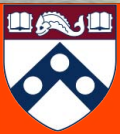


SCHEIE VISION



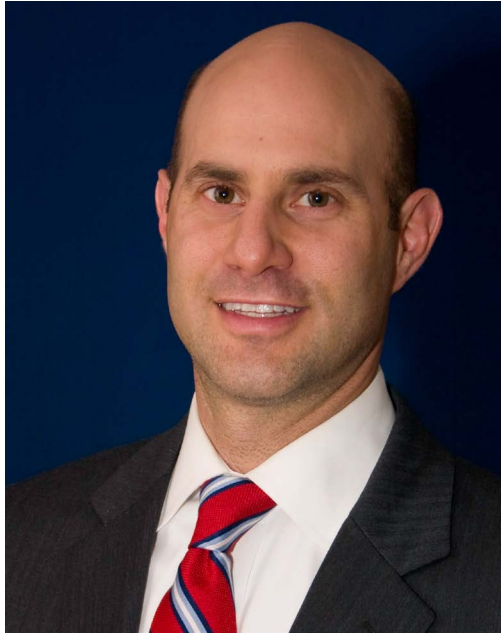
Raymond and Ruth Perelman School of Medicine at the University of Pennsylvania

Department of Ophthalmology

Scheie Eye Institute

Volume 1 Issue 1

Remarks From Scheie Alumni President



lot from Scheie over the years and I'm ready to give back."

Dr. Goldstein earned his M.D. from Boston University School of Medicine where he graduated with honors. After looking at a couple of different specialties, Dr. Goldstein decided on ophthalmology.

"I wanted something where I could work with children and adults, and do surgery and medical care," Dr. Goldstein explained. "When I entered the ophthalmology rotation, I knew it was a good fit."

Dr. Goldstein came to Scheie as a resident and earned the Department of Ophthalmology's Student Teaching award all three years of his residency. He became Chief Resident, and chose Oculoplastics as his specialty.

"I was really inspired by Dr. Roberta Gausas and Dr. Jim Katowitz. I liked the surgical procedures in Oculoplastics and the surgical complexity."

He became a full-time faculty member at the Scheie Eye Institute in 2002 and served as Director of Medical Education, earning the Golden Apple award from residents. Dr. Goldstein also oversaw the Oculoplastic surgery division at the Philadelphia Veterans Hospital. His education and administrative duties left him little time to care for patients.

"I began to miss working with patients," Dr. Goldstein said. "I wanted to put all of the skills I learned in my training to good use."

Dr. Goldstein moved to private practice

in 2003, where he now keeps a busy schedule. He is on staff at three local hospitals and works in a productive multispecialty ophthalmology practice. Dr. Goldstein said some of his most challenging and satisfying work comes in the form of reconstructive surgery for skin cancer patients.

He jokingly refers to his practice as Scheie North. "We have seven medical doctors and five of them trained at Scheie or CHOP," Dr. Goldstein said. His partners include Richard Prince, Sheryl Menacker, Jeff Gordon and Emily Decarlo.

Working with like-minded people is the key to a successful practice, Dr. Goldstein advised.

"You are very choosy about who you marry. You should be equally choosy about who you work with. You may be spending more time with them than with your spouse," Dr. Goldstein said. "Find people you like to work with."

Dr. Goldstein gives another piece of good advice to residents: "Life is short. Find something you like to do and do it well. If you like your work, every day will be great."

Dr. Goldstein said he has big plans to invigorate the Scheie Alumni Association.

"My goal is to get as many alumni engaged as possible," he explained.

We are all excited about Dr. Goldstein's new role as Scheie Alumni President and look forward to participating in the Scheie Alumni Association under his leadership.

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We'd love to hear from you! Please send contact information and career updates to camille.metcalfe@uphs.upenn.edu to be included in the Alumni Updates section of coming newsletters.

As the newest set of residents begin training at the Scheie Eye Institute, many of you may be thinking the same thing: "It feels like just yesterday that I began my residency." Like many Scheie Alums, you may have lost contact with friends, colleagues, and mentors from your time at Scheie.

The Scheie Alumni Organization can make connecting with old friends a little easier. Our new quarterly newsletter can help you share contact information, research updates, and referrals with colleagues all over the country. Scheie Alumni events and CME lectures can facilitate new professional relationships. Department Chair Joan O'Brien has appointed Dr. Scott Goldstein, class of 2000, to lead Alumni efforts as the new President of the Scheie Alumni Association.

"I feel honored," Dr. Goldstein said in a recent interview. "I've received a

Scheie Welcomes New Retina Specialist

The Scheie Eye Institute is pleased to announce the arrival of Dr. Brian VanderBeek, retina specialist and new full time faculty member at Scheie. Dr. VanderBeek will be mentored by Dr. Maureen Maguire as part of the Departmental K12 program.

"I am excited for the opportunity to work with the retina faculty here at Scheie and work under Dr. O'Brien," Dr. VanderBeek said.

Dr. VanderBeek grew up in Troy, Michigan, not far from Detroit. After completing his Bachelor's degree, Dr. VanderBeek earned a Master's degree in Public Health from the University of Michigan. It was during his training in public health that he realized he wanted to go to medical school and work closely with patients.

