 mm and 6 mm divided into 4 quadrants and centered on the fovea. We compared the postoperative OCT values to the respective preoperative values.
Results: Central foveal thickness (CFT) in the operated eyes was 201.0±18.4 microns (µ) preoperatively compared to 205.32±22.7 µ postoperatively (p=0.0220). Pre- and postoperative perifoveal outer temporal quadrant thicknesses were 219.94±15.98 µ and 225.48±14.63 µ, respectively (p=0008). There were no significant differences in any of the other quadrants of the operated eyes. No differences were found between pre- and postoperative retinal thickness measurements of the fellow eyes (controls). Changes in CFTs of eyes that underwent recti muscle operation were greater than changes in eyes following oblique muscle operation, but not significantly.
Conclusions: This is the first demonstration of an asymptomatic increase in foveal and perifoveal thicknesses following extraocular muscle surgery. These findings might be related to a very minimal subclinical macular edema secondary to the traumatic intervention, despite the fact that there is no direct involvement of the retina. Long-term follow-up studies are warranted to establish whether these increased thicknesses eventually return to preoperative levels

REFRACTIVE AND STRUCTURAL CHANGES OF INFANTILE PERIOCULAR CAPILLARY HEMANGIOMA TREATED WITH PROPRANOLOL

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Introduction: To evaluate optical and anatomical changes induced by oral Propranolol therapy for infantile periocular capillary hemangioma (IPCH).
Patients / Methods: Patients and Methods: A retrospective comparative study was conducted from 6/2008-6/2010 at SCMCI, on children diagnosed with IPCH. Infants underwent thorough multidisciplinary evaluation by a pediatric ophthalmologist, dermatologist and orthoptists, with/without MRI and digital measurements of the ocular extension area. Propranolol therapy was administered progressively up to 2mg/kg/day under combined multidisciplinary follow up including, blood pressure, heart, pulse and blood glucose level measurements. Clinical evaluations were performed after first week, then every 6-8 weeks up to lesions disappearance. Side effects were recorded. Parameters, like sphere, cylinder, axis and spherical equivalent were statistically analyzed in the involved eye before and post treatment as well as between the two eyes.
Results: Results: Thirty patients (8 males, 22 females) were diagnosed at 1.64±2.79 months of age, more on the right side (53.3%) and mainly located preseptal (83.3%). All pts were treated by Propranolol but 13.3% were treated initially for a short time by steroids. Mean age of treatment initiation was 5.0±4.55 months and interval gap till starting therapy was 3.34±4.33. Side effects were found in 11/30 babies but only in 4/30 infants treatment dose was reduced to 1mg/kg/day. Mean involved extra ocular area was reduced from 12.7±21.75cm2 to 6.03±9.5 cm2 ($p<0.0001$). Comparative analysis of refractive parameters showed a reduction of the mean cylinder component in the involved eye before versus post treatment (1.01±1.1D versus 0.607±0.67D respectively) $p=0.022$. Comparison of the cylinder changes between both eyes pre treatment (0.97±1.1D and 0.49±0.61D respectively) and post treatment (0.607±0.67 and 0.32±0.48D respectively) showed significant differences, $p=0.017$ and $p=0.008$ respectively.
Conclusions: Conclusions: Early diagnosis of IPCH with prompt Propranolol treatment is involved with a significant reduction of the involved ocular area as well as the astigmatism and prevention of ocular/face disfiguring without rebound. Propranolol is recommended as the treatment of choice for babies with IPCH.

THE EFFECTS OF OPTICAL DEFOCUSING AND MYOPIA ON VISUAL BEHAVIOR IN DOGS

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Introduction: Though the average refractive error of dogs is 0D, several dog breeds are genetically predisposed to myopia. Inherited myopia due to axial length and vitreous chamber elongation has been described in the Labrador retriever, making this dog breed a naturally-occurring model for human myopia. The aim of this study was to assess the effects of myopia on visual behavior in dogs.
Patients / Methods: Experimental animals included eight trained retriever dogs. A target launcher was used to launch targets at a distance of 150 meters. Each dog underwent three target retrieval trials, and the launcher was moved to a different location for each trial, to prevent a learning effect. For each trial, the dog was bilaterally and randomly fitted with either 0D, +1.50D or +3.00D contact lenses. The time for retrieval of target with the different lenses was measured. Dog performance was also subjectively evaluated by professional trial judges who were masked regarding the power of the lenses. All runs were filmed to allow later analysis of performance.
Results: The performance of the dogs was significantly affected by the power of the contact lenses. Time to target retrieval with 0D lenses was significantly shorter than retrieval times with both +1.50 and +3.00D lenses (P=0.04 and P=0.007, respectively; Friedman aligned rank test). No differences in retrieval times were found between +1.50D and +3.00D contact lenses (P=0.50). Myopia also had a significant effect on the subjective evaluation of the judges. Scoring by both judges was significantly correlated with the power of the lenses (P=0.05; Chochran-Mantel-Haenszel test), with the highest scores awarded for trials with 0D lenses, and the lowest scores awarded for trials with +3.00D lenses.
Conclusions: To date, visual acuity in dogs could only be assessed using pattern ERG or VEP recordings. While behavioral tests have been used to study color perception and contrast sensitivity in dogs, this is the first behavioral study of defocusing in dogs. Our results demonstrate that even mild defocusing of 1.50D has significant behavioral consequences in dogs. Refractive screening of dogs with demanding visual tasks, such as guide dogs for the blind, is recommended.

"HIDE AND SEEK" IN THE COMMON CHAMELEON'S (CHAMAELEO CHAMELEON) AVOIDANCE RESPONSE: VISUO-MOTOR PATTERNS, LATERALIZATION AND ONTOGENY."

