

**RESIDENT/FELLOW  
RESEARCH DAY**

**May 20, 2005**

**DEPARTMENT OF OPHTHALMOLOGY  
AND VISUAL SCIENCES**

**UNIVERSITY OF IOWA  
ROY J. AND LUCILLE A. CARVER  
COLLEGE OF MEDICINE**

**UNIVERSITY OF IOWA  
HOSPITALS & CLINICS**

**IOWA CITY, IOWA**

**Braley Auditorium  
01136 Lower Level  
Pomerantz Family Pavilion  
1:00 PM – 5:30 PM**

# **RESIDENT/FELLOW RESEARCH DAY - 2005**

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# **RESIDENT/FELLOW RESEARCH DAY - 2005**

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Stacy A. Sjoberg, M.D., Ph.D.

### **GLAUCOMA**

Michael K. Maley, M.D.

### **NEURO-OPHTHALMOLOGY**

Shannon C. Lynch, M.D.

### **OCULOPLASTICS**

Richard C. Allen, M.D., Ph.D.

### **OCULAR PATHOLOGY**

A. J. Bogdan, M.D.

### **PEDIATRIC OPHTHALMOLOGY**

Rahul Bhola, M.D.

### **RESEARCH**

John H. Fingert, M.D., Ph.D.

Michael A. Grassi, M.D.

Chan Y. Kim, M.D., Ph.D.

Hye Y. Kim, M.D.

### **VITREORETINAL DISEASE**

Judy C. Liu, M.D.

Chetankumar B. Patel, M.D.

Jason B. Sanders, M.D.

David S. Zumbro, M.D.

# **RESIDENT/FELLOW RESEARCH DAY - 2005**

## **THIRD-YEAR RESIDENTS**

Michael V. Boland, M.D., Ph.D.

Andrew P. Doan, M.D., Ph.D.

Lynn E. Fraterrigo, M.D.

James G. Howard, M.D.

Sudeep Pramanik, M.D.

## **SECOND-YEAR RESIDENTS**

James M. Coombs, M.D.

Reid A. Longmuir, M.D.

Jeffrey L. Maassen, M.D.

Erin E. O'Malley, M.D.

Erin M. Shriver, M.D.

## **FIRST-YEAR RESIDENTS**

Robert B. Dinn, M.D.

Jordan M. Graff, M.D.

Susannah V. Quisling, M.D.

Christopher C. Robinson, M.D.

Avinash P. Tantri, M.D.

## **ORTHOPTIC STUDENTS**

Rebecca K. Parrish, B.A.

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Department of Ophthalmology and Visual Sciences  
Resident and Fellow Research Program

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# RESIDENT/FELLOW RESEARCH DAY

## SCHEDULE OF EVENTS

Friday, May 20, 2005

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# RESIDENT/FELLOW RESEARCH DAY SCHEDULE OF EVENTS

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# RESIDENT/FELLOW RESEARCH DAY SCHEDULE OF EVENTS

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## RESIDENT/FELLOW RESEARCH DAY - 2005

### Long-term Outcome of Pediatric Aphakic Glaucoma

Rahul Bhole, M.D.

Ronald V. Keech, M.D., Richard J. Olson, M.D., sponsors



**Purpose:** To determine long term outcome of eyes with aphakic glaucoma following pediatric cataract extraction.

**Method:** A retrospective analysis of 130 patients diagnosed with aphakic glaucoma between 1969 and 2004 was performed. A total of 36 patients (55 eyes) were included in this study after excluding those that had cataract extraction after age 10 and patients with other ocular conditions, systemic syndromes, traumatic cataracts, congenital glaucoma or inadequate follow-up. Outcome variables studied included visual acuity, number of medication changes required over the course of the follow-up, maximum number of medications used at a time for more than 6 months to control intraocular pressures and surgical interventions required. Mean follow-up period was 18.7 years (range, 6.9-35 years).

**Results:** At the time of last follow-up 54.5% of the patients had visual acuity 20/40 or better, 34.5% had 20/50 to 20/200, and 11% had acuity worse than 20/200. Over the course of follow-up 34% required 1-2 medication changes for controlling glaucoma, 33% required 3-5 medication changes and 33% required 6 or more medication changes. Thirty-six percent of the eyes required a maximum of 1-2 medications for more than 6 months during the course of follow-up, 33 % required 3 and 31% required 4 or more medications or a surgical intervention for controlling intraocular pressure. Of the 55 eyes, 27% required surgical intervention (40% 1 surgery, 47% 2-3 surgeries and 11% 4-6 surgeries).

**Conclusion:** Patients with glaucoma following pediatric cataract surgery have a good visual outcome although most will require 3 or more medications and 1/4<sup>th</sup> will require one or more surgical procedures to control the glaucoma.

## RESIDENT/FELLOW RESEARCH DAY - 2005

### **Comparison of A-Scan Applanation Ultrasound to IOL-Master – Final Refractive Error Outcomes in a Teaching Setting.**

Reid Longmuir, M.D.  
Thomas Oetting, M.D., sponsor



**Purpose:** To determine the difference in predicted versus actual refractive error outcomes in patients receiving intraocular lens calculation performed with the traditional A-scan ultrasound device and the IOL-Master at the VAMC. Null hypothesis will be no difference between the groups.

**Population:** Patients receiving cataract extraction with intraocular lens implant using either method at the VAMC, Iowa City (resident-performed surgery) from approximately July 1, 2004 to June 30, 2005.

**Methods:** We will compare predicted outcomes for all patients receiving intraocular lens implants using the A-scan device and those receiving implants based on calculations from the IOL master, by chart review. The average error in predicted versus actual will be compared between groups.

**Results:** Pending.

**Discussion:** The importance in this project lies in determination not only of the relative accuracy of these two methods, but also the ability of residents to perform the A-scan accurately. The applanation required to do A-scan measurements could theoretically introduce falsely low axial eye lengths and resultant post-operative spherical equivalents more myopic than predicted. Additionally, residents do not routinely supervise the IOL master measurements as they are acquired, and we would like to know the accuracy of this method as it compares to our previous gold standard of the A-scan.

### **Clinical Characterization and Ptosis Surgery Outcomes of Hispanic New Mexicans with Oculopharyngeal Muscular Dystrophy**

Richard C Allen, M.D., Ph.D.