He earned his Medical Degree from the University Of Cincinnati College

Of Medicine, and chose a career in Ophthalmology because he enjoys the opportunity to perform surgeries as well as work with patients. He completed his ophthalmology residency at the New York Presbyterian Hospital Weill Cornell Medical College and completed a 2-year Retina Fellowship at the University of Michigan Kellogg Eye Center.

One of the biggest challenges of specializing in retina, Dr. VanderBeek said, is working with patients who are very likely to lose their vision and are often most at risk for blindness. Despite the challenges, Dr. VanderBeek remains optimistic about the difference good treatment can make.

"Every day I go to work, I help people keep their vision," he said.

During his fellowship Dr. VanderBeek received the Center for Research on Learning and Teaching Lecturers' Pro-

fessional Development Grant and the Retina Society Fellowship Research Award. Dr. VanderBeek's research interests, which include health care cost effective and cost comparative studies, were influenced by his training in public health.

"One of the biggest issues in public health," Dr. VanderBeek said "is the escalating cost of healthcare and the difficulty in defining quality of outcomes from use of health services."

Dr. VanderBeek will continue his research here at Scheie while also working as a retina surgeon.

The newly arrived doctor is expecting a new arrival of his own, and admits he is a bit nervous about being a first-time dad.

"I am probably more nervous to be a father than when I did my first surgery," Dr. VanderBeek said. "In the



surgery I had an attending there to step in if things got tough or I was heading in the wrong direction. As a parent, there is no training course like residency!"

The faculty and staff of the Scheie Eye Institute wholeheartedly welcome Dr. VanderBeek and look forward to a long and productive future together.



Iron Buildup & AMD

is more than they actually need, and it begins to build up in the heart, liver, brain and retina.

“We think that this stockpile of iron may be sort of like nuclear fuel,” Dr. Dunaief said. “If it is not shielded or there’s too much of it, or the cellular mechanisms that are supposed to shield it are damaged, it can kill cells.”

Dr. Dunaief’s lab compared the levels of iron in eyes with macular degeneration to age-matched controls, and found that the eyes with macular degeneration had significantly more iron.

Genetic testing also sheds light on the link between iron and macular degeneration. A rare genetic mutation in young people inhibits the gene ceruloplasmin, which exports iron from the retina. These patients develop macular degeneration at a young age, suggesting that patients with macular degeneration who have more iron in the eye may have the disease in part because of the iron.

Dr. Dunaief found that knockout mice without the ceruloplasmin gene developed a retinal degeneration very similar to macular degeneration. Both conditions developed drusen-like

material under the retina, caused the death of photoreceptor cells and RPE cells, and caused neovascularization.

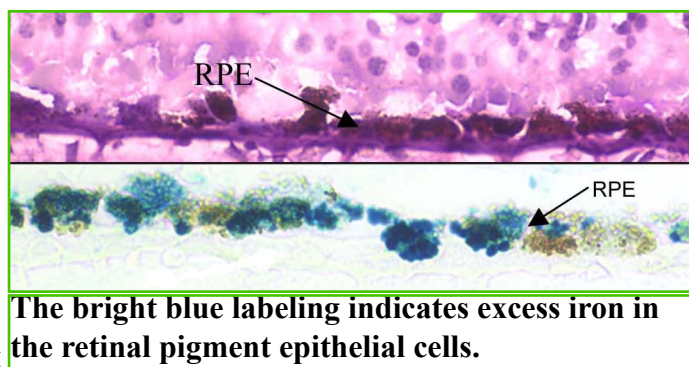
Dr. Dunaief’s lab is currently testing iron-binding drugs that remove excess iron in the retina. The results are encouraging.

“If we give the knockout mice an iron binding drug in their drinking water we can prevent the retinal degeneration,” Dr. Dunaief said. “There is a way to combat this iron-induced damage.”

Dr. Dunaief’s lab found that these drugs work not only in the retina, but also in the brain, preventing a Parkinson’s-like disease in knockout mice.

The drugs bind iron loosely enough that it does not eliminate the iron needed to make red blood cells or energy.

A drug of this type could provide hope for patients with a variety of diseases involving oxidative stress in the retina. Even when iron buildup isn’t the primary cause of retinal degeneration, it may exacerbate retinal degeneration



The bright blue labeling indicates excess iron in the retinal pigment epithelial cells.

caused by other factors. Removing iron could be therapeutic for a wide range of retinal diseases including diabetic retinopathy, retinal detachment, pathologic myopic, histoplasmosis, glaucoma and retinitis pigmentosa. In fact, an iron-binding drug has already been tested in mice that are a model of retinitis pigmentosa, and has proven protective in those mice.

Dr. Dunaief hopes to begin clinical trials in the next few years.

“We need to make sure that we’re picking the best possible drug,” Dr. Dunaief said. “There are hundreds of slight variants of this drug and we want to make sure that we’re picking the drug that has the best chance of being therapeutic and safe.”

Dr. Dunaief’s most recent research can be found in the September 2011 edition of the Journal of Inorganic Biochemistry.



Isolated populations, such as the Amish, provide valuable insight into the genetics of AMD.

analysis comparing associations between the disease and genetic changes found a number of new genes that were significantly more associated in cases of AMD than in controls. Additional analysis of all susceptibility loci showed that 329 of 331 individuals (99%) with the highest-risk genotypes had AMD, and 85% of these had advanced AMD.

New Genes Linked To AMD

“You can sequence the DNA of an Amish patient with AMD and the DNA of an unaffected sibling, and you can see genetic differences that may be associated with the disease. These differences would be harder to see when looking at unrelated cases and controls, simply because of normal genetic variation.”