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Introduction: Common chameleons (C. chameleon, Reptilia, Lacertilia) are arboreal lizards. Their optical nerves show full decussation, and visual information from each eye is conveyed to, and processed by, the contra-lateral optic tectum with minimal tectal connection. Chameleons have highly independent eye movements, allowing them to rapidly shift from monocular to binocular vision. From hatching, faced with a threat stimulus, a chameleon positions itself on the side of a perch opposite (~180°) to the stimulus, while keeping it under monocular or binocular viewing. Sideways motion of the stimulus results in the chameleon's counter-motion by the chameleon. Aims: Using the visuo-motor patterns of avoidance response as a model, to determine, under conditions of binocular and monocular viewing, (i) the visuo-motor patterns used by each of the eyes, (ii) evidence for lateralization, and (iii) ontogenetic changes.
Patients / Methods: Chameleons (n=25) were subjected to an apparently moving threat, by the slow rotation of their vertical perching pole. Pole motion was clockwise or anti-clockwise in discrete steps, relative to the stationary experimenter. Chameleons of 4 age groups (1, 120, 240, 360 days post hatching) were tested on a narrow or a wide pole, respectively allowing monocular and binocular viewing or only monocular viewing of the threat. Video films were computer analyzed for response parameters (duration in specific visual sphere areas, frequency of shifts between the visual sphere areas).
Results: (i) Three different VMPs were observed during threat avoidance (ii) VMPs were both context dependent and side dependent (lateralized) (iii) Differences in eye use were apparent only when binocular viewing of the threat was possible (iv) Binocular viewing of the threat stimulus increased during ontogeny.
Conclusions: Patterns of eye movement in chameleons are unique in their being "context dependent". That lateralization was apparent only under specific conditions (threat approaching from the right side with no visual obstruction), may indicate weak inter-hemispheric connections.

THE DEPENDENCY BETWEEN VITREAL DOPAMINE AND DIHYDROXYPHENYLACETIC ACIDS (DOPAC) ON AMBIENT LIGHT INTENSITY.

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Purpose: Light initiates a neuro-hormonal cascade that activates retinal amacrine cells to produce and release dopamine. Low luminance (3-80 lux) was shown to modify the accumulation and the release of dopamine in rats' retina (Brainard.,1987). Recently, we showed that ambient light that range from 50 to 10,000 lux modulates the development of chicks' refraction (Cohen., 2008, 2010). Since retinal dopamine is thought to be involved in the development of refraction, it is possible that its retinal concentration is modified by light intensity. The aim of the study was to examine the dependency between light intensity and vitreal dihydroxyphenylacetic acids (DOPAC) concentration that was shown to represent a more precise rate of retinal dopamine release (Megaw., 2001).
Method: Male chicks (N=77) were exposed for 3 days to light intensity of 0, 50, 500, 10 000 lux at either continuous or 12h-/-12h light-dark cycles, with the light on at 7 am until 7 pm. The vitreous was extracted either at 8 a.m. or at 1 p.m.. Vitreal dopamine and DOPAC were quantified by liquid chromatography with electrochemical detection.
Results: Light intensity modulates vitreal dopamine and DOPAC concentrations. Under continuous light, the mean diurnal DOPAC concentration of the high (10,000 lux)-, medium (500 lux)-, and low (50 lux)-intensity groups were 15.05±5.17, 8.55±2.1, 4.24±1.26 ng/ml, respectively (one-way ANOVA, $P<0.0001$). Under light-dark cycles, DOPAC concentration at 8 am and 1 pm were strongly correlated with light intensity ($r=0.84$, 0.72, respectively; $P<0.0001$). The mean diurnal DOPAC concentration was 2.7ng/ml greater in the high- vs. low-intensity groups. The peak vitreal dopamine concentration of the high- and low-intensity groups were 1.27±0.15 and 0.66±0.32 ng/ml, respectively (t-test, $P=0.004$).
Conclusions: Retinal dopamine release is dependent on ambient light intensity. Under light-dark cycle, retinal dopamine release showed significant variations according to light intensity. This study support the hypothesis and provides a putative mechanism for the neurohormon dopamine involvement in the control of refractive development

VISUAL ACUITY IN CHILDREN OPERATED FOR CONGENITAL CATARACT: COMPARISON OF OUTCOME OF SURGERY WITH AND WITHOUT INTRA-OCULAR LENS IMPLANTATION

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Introduction: The purpose of this study was to compare the resultant visual acuity in children undergoing congenital cataract surgery with and without intraocular lens (IOL) implantation.
Patients / Methods: A retrospective analysis of clinical data was performed on 227 eyes of 155 patients with congenital cataract who underwent cataract surgery with or without primary IOL implantation, between the years 1991-2008 at the pediatric ophthalmology unit at the Sheba Medical Center. Factors examined included demographic data, cataract characteristics, type of surgical procedure and type of IOL.
Results: The median age at surgery was 29.34 months (range 0.5-204 months). The median follow up time was 63.60 months (range 1.5-200 months). Initial analysis of the visual acuity (logMAR) as a function of the type of surgery found a significant advantage in favor of IOL implantation (0.520 ± 0.486 vs. 0.874 vs. 0.593, $p < 0.001$). However, in a linear regression model considering the type of surgical procedure and the age at surgery, the surgical type had no significant effect on the visual acuity. On the other hand, the age at surgery was negatively correlated with the visual acuity. This trend was statistically significant ($p = 0.002$).
Conclusions: No difference was found between the postoperative visual acuity in children operated with implantation of IOL or without it. It was found that the older the child at the time of surgery, the better his visual acuity.