J. Jaramillo, R. Black, D. Sandoval, C. Qualls, L. Morrison

Jeffrey A. Nerad, M.D., sponsor



**Purpose:** Oculopharyngeal muscular dystrophy is an autosomal dominant condition characterized by progressive ptosis and dysphagia. The disease is caused by expansion in a GCG repeat in the PABPN1 gene. The purpose of this study is to clinically characterize and evaluate ptosis surgery outcomes in Hispanic New Mexicans with OPMD who uniformly have a (GCG)<sub>9</sub> repeat expansion in the PABPN1 gene.

**Methods:** Hispanic New Mexicans with OPMD underwent a full ophthalmic examination pre- and post-operatively with attention to the following measurements: margin reflex distance (MRD), palpebral fissure height (PF), and levator function (LF).

**Results:** 86 patients were identified with OPMD. 50 patients were examined prior to any surgical intervention. The mean age of patients was 63.9 +/- 8.5 (SD) years. For MRD, PF, and LF, the right and left eye were highly correlated with Pearson correlations of 0.88, 0.86, and 0.89 ( $p < 0.001$ ), respectively. There was a high correlation between age and MRD ( $r = -0.75$ ,  $p < 0.001$ ), moderate correlation between age and PF ( $r = -0.45$ ,  $p = 0.001$ ), and a weak correlation between age and LF ( $r = -0.32$ ,  $p = 0.02$ ). 83 of 86 patients underwent ptosis surgery. 15 patients had a blepharoplasty, 17 patients had a levator advancement (LA), and 51 patients had a frontalis sling (FS) as their first surgery. 93.3% of patients who had a blepharoplasty, 47.0% of patients who had a LA, and 7.84% of patients who had a FS as their first surgery went onto reoperation for recurrent ptosis; these percentages differ (Fisher's exact,  $p < 0.001$ ). Of the 83 patients who underwent surgery, preoperative data was available for 47. Of these 47, 41 patients had a FS and 6 patients had a LA. There was no statistical difference between these two groups with respect to age, pre-op MRD, PF, and LF. For patients having a LA, the post-op change in PF was 0.33 mm OD and 1.1 mm OS. For patients having a FS, the post-op change in PF was 2.63 mm OD and 2.68 mm OS. These post-op differences were statistically different ( $p = 0.03$ , OD and  $p = 0.004$ , OS). Neither group experienced a significant post-op complication.

**Conclusions:** Hispanic New Mexicans with OPMD due to a (GCG)<sub>9</sub> expansion in the PABPN1 gene experience a symmetrical, progressive ptosis. Frontalis sling surgery is the most effective first surgery to treat the ptosis in these patients.

## RESIDENT/FELLOW RESEARCH DAY - 2005

### **Detection of Amyloid Precursor Protein in the Nerve Fiber Layer and Optic Nerve in Non Accidental vs. Accidental Injury of Infants**

A.J. Bogdan, M.D.  
Patricia Kirby, M.D.,  
Nasreen A. Syed, M.D., sponsor



**Purpose:** Amyloid Precursor Protein (APP) has been demonstrated to be a sensitive marker for axonal damage, seen as axonal spheroids, due to acceleration-deceleration and rotational (shearing) injury in the central nervous system. In this study, we investigate cases of non-accidental injury (NAI) in infants, formerly known as Shaken Baby Syndrome, to determine if APP is detectable in the optic nerve and retina as a result of tractional forces and shearing injury.

**Methods:** 34 cases of autopsy eyes were selected for study from the archives of the F.C. Blodi Eye Pathology Laboratory at the University of Iowa from 1995-2004. The ages of the patients ranged from <1.0-72.0 months. The eyes were categorized into three groups determined by cause of death, Non-Accidental Injury (NAI) 17 cases; Accidental Injury (AI) 2 cases; and 15 Normal (N) cases in which trauma did not contribute to cause of death. The eyes were evaluated grossly and microscopically for retinal hemorrhages, optic disc and optic nerve sheath hemorrhages, perimacular folds, and vitreous hemorrhage. Immunohistochemical staining for Amyloid Precursor Protein using an immunoperoxidase method was performed using APP monoclonal antibody. Slides were then evaluated by two masked observers; one being an ocular pathologist and the other a neuropathologist for the presence of axonal spheroids in the retina and optic nerve.

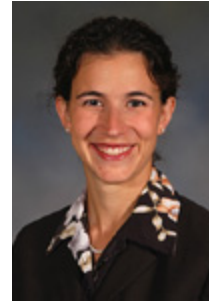
**Results:** 76% of the NAI group were found to be strongly positive in either the peripheral retina, posterior retina, optic disc or the optic nerve itself. One case of Accidental Injury had positive APP axonal spheroid staining in the nerve fiber layer, optic disc at the lamina cribrosa, and the optic nerve. The eyes of the Normal group were negative for APP. The inter-observer agreement in evaluating the slides was good overall.

**Conclusions:** Both Non-Accidental Injury and Accidental Injury cases demonstrated focal axonal staining for APP in the retinal nerve fiber layer, often adjacent to capillaries and retinal hemorrhages and in the optic nerve when compared with eyes from the Normal group. These findings support the theory that local tractional forces play a role in the etiology of the retinal and optic nerve hemorrhages in cases of infantile trauma without direct ocular injury.

### Central Retinal Vein Occlusion Associated with Cilioretinal Artery Occlusion

Lynn Fraterrigo, MD

Sohan Singh Hayreh, MD, PhD, DSc., sponsor



**Purpose:** Central retinal vein occlusion (CRVO) may be associated with cilioretinal artery occlusion. In case of non-ischemic CRVO, cilioretinal artery occlusion may be the primary cause of severe visual loss and presentation. Case reports/series describing this clinical entity are rare. No large systematic study has been performed to define the clinical presentation, features, and prognosis of CRVO with cilioretinal artery occlusion.

**Methods:** We performed a detailed review of the medical record of all patients with the diagnosis of CRVO with cilioretinal artery occlusion seen in the Ocular Vascular Clinic at the University of Iowa Hospitals and Clinics between 1974 and 2004. The total number patients presenting with this entity was 37. Demographic features, presenting clinical signs and symptoms, potential co-morbidities were recorded. The area of the retina affected by cilioretinal artery occlusion and its influence on the initial and final visual acuity and visual field were recorded and evaluated.