“These studies help identify individuals at high risk of disease,” Dr. Stambolian explained. “And provide clues about underlying cellular pathways that should eventually lead to new therapies.”

Many of Dr. Stambolian’s studies focus on the genetics of AMD in isolated populations. While there are around 10 known genes associated with AMD, genetic differences among populations mean that there are higher frequencies of AMD among particular groups. The Amish, for example, have a significantly higher prevalence of AMD than the national average, and, because of their isolated population, they provide a unique opportunity for genetic research.

“Within the Amish community you have a homogenous population that lives in the same environment, shares the same diet, and marries within their ethnic background.” Dr. Stambolian

African-Americans, on the other hand, have a much lower frequency of AMD. Dr. Stambolian’s team has just been awarded a grant to study why AMD appears so rarely in the African-American community. Dr. Stambolian is collecting DNA both from African-Americans with this eye disease and those without it. Dr. Stambolian’s team will sequence those regions of the genome already associated with AMD to identify genetic changes that exist between African-Americans and Caucasians.

“My hypothesis is that African-Americans have some protective genes which prevent them from getting AMD,” Dr. Stambolian said. “If you can define where those protections are in the genome, you could tailor drugs to implement some of those protective changes in DNA for individuals that are more prone to AMD.”

Identifying genes associated with AMD not only indicates who is at

high risk for the disease, it also reveals the biological pathways which underlie the disorder, and the particular enzymes and proteins that can be targeted with drug treatments. Studying the genetics of AMD can also help researchers by identifying biomarkers which may indicate the severity of the disease and the effectiveness of the therapy.

“Ultimately we want to be able to identify all the risk variants in an individual for AMD and then assess what dosage that patient needs, and how often they need it,” Dr. Stambolian said. “If you can predict the outcome based on a person’s genetic background or risk variance, it goes a very long way toward improving medical care. That is the ultimate goal. Personalized medicine is where the field is going.”



New research into Stargardt disease, a juvenile form of macular degeneration, revises a long-held hypothesis on disease severity, and identifies which patients are good candidates for the latest clinical trials attempting to slow disease progression.

Dr. Artur Cideciyan, Professor of Ophthalmology at the University of Pennsylvania, is a scientist who uses specialized vision tests to evaluate patients with Stargardt disease. His research, which has been funded by the National Eye Institute for more than a decade, has carefully defined the progressive stages of this hereditary condition, which is often caused by two mutations in the ABCA4 gene. There have been more than 300 different mutations described to date, but a predictive relationship between a specific pair of mutations and resulting disease severity is not yet established.

Dr. Cideciyan’s recent work focuses on designing a metric to measure

Gene Mutation & Severity

the severity of retinal degeneration in Stargardt disease in order to understand the contributions of genetic mutations patients inherit.

“Genotype-based inclusion criteria will be invaluable for selecting appropriate candidates for clinical trials in ABCA4 disease,” Dr. Cideciyan said.

Human vision starts upon capture of light photons by opsin proteins located on disk membranes at the specialized tips of photoreceptor cells in the retina. ABCR protein coded by the ABCA4 gene functions as a flip-flop, transporting accumulated vision byproduct across disk membranes, and eventually out of the retina. Most mutations in the ABCA4 gene are thought to affect the amount of ABCR protein produced and thus the rate of this transport function. Lack of complete and timely removal of vision byproducts from the retina results in accumulation of toxic bisretinoids which slowly destroy photoreceptors and RPE cells.

A long-held hypothesis stated that gene mutations that produced no ABCR protein resulted in the most severe forms of Stargardt disease, and those that produced mutant ABCR protein resulted in milder forms. Dr. Cideciyan’s research, however, has shown that some of the most severe phenotypes are caused by genotypes that are expected to produce mutant proteins. Greater severity of disease

compared to no protein production could occur because the misfolding of the mutant protein. Natural defenses of photoreceptor cells should remove misfolded proteins through unfolded protein response (UPR). However, Dr. Cideciyan believes that this UPR mechanism malfunctions under photoreceptor stress in Stargardt disease, leading to amplification and acceleration of the retinal degeneration.

“Production of a misfolded protein may actually be worse than no protein in this recessive condition,” Dr. Cideciyan said.

Current forms of experimental gene therapy are attempting to treat recessive forms of retinal degenerations by augmenting the mutant gene products with normal gene products. Dr. Cideciyan believes candidates without misfolding types of gene mutations, who would benefit from the addition of the normal protein, should be the first patients selected for upcoming gene therapy trials.

In Stargardt disease, different retinal regions progress through disease stages at different ages. Because gene therapy is administered locally into the eye, it is very important to choose appropriate regions to treat. Dr. Cideciyan evaluates the disease topography of patients with different genotypes to help them benefit the most from new therapies. He uses state of the art methods to detect regions with



Mutations in the the ABCA4 gene lead to varying degrees of severity in Stargardt disease.

photoreceptors and RPE cells that are showing evidence for early disease, but still remain viable and potentially treatable.

“Once we can predict the specifics of Stargardt disease progression based on genotype, then we can choose both specific patients and specific retinal locations that are appropriate for different types of therapy that are being planned,” Dr. Cideciyan said. “This will help better balance the risk and the potential benefit for patients volunteering to take part in clinical trials of experimental treatments such as pharmaceuticals to reduce toxic retinoid accumulation, stem cells to replace degenerated photoreceptor cells, and gene therapy to augment ABCR function.”