PERCEPTUAL TRAINING INDUCES VISUAL GAINS THAT OVERCOME THE OPTICAL DEFICITS IN PRESBYOPIA

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Introduction: Here we present a study performed at the University of California, Berkeley that supports and extends our initial experiment reported in ISVER-2010. Perceptual learning, prolonged practice of a visual task, can lead to improvement in visual function. In presbyopia, the visual input from the eye to the brain is limited by the optics of the eye. The purpose of this study was to ask whether perceptual learning in presbyopia leads to changes in optical functions that are not accounted for by directly measured pupil size and accommodation, but rather reflect improvement in cortical image processing after training.
Patients / Methods: Subjects were trained on contrast detection of Gabor targets under backward masking conditions, posing temporal constraints on the visual processing. The training covered a range of spatial frequencies and orientations that were modified in accordance with the improvement of the subjects. Visual acuity, spatial and temporal contrast sensitivity, contrast discrimination and reading speed were tested before and after the treatment. Front end aberrations, accommodation, depth of focus and pupil size were also measured before and after training. The subjects practiced for at least two sessions of about 30 min per week. The study included 29presbyopic subjects (52.44+/-0.83 years, mean+/-se). Seven young subjects (23.4+/-1.4 years, mean+/-se) served as control group.
Results: We found significant improvements in spatial and temporal contrast sensitivity, contrast discrimination and reading speed. After practice, perceptual functions reached the level of the young group. Visual acuity improved by ≈ 81% (2.57+/-0.017 ETDRS lines, mean+/-se), equivalent to a decrease in effective age of about 8 years. Processing speed improved as well. Moreover, after training, there was a real benefit for the subjects; many were able to read with no reading glasses. No changes in accommodation, and pupil size were found.
Conclusions: Perceptual learning produced substantial improvements in contrast detection, contrast discrimination and reading speed. The results are consistent with our previous studies in presbyopic and young subjects, and are not a result of improved optical functions. Thus, our method is effective in improving visual functions in people with blurred vision by enhancing the image representation in the brain.

Session VIII – Glaucoma and Cataract

MEDICATION ADHERENCE OF GLAUCOMA PATIENTS IN THE PRIMARY CARE SETTING IN ISRAEL

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Introduction: To understand the factors that influence glaucoma treatment adherence.
Patients / Methods: A retrospective cohort study was conducted using database of healthcare plan in the north of Israel (Clalit Health Services, Haifa & Western Galilee) between January 1 and December 31, 2007. From 10,000 persons who were prescribed glaucoma medications, a sample of 741 patients were selected for detailed abstraction. Adherent and nonadherent individuals, classified as such based on number of prescription claims for any ocular hypotensive medication during the study period. Demographics, and responses to telephone interview questions about glaucoma knowledge, drop-taking behaviors, experiences with medication, communication with the physician, and health-related beliefs associated with adherence behavior were obtained from each patient.
Results: Among 741 participants 481(65%) were poor adherers (1-5 prescription claims/ year) and 260(35%) were good adherers (11-12 prescription claims/year). Seven variables that affect adherence to glaucoma medication regimens were identified. Older age (OR=0.96, 95% CI 0.94-0.98), frequent dosing regimens (OR=0.77, 95% CI 0.70-0.85), and good communication with the ophthalmologist (OR=0.44, 95% CI 0.25-0.75), were promoters. Where, male gender (OR=1.55; 95% CI 1.1-2.19), lower income (OR=2.73, 95% CI 1.59-4.67), lack of knowledge of the benefits in taking the medication regularly (OR=1.42, 95% CI 1.19-1.68) and the request for help during application of eyedrops (OR=2.15, 95% CI 1.42-3.26) were barriers to adherence.
Conclusions: Strategies aimed at improving adherence in glaucoma patients need to address medication regimen, optimizing patient education about the benefits in taking the medication regularly, doctor-patient communications, and problem-solving regarding help during application of eyedrops.

TRABECULECTOMY AUGMENTED WITH MITOMYCIN C IS PROTECTIVE AGAINST INTRAOCULAR- PRESSURE RISE IN THE SUPINE POSITION

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Introduction: The intraocular pressure (IOP) increases substantially in the supine position. A new system (patent pending) was developed that enables accurate measurement of the IOP in the side-lying position using the standard Goldmann applanation tonometer. The purpose of this study was to measure and compare the amount of IOP elevation in the supine position between operated and medically treated glaucoma eyes.
Patients / Methods: Ten patients with chronic simple glaucoma or exfoliation glaucoma in whom only one eye was operated and their fellow-eye was treated with various topical preparations. The IOP was first measured in the sitting position. It was then measured in side-lying position after 15 minutes of lying supine.
Results: In the medically treated glaucoma eyes the IOP increased 5.7 ± 1.3 mmHg (range 4 to 8 mmHg) while in their fellow post-trabeculectomy eyes the increase in IOP while supine was only 1.8 ± 1.6 mmHg (range 0 to 5 mmHg). There was no significant correlation between the IOP elevation in the supine position in the glaucomatous eyes and their fellow trabeculectomy eyes.
Conclusions: Trabeculectomy but not topical anti-glaucoma medication may prevent IOP increase in the supine position.

LAMOTRIGINE, A VOLTAGE GATED SODIUM CHANNEL BLOCKER, IS NOT NEUROPROTECTIVE IN THE RAT GLAUCOMA MODEL.