**Results:** Average age of onset was 51 years. Depending upon the extent of supply by the cilioretinal artery and the type of CRVO, initial visual acuity ranged from 20/15 to hand motion, and final visual acuity from 20/15 to NLP; only 7 (19%) patients had a final visual acuity of 20/200 or worse - 4 of these were secondary to ischemic CRVO. Final visual acuity was 20/40 or better in 27 patients (72.9%), with 17 (45.9%) having 20/20 or better. Seven out of 21 patients, with cilioretinal artery occlusion touching the fovea, presented with initial visual acuity of 20/40 or better. The average time to final visual acuity was 265 days (median 40 days). Eyes with poor visual outcome appeared to take longer than those with good visual outcome. During follow-up, of the 37 patients, the visual acuity remained the same in 15 (7 of these patients had an initial visual acuity of 20/20), improved in 17 by 2 lines or greater, and declined in 5. The most common visual field defects were cecocentral (17/37) and other central/paracentral scotomas (19/37), most often corresponding to the area of retinal infarction by the cilioretinal artery occlusion. During the follow up period, the central visual field defects improved in 20/35 cases, and completely resolved in 4/35 cases.

**Conclusion:** Cilioretinal artery occlusion is a fairly common entity in association with CRVO. Overall, the visual prognosis associated with this entity is good. Association with ischemic CRVO, as expected, predicted poor visual prognosis. Cilioretinal artery occlusion extending adjacent to the foveal avascular zone but not involving it tends to show good recovery of visual acuity, despite often poor presenting initial visual acuity. Visual field defects corresponding to the area of retinal infarction are common. These defects frequently improve with time but do not often resolve completely..

## RESIDENT/FELLOW RESEARCH DAY - 2005

### Characterization of Wavefront Aberrations in Patients Who Underwent Deep Lamellar Keratoplasty (DLEK)

James M. Coombs, M.D.

Kenneth Goins, M.D. and John Sutphin, M.D., sponsors



**Purpose:** Deep lamellar keratoplasty (DLEK) is a new procedure to treat endothelial failure. A deep, 5.0 to 9.0 mm limbal incision is made, then a posterior lamellar dissection is performed throughout the entire cornea, and the posterior one-third of the central corneal tissue is replaced with a healthy endothelial layer. Early clinical results show less postoperative corneal astigmatism and faster visual rehabilitation compared with standard penetrating keratoplasty (PKP).

The purpose of this investigation is to characterize the wavefront aberrations in patients who undergo DLEK and to compare these findings with the wavefront aberrations present in PKP patients. In addition, we want to determine if higher order wavefront aberrations limit the final visual acuity in DLEK patients.

**Methods:** Thirty one (31) patients underwent DLEK at the University of Iowa between December 2003 to December 2004. Four patients required conversion to PKP at the time of surgery and served as our control. All patients were analyzed with Tracey iScan® wavefront mapping postoperatively. Six patients received a 9 mm limbal incision and 18 patients had a 5 mm incision. Ten of the 27 DLEK patients underwent a combined DLEK/phacoemulsification procedure while the other 17 had only DLEK.

Best corrected visual acuity was measured at each post operative visit and compared with the wavefront data. DLEK was performed by either of two surgeons (KG, JS). There were 3 patients whose Tracey scans were unreliable and were not included in the study. Of the studied 31 patients, 10 of 56 scans (18%) were discarded because >25% of ray points were rejected.

**Results:** Mean RMS value for total aberrations was 1.53, 1.10, and 1.06 for 5mm DLEK, 9mm DLEK and PKP respectively at 4-6 months post op. Mean RMS for high order aberrations was 0.48, 0.39, and 0.36 for 5mm, 9mm and PKP respectively at 4-6 months post op. In patients whose vision was worse than 20/40 there was a noticeable spike in 3rd order trefoil at 2-3 months post op as compared to those with vision better than 20/40.

**Conclusions:** In our retrospective analysis we found no significant difference in higher order aberrations among patients who underwent DLEK and those that had PKP. In patients who had vision worse than 20/40, only at 2-3 months post op a spike in HOA was noted. There was no difference, however after 4 months. The most notable trend in HOA after DLEK was a spike in 3rd order trefoil 2-3 months post op which eventually converted to coma. This trefoil spike is probably attributed to suture effect. With 18% of wavefront scans unreliable, Tracey may not be the best modality to measure HOA after DLEK..



### **Clinically Detectable Drusen Substructure in Fibulin 5 Associated Age-Related Macular Degeneration**

Chetankumar B. Patel, M.D.  
Edwin M. Stone, M.D., Ph.D., Stephen R. Russell, M.D.,  
sponsors



**Purpose:** On fluorescein angiography, cuticular drusen and early-adult onset grouped drusen exhibit regions of hyperfluorescence that are noticeably smaller than the drusen appear with color photography. This suggests that drusen associated with certain disorders possess clinically detectable, substructural domains (i.e., drusen cores). Recently, missense variations in the fibulin 5 gene were identified in seven patients with age-related macular degeneration (AMD). These patients all had small, round, uniform (i.e., cuticular-like) drusen. In this study, we examined whether patients with fibulin 5 mutations have findings suggestive of drusen substructure.

**Methods:** Prior IRB approval was obtained for this study. Of the seven patients with missense variations in the fibulin 5 gene, five had fluorescein angiography and color fundus photography performed on the same visit. The color and angiographic images of these five patients were evaluated by scanning the images on a Nikon Super Coolscan 4000 at 4,000 pixels per inch. These scanned images were normalized, registered and processed utilizing Adobe PhotoShop 7.0 to perform color fundus - fluorescein angiogram image subtraction. Drusen and hyperfluorescent core sizes were measured by overlaying the Zeiss 30° fundus images with the Age Related Eye Disease Study (AREDS) template.

**Results:** All five patients displayed evidence of coaxial central hyperfluorescent cores (CCHC) associated with a subset of drusen ranging in size from 63 to 180  $\mu\text{m}$ . CCHC were not evident in any drusen larger than 180  $\mu\text{m}$ . CCHC were found in several fibulin 5 phenotypic backgrounds such as scattered small macular drusen, near-confluent macular drusen, and in the presence of occult choroidal neovascularization.

**Conclusion:** Patients with missense variations in the fibulin 5 gene have drusen that exhibit drusen substructure. Further evaluation of this genotype and other patients with age-related macular degeneration will help to elucidate the pathophysiologic mechanisms underlying these cores as well as their prognostic significance.