Thanks to Dr. Cideciyan’s work, as new and safe treatments for Stargardt disease are ready for clinical trials, appropriate patients will be ready for treatment.



A new study by Dr. Dwight Stambolian, Associate Professor of Ophthalmology at the University of Pennsylvania, has identified additional genes that significantly influence susceptibility to macular degeneration. Dr. Stambolian’s research also sheds light on which populations are at risk for the disease, and how genetic tools can help treat it.

In the largest AMD genetics study to date, Dr. Stambolian’s team took blood samples from 2,157 AMD patients referred by a retina specialist and 1,150 controls confirmed to have no signs of AMD. Study samples were genotyped with Illumina Human 370 Chips, which capture more than ninety percent of common variants in European ancestry samples. Data

Avastin and Lucentis, Same Results

While only Lucentis has FDA approval for treatment of wet AMD, Avastin, which was created as a treatment for cancer, is commonly used off-label to treat wet AMD. The National Eye Institute funded the Comparison of AMD Treatments Trials to evaluate the safety and efficacy of the two drugs.

The multi-center study showed that vision in patients treated with Avastin, which costs \$50 per injection, improved just as much as vision in patients treated with Lucentis, which costs \$2,000 per injection. When the drugs were given monthly, those on Avastin on average gained 8.0 letters of visual acuity after a year, while those on Lucentis gained 8.5.

The study also showed that both drugs were nearly as effective when taken on an as-needed basis, averaging 7 doses per year, as opposed to monthly. Visual gains were about two letters less and there was almost no difference (within one letter) between

drugs when given on an as-needed basis.

The study evaluated 1,161 patients among 43 different centers. Study participants had active wet macular degeneration, characterized by fluid from abnormal vessels in the eye, based on examination with fluorescein angiography and ocular coherence tomography. Patients were divided into four groups: those treated with Avastin on a monthly basis, those treated with Avastin on an as-needed basis, those treated with Lucentis on a monthly basis, and those treated with Lucentis on an as-needed basis.

All groups received treatment at baseline. Those in the monthly treatment groups received injections every 28 days, while those in the as-needed groups were examined every 28 days. Participants in this group received treatment when OCT or fluorescein angiography showed signs of disease activity, such as fluid in the retina.

Incidents of death, heart attack and stroke were low and similar for both drugs; however rates of serious adverse affects were higher in Avastin treated patients. Twenty four percent of patients using Avastin experienced serious adverse affects, such as hospitalizations, compared to nineteen percent of patients treated with Lucentis.

Dr. Maguire said the finding was surprising, considering the adverse side effects are not the type usually seen with these drugs. In fact, most of the adverse affects have not been associated with Avastin treatment in cancer patients who receive doses 500 times higher than those administered in this study.

Further study will look at any differences that develop over the following year and will further examine adverse side effects associated with both drugs. The study was published in the May 19, 2011 issue of the New England Journal of Medicine.

A new drug trial shows that Avastin is just as effective as Lucentis in treating AMD



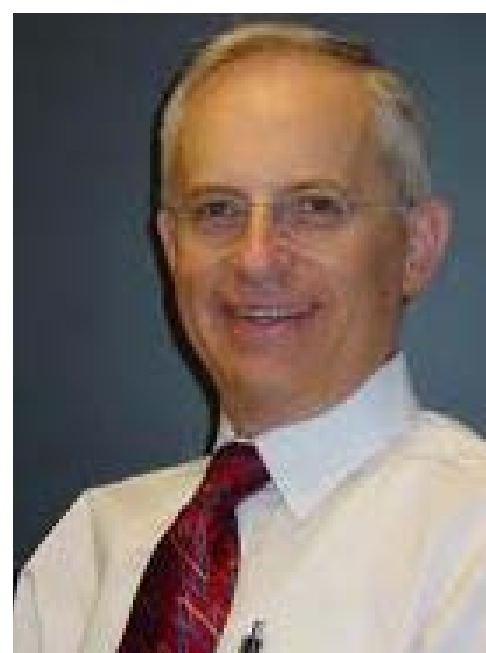


Open Studies at Scheie

One of your patients may be the perfect candidate for a study here at Scheie. Take a look at our open studies and call the contact listed to refer a patient or receive more information.