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Introduction: Sodium voltage gated (Na+v) channels are proposed to play a role in glaucomatous neurodegeneration, due to their potential to induce depolarization and intracellular sodium overload in neurons. Our aim was to evaluate the efficacy of lamotrigine, an anti epileptic Na+v blocker, as a neuroprotective drug in two rat glaucoma models.
Patients / Methods: Acute glaucoma was induced in 13 Lewis rats through unilateral anterior chamber cannulation. Intraocular pressure (IOP) was raised to 70-80 mmHg for 60 minutes. Chronic glaucoma was induced in 22 Wistar rats through unilateral translimbal laser photocoagulation, resulting in 14-20 days of elevated IOP (ca. 50mmHg). Lamotrigine was administered at doses of 20 and 12.5mg/kg/day for 17 and 52 days in the acute and chronic groups, respectively. In each model, half the animals served as untreated controls. Retinal function, retinal ganglion cell (RGC) and optic nerve (ON) survival rates, and inflammatory responses were evaluated by electroretinograms (ERG), retrograde RGC fluorogold staining, Bielschowsky silver staining and immunohistochemistry (IHC) for ED1 respectively. Na+v expression was evaluated by IHC for 1.2 and 1.6 channel subtypes.
Results: In both models we found overexpression of Na+v channels subtype 1.2. This finding was most noticeable in the optic nerve, where a meshlike pattern of positive 1.2 fibers was observed in glaucomatous eyes. No functional or morphological evidence for neuroprotection was found in the chronic model. In the acute model, functional recovery of the scotopic b-wave from day 6 to day 14 post IOP elevation was 56% in lamotrigine treated rats compared with 6% in controls ($p=0.004$ and 0.5 respectively). A recordable pattern ERG response was observed in 20-30% of lamotrigine treated rats compared with 0% in the controls ($p=0.15$). Other functional and structural parameters showed an insignificant trend towards lamotrigine neuroprotection in this model.
Conclusions: Lamotrigine is not neuroprotective in the rat glaucoma model, even though the disease induces increased Na+v channel expression. Some evidence for neuroprotection was found in the acute model where ischemic conditions exist. These results might reflect the true, partial, role of Na+v in glaucomatous pathogenesis, or might be caused by insufficient lamotrigine concentration in the retina and ON.

RETINAL NERVE FIBER LAYER IMAGING: COMPARISON OF CIRRUS OPTIC COHERENCE TOMOGRAPHY AND HEIDELBERG RETINAL TOMOGRAPH 3

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Introduction: Purpose: To study the relationship between retinal nerve fiber layer (RNFL) thickness measured by spectral domain optical coherence tomography (OCT) and confocal scanning laser ophthalmoscope.
Patients / Methods: One eye from each individual was selected randomly for retinal nerve fiber layer (RNFL) imaging by the spectral domain Cirrus HD-OCT (Carl Zeiss Meditec, Inc., Dublin, CA) and Heidelberg Retinal Tomograph 3 (HRT; Heidelberg Engineering, GmbH, Dossenheim, Germany). Glaucoma was defined based on the presence of visual field defects with the Humphrey visual field analyzer (Carl Zeiss Meditec, Dublin, CA). The mean RNFL thickness and measurements at the temporal, superior, nasal and inferior quadrants around the optic disc were compared (paired t test). The relationship between the measurements was evaluated using a Pearson correlation analysis. Differences were analysed using Bland-Altman method. The agreement of the categorical classification, were available, was evaluated (κ statistics). The diagnostic sensitivities, specificities and the area under the receiver operating characteristic curves (AUC) were examined.
Results: One hundred seventy-three subjects (88 glaucoma and 85 normal subjects) were included in this study. RNFL thicknesses as determined by HRT3 were significantly higher than measurements done by Cirrus OCT ($P<0.0001$). Strong significant correlation was found between the two technologies for all measurements ($P\leq0.009$). Bland- Altman plots demonstrated a pattern of proportional bias. The agreement of categorical classification ranged between poor to fair ($\kappa=0.183$ to 0.305). Cirrus OCT measurement for the inferior quadrant RNFL yielded the highest AUC (0.826). The highest sensitivities at fixed specificities were achieved by Cirrus OCT for the superior quadrant RNFL (37.65% at 99% specificity and 68.24% at 80% specificity).
Conclusions: RNFL thicknesses measurements by Cirrus OCT and HRT3 are strongly correlated but significantly different. The difference between paired RNFL measurements was proportional to the RNFL thickness (proportional bias). The normative diagnostic classification of the 2 technologies may not agree. The results preclude interchangeable use of these measurements in clinical practice. The highest AUC's, sensitivities and specificities were achieved by Cirrus OCT.

HEMATOLOGIC BIOMARKERS IN CHILDHOOD CATARACTS

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Introduction: To date, more than thirty nine genetic loci have been associated with congenital cataracts. Despite this progress, current diagnostic techniques are insufficient for unraveling the underlying genetic defect in sporadic patients and small families. We hereby demonstrate the contribution of routine laboratory tests in the search for genetic defects of childhood cataracts.
Patients / Methods: Two families with congenital cataracts and hematologic findings that included the "ii" blood type and hyperferritnemia underwent detailed ophthalmologic and clinical examinations. Mutation analysis of the GCNT2 and FTL genes was performed in the two families, respectively.
Results: In the first family we found a novel GCNT2 gene mutation (G312D) in the cataract patients with the "ii" blood group, while in the family with hyperferritinemia cataract syndrome we identified a G > C heterozygous mutation at position +32 of the FTL gene.
Conclusions: Hematologic biomarkers may simplify the search for the underlying molecular defect in families with congenital cataract