## RESIDENT/FELLOW RESEARCH DAY - 2005

### **Cataract Surgery: Assessment of Risk Factors for Anesthesia Consultation, and an Examination of Resulting Interventions**

Avinash Tantri, M.D.  
Connie Clark, R.N.  
Thomas Oetting, M.D., sponsor



**Purpose:** Cataract surgery is the most common surgical procedure in the VA hospital system. Most of these cases are done under local anesthesia. Some cases require intraoperative anesthesiology consultation. We will examine the risk factors for intraoperative anesthesiology consultation in cataract surgery performed under local anesthesia. We will then evaluate the results of those consultations. Availability of this data can assist both the ophthalmologist and anesthesiologist in preparation for surgery.

**Methods:** Retrospective chart review of 276 cataract surgeries performed under local anesthesia from April 1, 2002 to April 1, 2003 at the Iowa City VA Medical Center.

**Results:** The ASA (American Society of Anesthesiologists) classification of each patient was determined: 154 patients were classified as ASA 2. 121 patients were classified as ASA 3. Anesthesiology was consulted 24 times. Of these, 19 consultations involved patients who were ASA 3, while 5 consultations involved patients who were ASA 2.

The type of intervention was then examined: Oxygen flow rate was increased in 5 cases. Anesthesia consultation in the other 19 cases consisted only of observation, equipment repair, or starting of an intravenous line. Only one case (ASA 3) was converted intraoperatively to monitored anesthesia.

We will also examine resident training level, case length, and type of local anesthesia to determine if these are risk factors for consultation.

**Conclusions:** ASA classification is predictive of intraoperative anesthesia consultation in cataract surgery performed under local anesthesia. Most consultations resulted in no intervention. Intraoperative conversion to monitored anesthesia is rare. Results regarding resident training level, case length, and type of local anesthesia are pending.

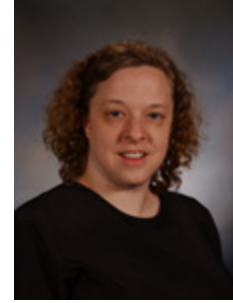


## RESIDENT/FELLOW RESEARCH DAY - 2005

### **Correlation Between Interface Opacity and Visual Acuity in Deep Lamellar Endothelial Keratoplasty (DLEK)**

Stacy A. Sjoberg, , M.D., Ph.D.

Kenneth Goins, M.D. and John Sutphin.M.D., sponsors



**Purpose:** It has been documented that the final Snellen visual acuity after DLEK may be reduced compared to conventional penetrating keratoplasty, despite lower astigmatism. The etiology of this is unclear, however some investigators suggest that interface opacity, posterior corneal vaulting, higher order wavefront aberrations or endothelial cell count may play a role. The purpose of this study is to determine if interface opacity has adverse effects on visual outcome in DLEK.

**Methods:** Thirty patients underwent DLEK. Postoperatively, the mean best corrected Snellen visual acuity, pachymetry, and interface, corneal anterior surface and lens opacities (Oculus Pentacam densiometry measurement) were determined at 3 months.

**Results:** Pentacam data and Snellen visual acuities were examined 3 months postoperatively in twenty-eight patients. The mean best-corrected Snellen vision at 3 months was 20/50. Early results show limited correlation between interface opacity and visual acuity with  $R^2 = 0.1344$  (Interface opacity may “explain” less than 13% of the variance in visual acuity). There were a few select cases where the interface densiometry measurement was greater than the anterior corneal surface densiometry measurement also corresponding to poor visual acuity.

**Conclusions:** While interface opacity may play a small role in decreased post DLEK visual acuities, other factors may play a more significant role such as lens opacities, or perhaps corneal topographic astigmatism, higher order wavefront aberrations, corneal or macular edema.

**Comparison of Oculus Pentacam and Orbscan IIz on Posterior Corneal Curvature Measurements in Keratoconus Eyes**

Susannah Quisling, M.D.  
Stacy Sjoberg, M.D., Bridget Zimmerman, Ph.D.  
Kenneth Goins, M.D., John Sutphin, M.D., sponsors



**Purpose:** To compare posterior curvature elevation and pachymetry by Pentacam and Orbscan IIz (OIIz) in keratoconus.

**Methods:** Measurements of posterior curvature topography were compared in 28 keratoconus eyes with reference to the apex and thinnest point. The mean difference, standard deviation (SD), and 95% limits of agreement were calculated and Bland-Altman plots were constructed.

**Results:** In 28 eyes, selection of best-fit sphere (average radii 5.91 mm Pentacam, 5.97 mm OIIz) and resulting posterior vault mean of 38  $\mu\text{m}$  for Pentacam and 53  $\mu\text{m}$  for OIIz showed mean difference of  $-0.06 \pm 0.29$  ( $p=0.112$ ) and  $-15.07 \pm 27.68$  ( $p=0.008$ ) respectively. The mean thinnest point was 441  $\mu\text{m}$  for Pentacam and 446  $\mu\text{m}$  for OIIz with a mean difference of  $-4.96 \pm 39.06$  ( $p=0.507$ ).

**Conclusion:** The OIIz and the Pentacam provide similar measurements of the thinnest point in keratoconus eyes, but posterior vault is greater in OIIz. Causes will be discussed, which include lid artifact and apical scar.

## RESIDENT/FELLOW RESEARCH DAY - 2005

### Vertical Optokinetic Nystagmus Testing in Patients with Congenital Nystagmus

Rebecca Parrish, B.A.

Ronald Keech, M.D. and Wanda Pfeifer, O.C.(c), sponsors

**Purpose:** It is a widely held belief that testing vertical optokinetic nystagmus in young children with congenital nystagmus provides insight in regard to their optimal visual acuity outcome. To date, there are no studies that clarify the prognostic value of optokinetic nystagmus testing in congenital nystagmus patients.



This research study is to determine if there is a correlation between the vertical optokinetic response and the visual acuity in patients with congenital nystagmus. It is our hypothesis that a positive vertical OKN response in patients with congenital nystagmus will confer a good visual prognosis. If this hypothesis is correct, then it may be valuable to the clinician in prognosticating vision in the infant with congenital nystagmus.

**Methods:** We will include 25 patients with congenital nystagmus. Test best corrected visual acuity at 20ft and 1/3m. Elicit an OKN response with a computer program with 9 different stripe sizes and speeds. In addition to the computer program, we will use a standard OKN drum at 33cm rotated at approximately 4degrees/sec.

**Results:** Pending.

### **Reduced Visual Outcomes Correspond to Increased Circularity of AMD Associated CNV Following Sequential PDT**

David S. Zumbro, M.D.  
J.S. Slakter  
Stephen R. Russell, M.D., sponsor



**Purpose:** We have shown that persistent or recurrent choroidal neovascularization (CNV) following initial and sequential PDT results in increasingly circular CNV shape. To determine the implications of circular CNV shape, we evaluated standardized best corrected visual acuities (BCVA) following PDT treatments in a well studied cohort.