Study Name	Inclusion Criteria	Exclusion Criteria	Compensation	Contact
Nordic: Udiopathic Intracranial Hypertension Treatment Trial	<ul style="list-style-type: none"> 18-60 years old Diagnosis of IIH by modified Dandy criteria for < 6 weeks Reproducible visual loss present on automated perimetry in eye with greatest loss Average perimetric MD -2 dB up to -5 dB in the worst eye Presence of bilateral papilledema 	<ul style="list-style-type: none"> Total treatment of IIH of more than 1 week in the past 6 weeks Corticosteroids used for IIH treatment within the past 6 weeks Previous surgery for IIH, or previous gastric bypass surgery Abnormal CSF contents: increased cells >5 cells, elevated protein >45 mg%, low glucose <30 mg % 	\$30 per visit	Joan Dupont 215-662-8038
Pfizer: NAION Study	<ul style="list-style-type: none"> Male > 45 years old Experienced abrupt visual change Experienced monocular symptoms Afferent papillary defect present in affected eye Presented to an ophthalmologist within 3 weeks of symptom onset 	<ul style="list-style-type: none"> Pain consistent with arteritic/inflammatory process or optic neuritis Acute visual loss, e.g. traumatic injury, tumor, ocular inflammation, retinopathy History of prior optic neuropathy in affected eye or optic neuritis in either eye 	\$25-\$50 per visit	Joan Dupont 215-662-8038
Abbott 880: Inactive Uveitis	<ul style="list-style-type: none"> >18 years old Diagnosed non-infectious intermediate-, posterior-, or pan-uveitis Inactive disease for at least 2 weeks prior to baseline On prednisone 10-25 mg/day (or equivalent) History of having failed to taper off his or her oral corticosteroid therapy 	<ul style="list-style-type: none"> Active uveitis Isolated anterior uveitis Confirmed or suspected infectious uveitis Presumed ocular histoplasmosis syndrome Ocular masquerade syndromes, such as ocular lymphoma Serpiginous chorioidopathy 	\$50-\$100 per visit	Joan Dupont 215-662-8038
Abbott 877: Active Uveitis	<ul style="list-style-type: none"> >18 years old Diagnosed non-infectious intermediate-, posterior-, or pan-uveitis Active disease despite at least 2 weeks of prednisone >10 mg/day Prior adequate response to corticosteroids 	<ul style="list-style-type: none"> Isolated anterior uveitis Prior inadequate response to or intolerance to high-dose corticosteroids Confirmed or suspected infectious uveitis Presumed ocular histoplasmosis syndrome 	\$50-\$100 per visit	Joan Dupont 215-662-8038
Can-Fite: Orally Administered CF101 for Moderate-to-Severe Dry Eye Disease	<ul style="list-style-type: none"> >18 years old Diagnosis of moderate-to-severe Aqueous-Deficient Dry Eye Central cornea FS score of .2 in at least 1 eye 	<ul style="list-style-type: none"> Sjogren's Syndrome with significant systemic non-exocrine gland involvement which would interfere with the trial Stevens-Johnson Syndrome Use of methotrexate or systemic cyclosporine in the past 3 months 	\$35-\$50 per visit	Joan Dupont 215-662-8038
CASS (Cytokine Analysis in Sjogren's Syndrome)	<ul style="list-style-type: none"> >18 years old Diagnosis of Sjogren's Syndrome 	<ul style="list-style-type: none"> History of graft vs. host disease or sarcoidosis History of uveitis, ocular cicatricial pemphigoid Ocular surgery in the last 6 months 	\$50 per visit	Eliza Windsor 215-662-8198
ForeseeHome Study	<ul style="list-style-type: none"> 55-85 years of age Does not have advanced AMD in at least one eye BCVA of study eye >20/60 Comprehends instructions for Foresee-Home device 	<ul style="list-style-type: none"> Has evidence of macular or retinal disorders other than AMD Had adverse reaction to fluorescein dye Study eye is receiving evaluation by an eye care professional more often than every 4 months 	no compensation	Sherri Drossner 215-662-8177

Glaucoma Genetic Study	<ul style="list-style-type: none"> >35 years old Diagnosis of primary open angle glaucoma, normal tension glaucoma, ocular hypertension or glaucoma suspect Family members of subject diagnosed with glaucoma 	<ul style="list-style-type: none"> All potential secondary causes of glaucoma High myopia Optic nerve drusen 	No compensation	Glaucoma Genetics Team 215-662-8673
Diabetes Retinopathy Clinical Research Network DRCRN	<ul style="list-style-type: none"> 18 years old Diagnosed diabetes mellitus Known HbA1c >7.5% within the past 6 months 		\$25 per visit	Sheri Drossner 215-662-8177
Genentech: FCFD4514S ITV for Geographic Atrophy	<ul style="list-style-type: none"> 60-89 years old BCVA of 20/125 to 20/400 inclusive Well-demarcated area of GA secondary to AMD in the absence of choroidal neovascularization GA must be > 1 DA If GA is multifocal, at least 1 focal lesion must be > .5 DA in the study eye 	<ul style="list-style-type: none"> History of vitrectomy surgery, submacular surgery or other surgical intervention for AMD Previous subfoveal focal laser photocoagulation Diabetic retinopathy in either eye Prior treatment with Visudyne, external beam radiation therapy, or transpupillary thermotherapy 	\$50-100 per visit	Joan Dupont 215-662-8038
Improving Vision and Preventing Visual Impairment in Urban African Americans	<ul style="list-style-type: none"> African American subjects > 50 years of age with diagnosis of AMD African American controls > 65 years of age with no signs of drusen or CNV 	<ul style="list-style-type: none"> Any subject in whom we cannot obtain a photo for such reasons as opaque media 	\$215 for participation	Laura Hall 215-662-8496
Primary Tube vs. Trabeculectomy	<ul style="list-style-type: none"> 18-85 years old Glaucoma that is inadequately controlled on tolerated medical therapy with IOP > 18 mmHg and <40 mmHg No previous incisional ocular surgery 	<ul style="list-style-type: none"> No light perception vision Active iris neovascularization or active proliferative retinopathy Iridocorneal endothelial syndrome Epithelial or fibrous downgrowth 	No compensation	Sheri Drossner 215-662-8177
Quark Stratun II: Dose Escalation Trial of QPI-1007 to Patients With Acute Naion	<ul style="list-style-type: none"> >50 years Positive diagnosis of NAIO BCVA in the study eye <20/64 or > light perception 	<ul style="list-style-type: none"> Macular disease, retinopathy, other eye disease limiting visual acuity in study eye Prior intraocular surgery other than Lasik 	\$100 per visit	Joan Dupont 215-662-8083



New research by Dr. Juan Grunwald, Director of the Vivian S. Lasko Ocular Vascular Laboratory at the Scheie Eye Institute, has shown a link between the progression of macular degeneration and decreased blood flow in the choroid.