DIFFERENT PHOSPHATASES ARE ACTIVE IN CATARACT AND GLAUCOMA PATIENT AQUEOUS HUMOR AND CORRELATES WITH ITS REDOX STATE

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Introduction: Direct and proteomics analysis of aqueous humor (AH) in the last years revealed the presence of many signaling proteins. Additionally, changes in the AH antioxidant capacity was found in cataract and glaucoma in humans AH. In our laboratory we were able to show that several members of the Mitogen Activated Protein Kinases are presented in the AH of rats and are subjected to changes depending on the intraocular pressure. In the present study, phosphatases activity was analyzed in human AH samples taken from cataract and glaucoma patients. Aim: (1) To analyze and compare the activity of serine/threonine phosphatases and tyrosine phosphatases (PTP) in cataract and glaucoma AH samples. (2) To evaluate the tested AH sample redox state. (3) To look for correlation between the redox state and the phosphatase activity.
Patients / Methods: AH samples were taken from 118 patients suffering from Cataract +/- exfoliation only (n=89) or with Glaucoma +/- exfoliation (n=29). Medical backgrounds were recorded. The AH samples were tested for different phosphatases presence and activity (Promega V2460 & V2471). AH total antioxidant capabilities (FRAP & ORAC), superoxide dismutase activity and glutathione content were evaluated
Results: Two Serine/Threonine phosphatases, PPase2A and PPase2C and PTP were detected in part the AH of cataract and glaucoma patients. The tested phosphatase mean levels did not differ between the groups. However significant differences were found among the percentage of negative/positive in the PTP assay among Cataract versus Glaucoma (p=0.0122), Cataract+exfoliation versus Glaucoma+exfoliation in PPase2A (p=0.0172) and PTP (p=0.0902). There was no effect of the patient age, sex and medical maladies background. In all the tested AH samples from the different groups similar Redox state were found. Positive correlation were found between PPase2A and PPase2C (Pearson 0.368), PTP and the antioxidant assay-FRAP (Pearson 0.362)
Conclusions: Different phosphatases can be detected in cataract and glaucoma patients' aqueous humor. The incidence of the tested phosphatases presence among the different maladies, vary. These phosphatases target proteins who are obscure for moment, might serve as new local target for intervention in glaucoma and cataract

Session IX – Retina 2

INCOMPLETE PVD AND EPIRETINAL MEMBRANES IN DIABETIC MACULAR EDEMA USING SPECTRAL-DOMAIN OCT

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Introduction: The association between the various stages of posterior vitreous detachment (PVD) and the epiretinal membrane (ERM) in eyes with diabetic macular edema (DME) is not determined as yet, although it draws much attention for years.
Patients / Methods: The study took place in one eye per consecutive patients with DME. In order to base our data on objective findings, we studied only eyes that presented with incomplete PVD and ERM that were confirmed by the spectral-domain optical coherence tomography (SD-OCT). Excluded were eyes that had undergone vitreoretinal intervention or that had complete PVD or complete vitreous attachment.
Results: Of 44 eyes with DME and adherent ERM, the posterior hyaloid was incompletely detached in 23 eyes (52.3%). Continuation between the detached posterior hyaloid and the ERM was apparent in 20 (87.0%) of the 23 eyes. Various OCT presentations of the partial PVD were encountered: A) Incomplete posterior vitreous detachment from the optic nerve head (ONH; n = 11; 25%), but attached to the macula; B) Incomplete posterior vitreous detachment from the macula (n = 7; 15.9%) in two manifestations; C) Complete posterior hyaloid detachment from the ERM (n = 2; 4.5%) with attachment to the ONH; D) Complete detachment of the ERM/ posterior hyaloid complex from the macula (n = 1; 2.3%); E) Incomplete detachment of a torn ERM/ posterior hyaloid complex from the macula (n = 2; 4.5%).
Conclusions: In eyes with DME, ERM and incomplete PVD, the posterior hyaloid and ERM appeared as one continuous membranous complex in most eyes. If this observation is verified by further studies, it may explain some of the ERM characteristics in DME and may have clinical importance in the context of removal of the ERM.

LAMELLAR MACULAR HOLES ASSOCIATED WITH END STAGE AMD STUDIED BY OCT

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Introduction: LMH due to an incomplete macular hole formation are usually stable in time and visual acuity of the involved eyes is often moderately good. Age-related macular degeneration (AMD) is the most prevalent cause of irreversible blindness in developed countries. The aim of the study was to describe morphologic abnormalities associated with LMH with underlying end stage AMD using OCT.
Patients / Methods: A retrospective study on consecutive patients with LMH with underlying end stage AMD. Analysis was referred to LMH-associated abnormalities at the residual fovea, mainly an epiretinal membrane (ERM), intraretinal split between the inner and outer retina, intraretinal fluid appear as cystoid spaces, and window defect excessively depicting the choroid.
Results: A total of 16 eyes of 14 patients (mean age, 80.6 years; range, 50–94) were included in the study. Best-corrected visual acuity ranged from 6/20 to 6/360. ERM, intraretinal split and cystoid spaces was detected in all the eyes, window defect was found in 14 eyes (87.5%). Foveal vitreous attachment was seen in only 1 eye (6.25%).
Conclusions: LMH with underlying AMD is a pathology that had not been acknowledged until now. It is possible that tangential traction exerted by an epiretinal membrane on the surface of juxtafoveal retina could have contributed to the LMH formation. Further studies are required to verify these observations, which may merit clinical and surgical considerations.

THE EFFECT OF THROMBIN ON THE STRUCTURE OF TIGHT JUNCTIONS AND THE PERMEABILITY OF RPE AND ENDOTHELIAL CELLS.

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Introduction: The blood retinal barriers (BRB) integrity is essential for normal retinal function. Any damage to the BRB is accompanied by infiltration and edema. BRB integrity is maintained by a dynamic system of tight junction proteins that are capable of regulating the intercellular space volume. Damage to the BRB accompanied by elevated thrombin levels was found in retinal pathologies such as diabetic retinopathy, inflammation, vascular occlusions, surgical complications and tumors. Understanding the effects of thrombin on BRB integrity is of great importance. The aim of the study was to explore the effects of thrombin on the permeability of endothelial and retinal pigment epithelial (RPE) cells layers. This effect was evaluated by measuring the changes in the expression and distribution of tight junction proteins.
Patients / Methods: We used a microvascular endothelial cell line and a retinal pigment epithelium cell line. The expression of genes encoding tight junction proteins (claudin1, 5, Jam1and ZO1) was evaluated using real time PCR. Permeability was evaluated based on spectrophotometric monitoring of the leakage of labeled dextran molecules of varying size. Intracellular localization of tight junction proteins was studied using immunohistochemistry staining.
Results: In both endothelial and RPE cell lines, addition of thrombin induced elevation in cell permeability as indicated by increased dextran leakage through endothelial and RPE monolayer. The effect of thrombin occurred in a few minutes after thrombin addition to the cells. The expression of genes of the tight junction family was altered in both cell lines. In both endothelial and RPE cells, thrombin induced downregulation of JAM1 expression while ZO1 mRNA levels were not affected by thrombin. Upregulation of claudin 5 and caludin 1 expression was detected in endothelial and RPE cells respectively. Changes in the tight junction proteins localization were demonstrated in the immunohistochemical staining.
Conclusions: The data indicate that elevation in thrombin level may cause alterations in the blood barriers of the retina through changes in endothelial and RPE permeability. Changes in the expression and localization of tight junction proteins induced by thrombin may partially contribute to increased permeability.