**Methods:** Thirty patients with TAP eligible PDT lesions were enrolled in a controlled, randomized masked trial (for anecortave acetate evaluation, C-00-07). Standardized BCVA, CNV greatest linear dimensions (GLD), and angiographic images of the control-PDT treated subgroup were provided to us for analysis, masked of patient identifiers. As a measure of CNV circularity or eccentricity, we measured the GLDs and the CNV dimensions perpendicular to the GLD, at study entry, and 3 and 6 months. Findings were tabulated and graphical distributions evaluated.

**Results:** At entry, 3 months and 6 months the frequency of greatest CNV lesions circularity (circularity index or eccentricity of 0.9 or larger) were 28%, 43%, 52%. At 6 months, the average logMAR visual acuities for the most circular (0.9 – 1.0 eccentricity) and less circular lesions (< 0.89 eccentricity) was 0.98 and 0.61.

**Conclusions:** Distribution of CNV shape following initial and sequential PDT demonstrates a consistent increase in circularity and a reduced BCVA. CNV that become more circular in shape following PDT suggests a reduced visual outcome.

### **Vitreopapillary Traction as a Cause of Chronic Optic Disc Edema**

Shannon C. Lynch, M.D.

Randy H. Kardon, M.D., Ph.D., sponsor

**Purpose:** To describe patient characteristics and optical coherence tomography (OCT) findings in chronic optic disc edema caused by vitreopapillary traction.

**Methods:** Six patients, aged 44 to 76, with chronic disc edema of unknown cause underwent detailed ophthalmologic exam including optical coherence tomography. OCT was performed using the retinal nerve fiber layer and map fast scans, optic nerve head fast scans, and line scans from the optic nerve to the macula. Stereo disc photos and perimetry were also obtained.

**Results:** In all six cases, vitreous traction as the cause of chronic disc edema was not initially appreciated on examination until discovery by optical coherence tomography. OCT demonstrated vitreous attachments to the optic nerve head with associated elevation in all cases and neurosensory detachment in four. Epiretinal membranes were present in all six cases. Only two of the six patients were diabetic. One patient, who also had a neurosensory detachment involving the macula, underwent vitrectomy with resolution of disc edema.

**Conclusions:** Vitreopapillary traction can be a cause of chronic optic disc edema and associated neurosensory retinal detachment in eyes with and without diabetic retinopathy. The presence of an epiretinal membrane may partly explain continued, chronic traction. Neurosensory detachment of the retina may contribute to the enlarged blindspot and the clinical appearance of disc elevation. Vitreous traction is easily demonstrated with optical coherence tomography and should be considered in the differential diagnosis of chronic disc edema.



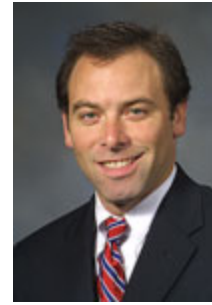
## RESIDENT/FELLOW RESEARCH DAY - 2005

### Aqueous humor factors and open angle glaucoma

J.H. Fingert, M.D., Ph.D.

A.T. Johnson, M.D., Ph.D., Y. H. Kwon, M.D., Ph.D., W.L.M.

Alward, M.D., and E. M. Stone, M.D., Ph.D., sponsors



**Background:** Immune mechanisms have been implicated in the pathogenesis of glaucoma. Preliminary studies have identified altered cytokine and growth factor levels in the serum of glaucoma patients. Abnormalities in the aqueous humor of a small number of glaucoma patients have also been identified, suggesting that cytokines may have a role in the development of glaucoma.

**Purpose:** Determine the concentration of a comprehensive panel of cytokines and immune factors in the aqueous humor in 50 normal subjects and in 50 patients with open angle glaucoma.

**Methods:** Aqueous humor will be collected intraoperatively from patients undergoing cataract or trabeculectomy surgery. The concentration of a panel of cytokines and immune factors in the aqueous humor will be measured using a micro-bead based immunologic detection assay.

**Results:** Preliminary studies of the aqueous humor of two cataract patients revealed measurable levels of several cytokines (IFN- $\gamma$ , TNF- $\alpha$ , IL-1b, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-13, MCP-1, MIP-1). IL-2 and IL-17 were not detectable.

**Conclusions:** Preliminary results indicated that a micro-bead based assay is an effective technique for detecting the concentration of cytokines in the aqueous humor. Analysis of additional samples is underway. The concentration of cytokines in the aqueous humor of open angle glaucoma patients and normal subjects will be compared to determine if these factors have a role in the pathogenesis of glaucoma.

## RESIDENT/FELLOW RESEARCH DAY - 2005

### **Diurnal Fluctuation and Concordance of Intraocular Pressure in Glaucoma Suspects and Ocular Hypertension Patients**

Andrew P. Doan, M.D., Ph.D.  
Miriam B. Zimmerman, M.S., Ph.D.  
Wallace Alward M.D., Emily Greenlee, M.D., and  
Young Kwon M.D., Ph.D., sponsors



**Purpose:** The one-eye drug trial for glaucoma medications reducing the intraocular pressure (IOP) assumes that the diurnal fluctuation of the IOP in both eyes is concordant. Our study objective was to determine the diurnal variation and concordance of IOP measured in glaucoma suspect (Suspect) and ocular hypertension (OHTN) patients.

**Methods:** Amongst the 142 diurnal curves on record, charts were excluded from the study if there was evidence of: glaucoma, glaucoma surgery, trauma, use of anti-glaucoma drops, or an incomplete diurnal curve record. The remaining 83 diurnal curves (68 Suspect and 15 OHTN) were included in our analysis. The IOPs were measured using Goldmann applanation tonometry at 07:00, 10:00, 13:00, 16:00, 19:00, and 22:00. The diurnal curves were analyzed to determine if there was concordance in the diurnal fluctuation between the eyes. The average Pearson correlation coefficient ( $r$ ) for the two patient groups was estimated to measure the linear association of IOP over the 6 time points between the two eyes within each subject. The correlation between the IOP OD and OS was first computed for each subject from each set of diurnal curves with the estimate of the average correlation calculated from the z-transform of these individual correlations.