The choroid is a thick layer of very high blood flow that nourishes the most important parts of the retina and removes metabolic waste products. Dr. Grunwald uses non-invasive technology to measure choroidal blood flow in patients with macular

AMD & Choroidal Blood Flow

degeneration who are at high risk for developing wet AMD.

"We use a very weak laser beam that goes into the eye of the patient," Dr. Grunwald said. "From the light coming back we measure how fast the blood is flowing and how much blood is flowing through the retina, without causing any damage to the eye."

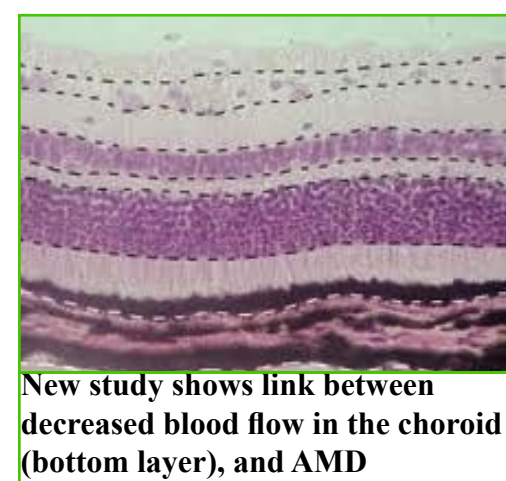
Dr. Grunwald has been following patients for up to 12 years, measuring their blood flow at yearly intervals. He found that one to two years prior to the transformation of the dry disease into the wet disease, and prior to the appearance of choroidal neovascularization, there was a significant decrease in blood flow.

"We saw a decrease that was much steeper than the decrease shown in people who did not go on to develop wet AMD," Dr. Grunwald said. "This strongly suggests that a decrease in blood flow may have something to do with the progression of AMD."

Dr. Grunwald also looked at the biggest risk factors in developing wet AMD such as age, drusen, hypertension, pigmentary changes in the retina,

and others. His lab found that each of these individual risk factors is also linked to decreased choroidal blood flow. The older you get, the worse the blood flow. The more drusen you have, the lower the blood flow to the choroid. If you have hypertension, blood flow in the choroid is lower, and if you have pigmentary hypertrophy in the eye, choroidal blood flow is also lower.

The exact cause of the decrease in blood flow is unknown, but Dr. Grunwald thinks it may be associated with the accumulation of drusen material between the retina and the choroid. In a healthy eye this material is removed by the choroid, but in eyes with macular degeneration, this process is interrupted and waste material begins to build up. This extra material disturbs the passage of trophic substances produced by the retina that nourish capillaries in the choroid and help the choroid to thrive. When the substances do not reach the choroid, the capillaries shrink. This theory is consistent with earlier studies that show that once the retina degenerates, the choroid also atrophies because it is no longer receiving the trophic sub-



New study shows link between decreased blood flow in the choroid (bottom layer), and AMD

stances that sustain it. "Now that we've identified this as a potential factor, we can start devising treatment modalities to perhaps improve the circulation in the choroid," Dr. Grunwald explained. "We are hoping that some studies will be coming in the near future, looking at whether improving circulation within the eye may prevent or delay the onset of AMD. It is very exciting."

Dr. Grunwald's results may provide a new research approach to other eye diseases with a vascular component, such as diabetes, retinal vascular occlusions, and glaucoma. His most recent work on choroidal blood flow can be found in the August 2011 edition of the Retina.