THE EFFECT OF MACULAR SURGERY ON THE VITREO-MACULAR INTERFACE

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Introduction: Vitreoretinal interface plays a major role in the pathogenesis of macular diseases such as macular pucker (MP), macular holes (MH), vitreo-macular traction (VMT) and macular edema (ME). Surgery is usualy the treatment for the vitreoretinal interface pathology. It is only since the appearance of the OCT technology that one can study in vivo this important antomical structure in health and disease. The purpose of this study was to shed more light on the pathogenesis of the macular diseases by comparing the vitreoretinal interface (VRI) imaging by OCT prior and after vitreo-macular surgery
Patients / Methods: 12 patients suffering from MP or VMTS or MH or ME were thoroughly evaluated by the OTI/OPKO OCT before undergoing vitreomacular surgery and 2 months after the surgical intervention. High quality pictures from the same area before and after the surgery were compared. All eyes were examined biomicroscopicaly as well.
Results: The contrast reflectivity of acellular vitreous and the parallel fiber orientation of the inner retina enabled clear interpretation of VRI at the diseased macula. Incomplete PVD was oserved in most of the eyes preoperatively. Traction on the macula by the vitreous (as in VMTS and ME) or by epiretinal membranes (ERMs) (as in MP) or by both (as in MH) were clearly observed before surgery. Postoperatively only few remnants of ERM were seen at the macula.
Conclusions: OCT as a non contact, non invasive imaging modality is essential in assessment of macular disorders that are difficult to characterize by biomicroscopy. Perifoveal PVD seems to induce macular complications by AP traction in VMTS and ME and by tangential traction in MP and MH. OCT enables us to better understand VR interface pathology and thus is essential for monitoring pre and postoperative course and also for the research of new treatment modalities for macular diseases.

DIAGNOSIS OF POSTTRAUMATIC STRESS DISORDER FOLLOWING SURGERY FOR PRIMARY RHEGMATOGENOUS RETINAL DETACHMENT

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Introduction: To investigate the prevalence of posttraumatic stress disorder (PTSD) in patients that underwent surgery for primary rhegmatogenous retinal detachment (RRD) and to determine variables associated with the disorder.
Patients / Methods: We approached 547 patients with a previous primary RRD, of which 363 (mean age 58 ± 15 years, 64% were men) were enrolled in the study. PTSD was assessed by the Clinician Administered PTSD Scale and the 25-Item National Eye Institute Visual Function Questionnaire (NEI-VFQ-25) was used as a measure of vision-related quality of life. Objective clinical measures were obtained from the patient's medical records. Psychological and ophthalmological variables were compared between PTSD diagnosed patients and a subset of PTSD-negative patients, who served as controls.
Results: Nine patients (2.5%) met the criteria for PTSD diagnosis and 9 PTSD-negative patients were randomly assigned to the control group. PTSD patients reported of significantly more traumatic events in their past (P=0.002) and for these patients NEI-VFQ-25 composite score was significantly lower (P<0.001). Clinical measures were not found as independent risk factors for PTSD prediction.
Conclusions: PTSD may develop in the aftermath of primary RRD. Previous traumatic events and NEI-VFQ-25 scores, in contrast to objective measures, were found as independent risk factors for PTSD prediction.

CHARACTERIZING THE RETINAL PHENOTYPE OF CCR2/CX3CL1 DOUBLE KNOCKOUT MICE

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Introduction: Chemokine receptor signaling and macrophages were implicated in the pathogenesis of Age-Related Macular Degeneration (AMD); however, their specific roles in AMD are not well understood. We aim to test the involvement of the CCL2/CCR2 and CX3Cl1/CX3CR1 chemokine signaling pathways in macrophage recruitment and their possible role in AMD in a mouse model.
Patients / Methods: Mice deleted for the CCR2 receptor and the CX3CL1 chemokine were generated (dKO mice), resulting in ablation of both signaling pathways. Eyes of wild type (WT) and dKO mice were analyzed histologically, the Outer Nuclear Layer (ONL) thickness was measured at 250 and 750 microns from the optic nerve (ON). Electroretinogram (ERG) recordings were performed on WT and dKO mice aged 4 and 8 months. Finally, we analyzed CD11b immunoreactivity on retinal flatmount preparations from dKO and WT eyes.
Results: Similar ERG recordings were obtained from dKO and WT mice at both ages tested. Increased subretinal accumulation of CD11b+ macrophages and microglia was observed in dKO mice, (average number of CD11b+ cells per retina: WT = 21.13, dKO = 43.07; P=0.0095). Many CD11b+ cells were morphologically large and ameboid in shape, and contained pigment within their cell bodies, indicating they might be phagocytically active. The ONL thickness in dKO mice was reduced by 12% medially (at 250 microns from the ON; P=0.005), and by 10.1% peripherally (at 750 microns from the ON; P=0.17). The overall retinal thickness was similar, suggesting a specific loss of photoreceptors.
Conclusions: We have generated a novel mouse model deleted for CCR2 and CX3CL1. Analysis of eyes from dKO mice revealed subretinal accumulation of pigment-containing, activated CD11b+ macrophages and microglia. This suggests enhanced recruitment of CD11b+ cells to sites of injury and inflammation, or their extended subrtinal presence. The normal overall retinal thickness, but reduced ONL thickness suggest photoreceptor loss in dKO mice. Microglia accumulation and mild photoreceptor loss in the presence of normal ERG amplitudes are reminiscent of AMD pathology in humans.