**Results:** The pooled mean IOP were 14.9 and 23.1 mmHg for Suspect and OHTN groups respectively. The average correlations between OD and OS IOP were 0.78 (95% CI: 0.71, 0.82) for Suspect, and 0.86 (95% CI: 0.77, 0.92) for OHTN. The standard deviation of the IOP between eyes within each subject was found to be similar for all the time points. This was at most 1.60 mmHg (95% CI: 1.37, 1.92) with a coefficient of variation (CV) of 10.76% for Suspect, and 2.63 mmHg (95% CI: 1.94, 4.07) with 10.06% CV for OHTN. Observed difference in IOP between eyes was less than 3.81 and 6.06 mmHg in 90% of Suspects and OHTN patients respectively.

**Conclusions:** These findings indicate the IOP of both eyes change in the same direction (positive correlation) and with similar magnitude. We conclude the diurnal variations in IOP between eyes are largely concordant.

## RESIDENT/FELLOW RESEARCH DAY - 2005

### **Diurnal Concordance of Intraocular Pressure Between Fellow Eyes in Normal Tension Glaucoma**

Michael Maley, M.D.  
Andrew Doan, M.D., Ph.D., Robert Dinn, M.D.  
Young Kwon, M.D., Ph.D., Wallace Alward, M.D., Emily  
Greenlee, M.D., sponsors



**Purpose:** Monocular drug trials are commonly used to assess the efficacy of glaucoma medications in lowering intraocular pressure. By using fellow eyes as controls, this practice assumes that the diurnal fluctuation of intraocular pressures is concordant between the two eyes. This study attempts to determine whether this is a valid assumption in normal tension glaucoma patients.

**Methods:** An IRB approved retrospective chart review of over 100 patients will be performed. Selected patients will have met the clinical criteria of normal tension glaucoma as diagnosed by the attending faculty in the glaucoma clinic at the University of Iowa. Patients who underwent a diurnal curve of intraocular pressure will be included. Those patients with a history of treatment with intraocular lowering medications, glaucoma surgery, a history of eye trauma, or incomplete diurnal curve will be excluded. Intraocular pressures will be compared between the two eyes from Goldmann applanation tonometry measurements at 7:00 AM, 10:00 AM, 13:00 PM, 16:00 PM, 19:00 PM, and 22:00 PM.

**Results:** Pending

**Conclusions:** Pending



## RESIDENT/FELLOW RESEARCH DAY - 2005

### **Diurnal concordance of intraocular pressure between the two eyes in primary open angle glaucoma patients**

Robert B. Dinn, M.D.

Andrew Doan, M.D., Ph.D., Michael Maley, M.D.

Young Kwon, M.D., Ph.D., Emily Greenlee, M.D., Wallace Alward, M.D., sponsors



**Purpose:** The one-eye drug trial is routinely used to assess the efficacy of glaucoma medications to lower intraocular pressure (IOP) by using the fellow (untreated) eye as a control. This approach assumes that the concordance in intraocular pressures between the two eyes is similar. Recently, an evaluation of diurnal pressure curves in glaucoma suspects and patients with ocular hypertension indicated fairly concordant diurnal fluctuations in IOP between the two eyes (Doan et al. Determination of the Diurnal Fluctuation of Intraocular Pressure in Glaucoma Suspects and Ocular Hypertension Patients ARVO 2005 Program 4833 Poster B36.). The concordance between the two eyes in patients with primary open angle glaucoma (POAG) has yet to be determined.

**Methods:** A retrospective chart review approved by an IRB will be undertaken on 291 charts in patients diagnosed with POAG who underwent bilateral diurnal IOP measurements. Subjects with a history of eye trauma, eye surgery, ocular vascular occlusive diseases, or asymmetric use of eye drops prior to having had the diurnal IOP curve being measured will be excluded from the analysis. In the remaining patients, the IOP in each eye will be compared for concordance based on Goldmann applanation tonometry measurements at 07:00, 10:00, 13:00, 16:00, 19:00, and 22:00.

**Results:** Pending

**Conclusion:** Pending

## RESIDENT/FELLOW RESEARCH DAY - 2005

### **Internet Use Among Ophthalmology Patients: Search Modalities for Eye Information**

Jordan M. Graff, M.D., Andrew P. Doan, M.D., Ph.D  
Thomas A. Oetting, M.D., Thomas A. Weingeist, Ph.D., M.D.,  
sponsors



**Purpose:** The Internet provides a potentially powerful tool for patient education. Surveys of patients in other fields of medicine generally reveal that a majority of patients are now using the Internet to search for information related to their medical conditions, though this is not universally the conclusion. There has been no formal study of internet use and search modalities among ophthalmology patients in the United States. We seek to describe the use of the Internet to search for eye and health related information in this population.

**Methods:** Cross-sectional survey administered in ophthalmology waiting rooms of university-based health care center. Anonymous survey of at least 250 patients will be obtained.

**Results:** To be discovered.

**Conclusions:** We hypothesize that a high percentage of Midwestern ophthalmology patients use the Internet to search for information related to their eye care. We also hypothesize that the majority of these patients are likely to employ broad-based, commercial search engines to find this information. Whether or not this is true will be discovered.

## RESIDENT/FELLOW RESEARCH DAY - 2005

### **The Effect of Panretinal Photocoagulation on Nerve Fiber Layer and Outer Retinal Layer Thickness**

Christopher Robinson, M.D.  
Randy H. Kardon, M.D., Ph.D.,  
Young H. Kwon, M.D., Ph.D., sponsors



**Purpose:** To determine the effect of laser-mediated retinal destruction on the nerve fiber layer

**Methods:** Patients requiring PRP, without a diagnosis of glaucoma, will be prospectively recruited from the retina clinic prior to their first PRP treatment. They will receive an OCT measuring RNFL and total retinal thickness prior to the first treatment, midway through treatment, and after treatment. A retrospective study will examine patients who have already received unilateral PRP or heavy regional laser treatment on nerve fiber layer and total retinal thickness.

**Results:** None yet.

**Conclusions:** None yet.

### **Modified Levator Recession and Muellerectomy for Lid Retraction Secondary to Thyroid Ophthalmopathy**

Erin Shriver, M.D.