2011-2012 Residents



Jason J. Jun, MD, MPP



Marc H. Levin, MD, PhD



Joshua J. Ney, MD



Sriranjani Padmanabhan, MD



Maulik S. Zaveri, MD, MS



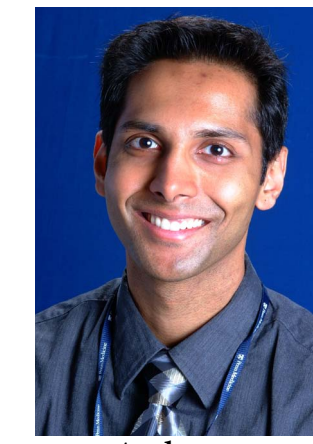
Dina Y. Gewaily, MD, MS



Esther R. Bisker, MD



Luxme Hariharan, MD, MPH



Ankoor Shah, MD



Deepika N. Shah, MD, MPH



Tomas S. Aleman, MD



Hilary S. Brader, MD



Kian Eftekhari, MD



Devon H. Ghodasra, MD

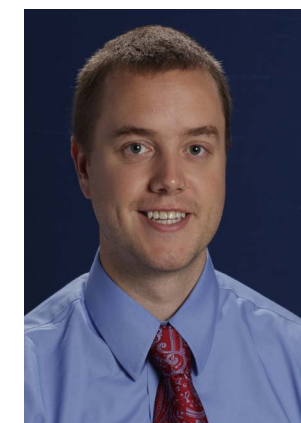


Dana H. Hornbeak, MD, MPH

2011-2012 Fellows



Collin M. McClelland, MD
Neuro-Op



Ryan D. Walsh, MD
Neuro-Op



Tony T. Choi, MD
Glaucoma



Stephanie Dotchin, MD
Pediatric Ophthalmology



Yasmin Shayesteh, MD
Oculoplastics



Jason P. Ruggiero, MD
Vitreoretinal Surgery



Javaneh Abbasian, MD
Pediatric Ophthalmology



Christina H. Choe, MD
Oculoplastics



Detecting Progression Earlier

tients to indicate whether or not there is a change in their vision," said Dr. Alexander Brucker, Professor of Ophthalmology at the University of Pennsylvania and principal investigator. "This can be very subtle over many days and weeks, and the patient may not appreciate a very subtle change. This new instrument may be able to tell us very specifically whether there is a change from one day to another, and therefore a problem."

Previous studies have shown that treatment is more beneficial if choroidal neovascularization is detected early, when visual acuity is good and the CNV lesion is small. Identifying progression can be difficult. Visual abnormalities such as metamorphopsia, scotoma or blurring often precede neovascularization, but patients are not always aware of these changes.

Study participants using the ForeseeHome device test their vision daily from their homes by looking through a small viewer at a screen which flashes a horizontal or vertical line. This line may or may not have a wave and participants use a computer mouse connected to the device to indicate when

they see a wave in the line, and where in the line the wave is located. The test takes about three minutes per eye.

The device employs hyperacuity stimuli to probe the functional integrity of the macula, the central portion of the retina responsible for sharp central vision. At the end of each test, a score measuring metamorphopsia/scotoma is transmitted by modem to a central database, where it is monitored daily by experts. Tests scores are continuously compared with the patient's baseline pattern, and in the event of a significant change, the longitudinal algorithm generates an alert which is sent to the participant and the clinical center of the treating ophthalmologist.

Study participants are evaluated to make sure they understand how to use the ForeseeHome device, and then they are randomized to receive either a ForeseeHome device or standard care. If participants in either group experience symptoms, or those in the home monitoring group receive an alert triggered by the ForeseeHome device, they are instructed to notify their clinical center within 72 hours. Early treatment can then be initiated if



The ForeseeHome device may detect progression of AMD earlier than standard care.

indicated by the patients physician.

"If this new device proves to be effective and reliable in giving us early notification that a patient has a problem, it might be a tremendous benefit to the patient, and prevent severe vision loss before it occurs," Dr. Brucker said.

Analysis of the results of the study will be conducted after patients have completed 24 months of follow-up. Doctors at the Scheie Eye Institute hope to enroll fifty participants. Please see the Study Recruitment box on page 4 for inclusion criteria.

A new monitoring device under study at the Scheie Eye Institute may save sight in patients with age-related macular degeneration by detecting progression earlier than previous methods.

The Scheie Eye Institute is one of 44 sites studying the ForeseeHome system to determine if the monitoring device improves detection of progression to choroidal neovascularization (CNV) when compared to standard care.

"Right now we depend upon the pa-



Gene Transfer & AMD

associated virus or AAV. This virus has been used successfully to deliver genes to the retinal pigment epithelium, and was an essential factor in restoring vision to patients with Leber Congenital Amaurosis. However, that particular virus does not deliver genes as efficiently to photoreceptors, the cells which deteriorate in the macula in most forms of AMD.

Dr. Bennett and colleagues have tested a number of modified AAVs in the macula of large animals with encouraging results. A recent side by side comparison with the original AAV and a modified version shows that the modified version is ten times more efficient than the original at delivering genes to cells in the macula. This could mean smaller doses, and a safer immune response.

"We can definitely target the entire macula now, in a stable and safe fashion, using that one particular virus," Dr. Bennett said.

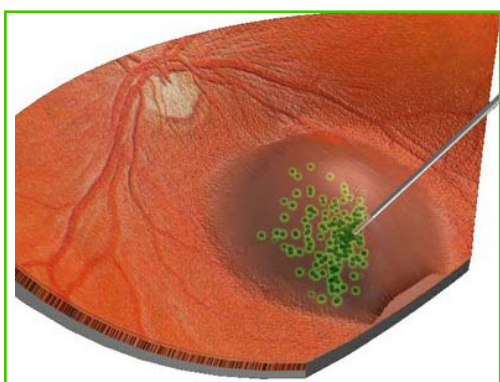
The size of the ABCA4 gene presents another challenge to gene therapy with Stargardt disease. The gene is too large for the cargo capacity of the special virus Dr. Bennett is using. Her lab is currently designing ways to use two different viruses that will each deliver one half of the gene which will then be spliced together by the cells.

"It is really kind of neat, technically," Dr. Bennett said. "I expect we're going to have promising results."

Dr. Bennett's team will have an easier time measuring their results thanks to a new \$3 million dollar piece of equipment from Canon. It is called the Adaptive Optics Scanning Laser Ophthalmoscope, and Dr. Bennett's team is the first group in the country, and the second group world-wide, to use it. The equipment scans a patient's retina, and output images show how many cone photoreceptors are in specific portions of the retina, as well as how tightly they are packed.