Session X – Cornea 2 and Oncology

SUB-TENON'S VERSUS RETROBULBAR ANESTHESIA IN CORNEA SURGERY

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Introduction: One of the biggest advances in ophthalmic surgery has been the use of progressively less invasive anesthesia for the control of intra-operative pain. Our purpose was to determine if intra-operative pain control during cornea and anterior segment surgery is as well controlled with sub-Tenon's anesthesia as with retrobulbar anesthesia.
Patients / Methods: On alternate operating room days,38 patients received either sub-Tenon's (n=20) or retrobulbar blocks (n=18). All patients received 3 mL of a 50:50 mixture of lidocaine (2%) and marcaine (0.5%) as well as mild IV sedation (propofol, midazolam and fentanyl). 10 minutes post-operatively the McGill Pain Questionnaire was administered by the fellow to the patients. The degree of pain at 10 minutes post-op was recorded on scale from 1-10 (10 being most pain ever).
Results: There were no complications from either sub-Tenon's or retrobulbar blocks. A paired t-test revealed no statistically significant difference in intra-operative pain control as assessed by the McGill Pain Questionnaire between the sub-Tenon's and retrobulbar groups ($p = 0.28$) Six patients in the sub-Tenon's group and 7 patients in the Retrobulbar group required "top-up" anesthesia (NS)
Conclusions: The results suggest sub-Tenon's anesthesia is as effective in controlling pain as retrobulbar anesthesia during anterior segment surgeries

CYTOTOXIC AND INFLAMMATORY EFFECTS OF CONTACT LENS MULTIPURPOSE SOLUTIONS (MPS) ON CULTURE HUMAN CORNEAL EPITHELIAL CELLS AND CONJUNCTIVAL FIBROBLASTS

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Introduction: Clinical data show that multi-purpose solutions (MPS) damage the ocular surface. This study examined the cytotoxic and inflammatory effects of seven commercial multipurpose contact lens solutions and hydrogen peroxide lens disinfection solution on human corneal epithelial cells and conjunctival fibroblasts.
Patients / Methods: MPSs (A to G) were applied on cells for 60 min to evaluate the cytotoxic effects with concentrations of 10 to 50% v/v (FITC-Annexin V/ PI, CellTiter-Blue and DNA Fragmentation ELISA assays). Cells were incubated with 30 and 50% v/v contact lens solutions for 12 hour. The mRNA levels of interleukin (IL)-6, IL-8, IL-1β, tumor necrosis factor-α (TNF-α) were tested by real time PCR. Cytometric Bead Array (CBA) was used to measure the respective protein contents in the culture supernatants. Cultures were also treated with phosphate-buffered saline (PBS) or benzalkonium chloride as negative and positive controls, respectively.
Results: All of the MPSs solutions showed different levels of toxicity compared to the negative control ($p<0.001$). Specifically, MPSs A and B solutions showed a significantly higher level of toxicity than the other MPSs ($p<0.05$). Incubation of MPSs with human corneal epithelial cells and conjunctival fibroblasts showed a significantly higher expression of inflammatory cytokines in MPSs A to C than the other MPSs ($p<0.05$). In contrast, there were no significant differences between hydrogen peroxide solution and the negative control on the various cytotoxic and inflammatory effects.
Conclusions: MPSs induced significant cytotoxic and inflammatory effects on ocular surface cells compared to the negative control. In contrast, hydrogen peroxide solution was the least cytotoxic and did not induce any inflammatory effects on human corneal epithelial cells and conjunctival fibroblasts. Taken together, these data suggests that hydrogen peroxide lens disinfection solution may be safer for use in contact lens wearers compared to the various multi-purpose soluitions.

HUMAN LIMBAL EPITHELIAL STEM CELL MARKERS AND MRNA EXPRESSION IN LONG-TERM REPEATED EXPLANT CULTURES FROM CORNEOSCLERAL RIMS

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Introduction: Limbal epithelial stem cell deficiency is a sight threatning condition that can be treated by stem cell transplantaion. This work was set to ascertain the feasibility of cultivating epithelial stem cells from cadaveric corneas in repeated sequential primary culturing.
Patients / Methods: Fresh and frozen human corneoscleral rims were cut into explants and cultivated. After 14 days each explant was removed and replaced in a new culture dish. Explants were re-cultured until no cellular growth was evident. Cultures were named according to the passage: P1, P2 and so on. Cultured cells were subject to either immunostaining or RT-PCR. Cultures dedicated for immunostaining were immunostained with antibodies against p63 and ABCG2, and the percentage of positive immunostained cells was recorded in the different passages. Cultures dedicated for RT-PCR underwent total RNA extraction and cDNA was synthesized using the RNA as template. cDNA was then amplified by PCR using primers for p63 and ABCG2 genes, and A relative standard curve method was used to quantify the expression
Results: Cultures from fresh explants contained positive immunostained cells for p63 and ABCG2 through P5 and P6, respectively. There was a gradual decline in the mean of the cells immunostained from P1 through P6; however- this trend was not statistically significant. When compared to fibroblast cultures, the presence the immunostained cells which were positive for p63 and ABCG2 was statistically significant throughout P5 and P6, respectively (Wilcoxon signed rank test). In explants that underwent freezing and thawing before cultivation, a statistically significant expression of both p63 and ABCG2 was evident up to P2. A relative standard curve of the RT-PCR results demonstrated that the p63 gene was expressed in 70% of the cultures expressing ABCG2.
Conclusions: Limbal epithelial progenitor cells, with typical stem cell markers and expressing mRNA unique to these cells, can be generated from repeated sequential explant cultures. This culture system may be used to expand large viable populations of progenitor epithelial cells for the purpose of cell expansion and transplantation in patients with limbal stem cell deficiency