Keith Carter, M.D., sponsor



**Purpose:** Eyelid retraction is the most common sign of thyroid ophthalmopathy. Lid retraction results when the horizontal tarsal ligamentous band and vertical eyelid retractors cannot lengthen to accommodate increasing exophthalmos. Upper eyelid retraction has been associated with a startled appearance, ocular discomfort, and keratopathy. Non-surgical treatments have been tried with minimal success. There is no clear agreement on the best surgical lengthening technique for upper eyelid retraction. One popular technique is the levator recession and muellerectomy. This surgery is often successful at restoring the natural lid length, however the upper lid crease is often sacrificed in the process. We are (Instead of Keith Carter is) currently performing a modified version of levator recession and muellerectomy aimed at lengthening the lid while preserving the upper lid crease. The purpose of this study is to assess if the modified levator recession and muellerectomy successfully restores the upper lid crease.

**Methods:** We will be assessing the prominence of the upper lid crease after modified levator advancement and muellerectomy. The extent of scleral show, palpebral fissure height, margin-reflex distance, and upper eyelid crease (will be determined) from photographs taken before and after the patient's surgery (and review of the patient's chart). The prominence of the upper lid crease will be scored in both pre and post-operative photos.

**Results and Conclusions:** Pending.

## RESIDENT/FELLOW RESEARCH DAY - 2005

### Long-term Outcomes of Strabismus Surgery in Thyroid Ophthalmopathy

Erin O'Malley, M.D.

Ronald Keech, M.D. and Richard Olson, M.D., sponsors



**Purpose:** Thyroid ophthalmopathy is one of the most common causes of adult strabismus. This restrictive strabismus results from inflammatory infiltration and fibrosis of the extraocular muscles, most commonly the inferior and medial rectus. Although some patients achieve functional benefit from non-surgical modalities such as prisms, often surgical intervention is necessary. This study will examine the long-term functional and motor outcomes of extraocular muscle surgery in patients with strabismus secondary to thyroid dysfunction.

**Methods:** We have identified 181 patients with strabismus secondary to thyroid dysfunction treated at the University of Iowa Hospitals and Clinics.

We plan to perform a retrospective chart review of all thyroid patients with strabismus who had surgery as part of their treatment. We are studying the type and number of strabismus surgeries performed over the course of follow-up as well as the long-term functional and motor outcomes.

**Results/Conclusions:** Pending.

## RESIDENT/FELLOW RESEARCH DAY - 2005

### **Natural History of Contact Lens Treatment for Aphakia in Children and Its Effect on Long Term Visual Outcomes**

Jeffrey L. Maassen, M.D.  
Richard Olson, M.D., Ronald Keech, M.D.,  
Christine Sindt, O.D., sponsors



**Introduction:** Pediatric cataract removal presents the ophthalmologist the challenge of providing proper aphakic correction to the developing child. Several techniques are available for visual rehabilitation in children, including spectacles, intraocular lenses, epikeratophakia, and contact lenses. Epikeratophakia is disadvantageous given it is a fixed correction and does not allow for the correction to change as the child develops. Intraocular lenses have questionable safety and long-term implant data is lacking for infants. Aphakic spectacle correction presents problems in monocular aphakia given anisocoria and image distortion. Contact lenses provide good optics without the distortion of aphakic spectacles, and they are readily adapted to the infants changing eye. However, data correlating keratometric changes, refractive error changes, and end-point visual acuity changes are lacking.

**Design:** We will retrospectively review our database of aphakic children (approximately 250 patients) according to age of cataract surgery, cause of cataract, unilateral or bilaterality, type of contact lens correction (silicon vs. RGP), and complicating factors. Amongst these groups, we will analyze amount of occlusion therapy, keratometric changes, refractive error changes, frequency of contact lens changes, and final visual acuity following treatment.

**Results:** pending

**Conclusions:** pending

### **The Prevalence of Unrecognized Refsum Disease in Patients with Retinitis Pigmentosa**

Michael A. Grassi, M.D., R. M. Johnston, A. R. Philp, Ph.D  
Edwin M. Stone, M.D., Ph.D., sponsor



**Purpose:** Refsum disease is a progressive neurological disorder characterized by retinitis pigmentosa, polyneuropathy, and cerebellar ataxia associated with elevated levels of phytanic acid.

The condition is caused by mutations in the gene encoding the enzyme, phytanoyl-CoA hydroxylase (PHYH). The ophthalmologic manifestations precede the other neurologic symptoms of Refsum disease by 10-15 years. Dietary modification can prevent progression of Refsum disease, placing the ophthalmologist in a unique position to profoundly alter the natural history of this condition. The purpose of this study is to determine the prevalence of undiagnosed Refsum disease in a cohort of patients with retinitis pigmentosa.

**Methods:** Genomic DNA was screened for mutations in PHYH exons using single strand conformational polymorphism analysis and DNA sequencing. 340 patients diagnosed with either simplex or autosomal recessive retinitis pigmentosa were evaluated. All nonsynonymous coding sequence changes were compared to a panel of 180 control patients as well as to all previously published mutations implicated in Refsum disease. Serum phytanic acid in conjunction with clinical examination by a neurologist was obtained in individuals harboring mutations in PHYH to confirm disease status.

**Results:** To be discussed.

**Conclusion:** To be discussed.

## RESIDENT/FELLOW RESEARCH DAY - 2005

### Ultra Long-Term Outcomes of Penetrating Keratoplasty for Keratoconus

Sudeep Pramanik, M.D., M.B.A.

John E. Sutphin, M.D., Ayad A. Farjo, M.D., sponsors



**Purpose:** To report graft survival data for initial penetrating keratoplasty performed more than 20 years ago for keratoconus. Secondary outcomes included recurrent keratoconus, steroid-induced glaucoma, and best-corrected visual acuity.

**Methods:** A retrospective, consecutive series of patients with keratoconus who underwent initial penetrating keratoplasty at the University of Iowa from 1970 to 1983 was performed. Baseline data included age, best spectacle corrected visual acuity (BSCVA), astigmatism, and graft size. Visual acuity and intraocular pressure were followed until the eyes reached one of four endpoints: graft failure, recurrent keratoconus, loss to follow-up, or death.

**Results:** Among the 112 eyes of 84 patients with a mean follow-up of 13.7 years, the mean age at transplant was 33.7 years, the mean preoperative BSCVA was 20/200, and the mean astigmatism was 6.65 diopters. Greater than 15 years of follow-up was available on 52 eyes. Seven eyes experienced graft failure and recurrent keratoconus was noted in 14 eyes, with a mean time to recurrence of 18.4 years. Six eyes developed a steroid-responsive glaucoma and two required trabeculectomy. Among those with more than 15 years of follow-up, 2/3 had a BSCVA better than 20/40.

**Conclusion:** Penetrating keratoplasty offers good long-term visual rehabilitation for keratoconus. There is a low rate of graft failure, but a moderate rate of late postoperative recurrence.



## RESIDENT/FELLOW RESEARCH DAY - 2005

### Changes in Nerve Fiber Layer Reflectivity using Optical Coherence Tomography in the Setting of Optic Neuropathy

M. V. Boland, M.D., Ph.D.

R. H. Kardon, M.D., Ph.D., faculty sponsor



**Purpose:** It has been observed in some patients with severe visual field loss from glaucoma and other optic neuropathies that the optical coherence tomography (OCT) estimate of the retinal nerve fiber layer is thicker than expected. Patients with acute optic neuropathy have been followed over time and showed initial thinning of the retinal nerve fiber layer, followed by some degree of re-thickening. The purpose of this work is to determine whether there are features of retinal OCT that can be used to differentiate a healthy nerve fiber layer from the damaged and paradoxically thickened ones described above.

**Methods:** Four patients with various optic neuropathies and subsequent nerve fiber layer thinning and re-thickening on longitudinal OCT data were identified. All OCT data were collected using a Zeiss Humphrey OCT 2000 and each patient had at least 12 months of follow up. Scans of the retina adjacent to the optic nerve in both the healthy and diseased eye were processed using third party software (OCTPro 2k1) to identify the nerve fiber layer. The raw reflectivity data from the nerve fiber layer were then exported and analyzed using simple statistics (e.g., mean, standard deviation) and histograms.

**Results:** The mean reflectivity of the nerve fiber layer in a patient with traumatic optic neuropathy and no light perception vision decreased over time and then remained low even as the layer re-thickened. Analysis of data from patients with less severe injury did not show similar changes in reflectivity. Histogram analysis of reflectivity data for the patient with traumatic optic neuropathy are consistent with a decrease in the average reflectivity and do not demonstrate a multi-modal distribution of reflectivity.

**Conclusions:** The reflectivity of the nerve fiber layer is an important feature that is not currently used in analysis of OCT data. Furthermore, thickness of the nerve fiber layer alone is not a perfect predictor of visual field loss. We hypothesize that one reason for this discrepancy is the re-thickening phenomenon mentioned above. We also believe that the re-thickened nerve fiber layer may contain gliotic tissue that has replaced damaged nerve fibers. The observed change in the reflectivity of the nerve fiber layer, even after re-thickening, is consistent with the presence of non-nerve tissue. Finally, given the changes we have observed in the reflectivity of the nerve fiber layer, it may be possible to distinguish normal from abnormal tissue and better correlate thickness with function.

## RESIDENT/FELLOW RESEARCH DAY - 2005

### Identification Of A Novel Mtdna Mutation In A Family With An Anterior Ischemic Optic Neuropathy Phenotype

James G. Howard, MD

Sohan S. Hayreh, MD, PhD, DSc, Edwin M. Stone, MD, PhD,  
sponsors



**Purpose:** Six members of a pedigree were each diagnosed with anterior ischemic optic neuropathy (AION) in their 40's or 50's. These patients were screened for mitochondrial mutations to determine if they were actually affected with a late-onset form of Leber's hereditary optic neuropathy (LHON) rather than true AION.

**Methods:** The mitochondrial DNA of the proband was sequenced and then compared against the revised Cambridge reference sequence. When a novel mutation that changed an amino acid was identified in the ND1 gene of the proband, other family members, 41 AION patients, and 1488 LHON probands were screened for this mutation.

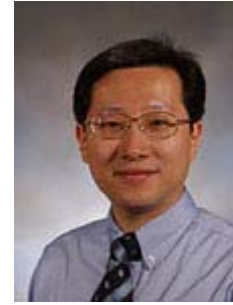
**Results:** Six affected members of this family first developed symptoms of AION in their forties or fifties, and all were related to one another through females. A novel mitochondrial mutation was identified in all six family members who had been diagnosed with AION. A guanine to adenine change was identified at position 4132 which would be expected to cause an ALA276THR change in the protein encoded by the ND1 gene. Four unaffected family members also harbored this mutation, but it was not identified in any of the 41 AION or the 1488 typical LHON probands in the study.

**Conclusions:** A novel mitochondrial DNA mutation (4132 G->A) is associated with late onset Leber's hereditary optic neuropathy. This mutation appears to be rare since it was not identified in a large group of LHON patients.

### **Comparative analysis of optic nerve head gene expression changes in human glaucoma and in rodent models of ocular hypertension**

Chan Y. Kim, MD, PhD

Markus H. Kuehn, PhD, Young H. Kwon, MD, PhD, sponsors



**Purpose:** To globally characterize abnormal gene expression patterns in the glaucomatous optic nerve head and to evaluate whether surgical rodent models of ocular hypertension accurately reflect the molecular events in human glaucoma.

**Methods:** Ocular hypertension (OHT) was induced in one eye of Brown Norway rats through diode laser cauterization of the trabecular meshwork. The second eye was left untreated and served as a control. The development of OHT was monitored by applanation tonometry and the pupil light reflex was recorded to assess the degree of visual loss. Several days after surgery the optic nerve heads from both operated and control eyes were isolated. Following RNA extraction the gene expression patterns were determined using Affymetrix gene chips. The analyses was repeated using a second group of animals. Likewise, RNA was extracted from the optic nerve heads of carefully selected human eye donors with glaucoma and from healthy controls. Gene expression profiles were established using gene chips, as above. Data were analyzed to identify those genes whose expression patterns were conserved between our rat model and human glaucoma.

**Results:** Statistical analyses of data obtained from ONH of rats with ocular hypertension identified approximately 60 genes which are more prominent in the degenerating optic nerve head. At least 75% of these also exhibited increased transcript levels in human glaucomatous ONH. Functionally, many of these genes can be classified as extracellular matrix constituents (e.g. COL10a1, TIMP1), regulators of cell division (e.g. GAS6), and adhesion molecules (e.g. CHAD).

**Discussion:** The gene expression changes observed in our rodent model of ocular hypertension largely reflected those evident in human glaucomatous tissue. Thus, our data demonstrate the suitability of this model for the study of human disease. Frequently, the magnitude of the observed expression change was less pronounced in human tissue than in the rodent model. These findings can perhaps be explained with the extended time period during which human glaucoma develops. Using a global data analysis approach and human tissue alone, these changes could easily remain undetected. Thus, the comparative analysis data derived from this animal model and human glaucomatous tissue not only highlights universally active pathways but also allows the identification of minor gene expression changes through focused data analysis.