"This equipment is amazing because it gives exquisite resolution of cone photoreceptors," Dr. Bennett said. "As we study macular degeneration this will give us a lot of information on how many healthy cones are present, where they are, and whether they're staying around or dying off as we treat patients."

Dr. Bennett is also working with research teams in Switzerland, France, and Germany to treat blindness through optogenetics. This approach entails rescuing vision in a completely blind eye by delivering light sensitive molecules to the remaining cells in the retina. An eye that has suffered AMD over the years may no longer have functioning photoreceptors. Optogenetics takes advantage of the rest of the circuitry that is intact, including the cells in the middle part of the retina and the cells in the inner part of the retina which connect to the optic nerve. The study has proven effective



By using a modified AAV, (shown in green) healthy genes can be delivered directly to cells in the macula.

in mice models of blindness, and while the therapy does not result in 20/20 vision, it could restore enough vision to allow people to navigate and see large shapes.

"This level of vision would be very meaningful to people who have basically lights-out vision right now," Dr. Bennett said. "The advantage to this approach is that it would be a generic strategy. We would not need to know the genetic or environmental cause of blindness. It would be something that could be applied to anybody that is blind. And that is pretty exciting."

On September 20, 2011, Dr. Bennett received the Pioneer Award from the Director of the NIH. This award is designed to support bold and innovative scientists who propose pioneering approaches to major research challenges. Dr. Bennett will use the award to fund her research on molecular therapy for blinding retina disorders.

Please join us for the Scheie Alumni Reception at the 115th annual meeting of the American Academy of Ophthalmology.

Saturday, October 22, 2011
7:00 p.m. to 9:30 p.m.
Hilton Orlando
Lake Lucerne Room, Lobby Level
6001 Destination Parkway
Orlando, Florida

Enjoy cocktails and hors d'oeuvres while reconnecting with old friends and meeting new Scheie alumni and faculty. Kindly respond by clicking on "Calendar of Events" at alumni.med.upenn.edu. You may also respond by calling (215) 898-9847 or sending an email to schester@upenn.edu

We'll see you there!



Dear Friends,

Welcome to the inaugural issue of the Scheie Vision newsletter. The mission of this quarterly newsletter is to inform Scheie Alumni, and the ophthalmology community, of new research and clinical activities happening here at Scheie Eye Institute and the Department of Ophthalmology at the University of Pennsylvania. Each issue will focus on a particular eye disease, and will highlight the research of Scheie scientists as they work toward greater understanding of disease pathogenesis and more effective translation treatments for our patients.

I chose macular degeneration, which is the leading cause of blindness among people over the age of 60, as the focus of our first issue. We have come a long way in improving diagnosis and treatment of this common eye disease, but there is still a long way to go. The talented faculty here at Scheie is studying the causes and treatments of AMD from a variety of angles. Their research includes insights into the genetics underlying AMD, factors such as iron load and choroidal blood flow variations that are associated with the disease, and new ways for detecting progression.

I am extremely happy to welcome a new retina specialist to our full time faculty. Dr. Brian VanderBeek brings an extraordinarily rich background in outcomes research to our retina practice. He started at Scheie just a few weeks ago, and has already made a big impact on both our faculty and our patients with his clinical and surgical skill set. We are grateful that he has joined the Retina Division.

As mentioned in our front page story, I have appointed Dr. Scott Goldstein as the new president of the Scheie Alumni Association. I look forward to working with Dr. Goldstein to reach out to the exceptional alumni who have made the Scheie Eye Institute a leader in both research and patient care. I hope this newsletter will help strengthen ties among Scheie Alumni and foster collaborations among researchers across institutions.

I look forward to the Alumni Association Reception at the American Academy of Ophthalmology annual meeting this October. I would welcome anyone who receives this newsletter and their friends to come and visit with us.

All my sincere regards,

Joan M. O'Brien

Chair's Corner

The Scheie Eye Institute

The Scheie Eye Institute, founded by Harold G. Scheie in 1972, is a leader in the field of ophthalmological research, education and patient care.

Our physician-scientists focus on translational research ranging in topic from age-related macular degeneration to glaucoma to retinitis pigmentosa. The Scheie Eye Institute is ranked #1 in funding from the National Eye Institute.

Our full time residency and fellowship program is devoted to training 15 residents and 8 fellows to become leaders in the future of ophthalmology. In fact, Scheie is now the first institute to receive a training grant in Ocular Genetics and Bioinformatics from the National Institutes of Health. This will enable us to train scientists and ophthalmologists to interpret the huge amount of genetic information which will become available to us in the next five years.

The Scheie Eye Institute employs 60 physicians and researchers to consult and treat eye problems of every kind. Last year alone Scheie received 81,129 patient visits. We have three locations in the city of Philadelphia, and three more in Radnor, Media and Darby Pennsylvania.

For more information about the Scheie Eye Institute, look us up online at www.ups.upenn.edu/ophthalmology or call 215-662-8415.



Your support is the key to our success

Private contributions have helped propel the Scheie Eye Institute to the forefront of research and patient care. Many of our greatest breakthroughs have been made possible through donations from individuals and organizations. These gifts benefit vision saving therapy for those in our community as well as people from around the world. If you would like to make a donation to the Scheie Eye Institute, please visit us online at www.pennmedicine.org/ophth/giving or send a check to Scheie Eye Institute, Attn. Camille Metcalf, 51 N. 39th Street, Philadelphia, PA 19104.