NON-CHEMICAL STERILIZATION OF EYE DROPS BY IRREVERSIBLE ELECTROPORATION

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Introduction: Contamination of eye drops and other drugs can have substantial detrimental effects on health necessitating the addition of preservatives in many pharmaceutical. Preservatives such as the common benzalkonium chloride [BAK] have substantial detrimental effects on the eye on chronic use. We tried the use of Irreversible Electroporation (IRE), a method whereby minute amounts of electricity kills living cells by perforating their membranes. for nonchemical sterilization of topical eye medications.
Patients / Methods: Commercially available Hylo-Comod® preservative-free eye drop solution was contaminated with 106 CFU/mL Escherichia coli bacteria. Electroporation parameters for sterilization were investigated by comparing electrical fields of 5.4, 7.2, and 10 kV/cm, delivered as 100-μs square pulses at 1 Hz in sequences of 10 pulses, 20 pulses, or 20 pulses delivered as four sets of five pulses with 1-min intervals between each set. Pour plate counting method was used to determine microorganism survival. Effects of the treatment on temperature and pH were recorded as well.
Results: Twenty pulses delivered as four separate sets resulted in three orders of magnitude reduction in bacterial load (to 0.14%±0.03%). This reduction complies with the FDA requirement for three orders of magnitude reduction in bacterial concentration. The solution remained at pH 7.5 and the temperature rose to 35.6°±0.2C when these IRE parameters were used.
Conclusions: IRE seems to be a simple method for sterilization of drugs in solution to regulatory requirements, making the use of toxic preservatives such as benzalkonium chloride and thimerosal unnecessary

TREATMENT OF UVEAL MELANOMA BY NON-THERMAL IRREVERSIBLE ELECTROPORATION - MATHEMATICAL MODEL, ANIMAL AND PRELIMINARY EX-VIVO HUMAN EXPERIMENTS

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Introduction: Non Thermal Irreversible Electroporation (NTIRE) is a novel technique which employs electrical pulses for selectively and permanently damaging cell membrane while sparing non- cellular structures. The purpose of this work was to evaluate the possibility to use NTIRE for uveal melanoma treatment by simulation, animal study as well as ablation of human uveal melanoma ex-vivo.
Patients / Methods: A 3D model of the eye with a moderate size uveal melanoma tumor was created by Comsol Multyphysics 3.5. We simulated NTIRE to the eye while changing various combinations of internal and external electrodes. The electric potential and electric field for each spatial point in the eye were calculated by the Laplace equation. The Joule heating rate per unit volume caused by the electrical field was added to the Pennes bio-heat equation for temperature calculation. Porcine eyes and live rats eyes were used for model validation and for studying the effect of NTIRE on ocular structures. The electric properties of human uveal melanoma tumor were measured immediately after enucleation in 2 patients. Tumors were treated by 90-150 pulses of more then 1000 Volts/cm and were sent for pathological examination.
Results: Highest intratumor electric fields were found for configurations of combined intra and extraocular electrodes. The fraction of tumor within the various target fields was dependent on the pulse potential, electrode configuration and tumor conductivity. Pulse duration of 100 microseconds was associated with significant increase in temperature in some electrode configurations. However, pulse duration of 1 microsecond was not associated with significantly increased scleral temperature in all electrode configurations and pulse frequencies. Animal data supported the results obtained by the mathematical model. Histopathology of treated tumor showed extensive destruction of the tumors on both the architectural and the cellular levels.
Conclusions: This research supports the possibility to consider NTIRE as a treatment option for uveal melanoma. Further animal and human research need be conducted to substantiate the efficacy of NTIRE for the treatment of uveal melanoma.

EXPRESSION OF CXCR4 IN PRIMARY AND METASTATIC UVEAL MELANOMA

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Introduction: The purpose of this study was to determine the expression of the CXCR4 chemokine receptor in primary and metastatic Uveal Melanoma (UM) tissues and in a UM cell line.
Patients / Methods: Immunohistochemistry to detect CXCR4 (monoclonal anti-human CXCR4, R&D systems, Minneapolis, USA) was performed on 17 eyes of 17 patients with UM, as well as on 9 liver sections of 9 metastatic UM patients. The tissues were analyzed and graded according to the intensity of the stain from 0-4 (0- being no staining, and 4- very intense staining). The primary tumors were examined for tumor cell type, vasculogenic mimicry patterns, mitotic figures, and tumor size (largest basal diameter and tumor height). mRNA from the OCM1 cell line was examined for the expression of CXCR4 and VEGF before and after stimulation with SDF1 (CXCL12), as well as expression of SDF1 mRNA.
Results: CXCR4 expression was observed in both primary and metastatic uveal melanoma. In the 17 primary tumors 10 (59%) tumors stained grade 3. The mean staining intensity was 2.59. In the metastatic tumor 3/9 (33.3%) liver sections stained grade 4. The mean staining intensity was 2.56. No correlation was found between CXCR4 staining intensity and any of the histopathologic parameters. SDF1 mRNA was not detected in OCM1 cells. mRNA levels for CXCR4 did not increase after stimulation with SDF1, but this stimulation increased the mRNA levels of VEGF after 24 and 48 hours.
Conclusions: CXCR4 was found to be expressed in both the primary and the metastatic tumors. mRNA levels of CXCR4 did not increase after stimulation with external SDF1. However, VEGF mRNA levels increased after SDF1 stimulation. An inhibiting agent for CXCR4 protein is presently available and may be a new direction of treatment for both primary and metastatic uveal melanoma. However, this pathway needs further investigation.

Notes: