Limits in laser photocoagulation therapy and an incomplete understanding of the pathogenesis of diabetic retinopathy are the impetus for increased investigation into the molecular mechanisms of proliferative diabetic retinopathy and diabetic macular edema (DME).

DME affects about 10 percent of all diabetic patients, but currently it is impossible to predict which patients will progress to this stage. However, Cleveland Clinic Cole Eye Institute researchers Bela Anand-Apte, MBBS, PhD and Jing Xie, PhD, have developed a new tool to help change that.

“We know that DME occurs when fluid leaks out of a blood vessel and into the macula, but in normal eyes, retinal blood vessels do not leak. They form a very tight blood-retinal barrier, unlike other tissues, in which vessels are more permeable to enable nutrients to penetrate,” says Dr. Anand-Apte.

“Better understanding the pathology of leaky blood vessels is crucial to understanding what allows retinal blood vessels to form and maintain these tight barriers. We hope to ascertain what changes occur during the diseased state and, armed with this information, work toward identifying putative therapeutic targets,” she says.

Current knowledge about the formation and maintenance of the blood-retinal barrier (BRB) is very limited, at least in part due to the fact that research has been based mainly on in vitro models of cultured cells and in situ vascular perfusion.

To develop an unbiased high throughput genetic approach to identify molecules involved in regulating retinal vascular permeability and the BRB, her team is using a model utilizing zebrafish that have been genetically engineered in her laboratory.

Continued on page 2
“We have generated a transgenic zebrafish line that expresses Green Fluorescent Protein (GFP) in the blood plasma whose retinal vasculature can be visualized in vivo. The broad long-term goal will be to use this zebrafish model to examine the disruption-reconstruction process of the blood-retinal barrier as well as in forward genetic screens to identify mutations that generate defects in blood-retinal barrier formation and increased vascular permeability.

“Because of its tissue transparency, external development and genetic amenability, we believe that zebrafish can be an excellent model system to examine the blood retinal barrier,” she adds. “Using this model, we will be able to examine the spatial and temporal development of the blood-retinal barrier, identify factors that can disrupt this barrier and examine the barrier in disease states like diabetes.”

Drs. Anand-Apte and Xie have identified two specific aims of the project:

- Determination of the developmental stage at which BRBs formed under normal conditions and evaluation of their disruption in disease states. Time-lapse confocal microscopy in vivo imaging will be performed on GFP plasma zebrafish to determine the timing of the BRB formation. Retinas of zebrafish will be evaluated from 1.5 dpf (days post fertilization) to 5 dpf at four-hour intervals. Two models of diabetic retinopathy will be developed in these transgenic zebrafish (induction of hyperglycemia and/or beta cell ablation) and progression to increased vascular permeability examined.

- Identification of factors involved in BRB formation or maintenance. Forward genetic screening will be used to identify mutations that cause increased retinal vascular permeability. Ethylnitrosourea (ENU) as the mutagen will be used and has previously been shown to generate hundreds of point mutations in the male premeiotic germ cells at high frequency. To identify the mutations regulating BRB formation, F3 embryos will be scored under fluorescent microscope from 2 dpf to 7 dpf for leakage of fluorescence. Morpholinos or mRNAs against previously identified genes will be injected into the embryos in these models for a reverse genetic approach to validate the zebrafish model. Results from this pilot project will provide the basis for future studies in which candidate genes involved in the formation and maintenance of the BRB can be studied for their ability to be targeted for potential.

“We hope to provide a unique model for future studies in which candidate genes involved in the formation and maintenance of the blood-retinal barrier can be studied for their ability to be targeted for potential therapeutics for macular edema or other diseases in which disruption of the blood-retinal barrier plays a major role,” Dr. Anand-Apte concludes.

For more information, contact Dr. Anand-Apte at ophthalmologyupdate@ccf.org.
For patients with central retinal vein occlusions (CRVO), no approved medical therapy exists. Investigations, however, continue into possible treatments for the estimated 60,000 Americans diagnosed with the disease each year.

At the Cleveland Clinic Cole Eye Institute, Rishi P. Singh, MD, and colleagues have completed enrollment in a multicenter Phase III trial studying the efficacy and safety of intravitreal ranibizumab (LUCENTIS®) compared with sham injections in subjects with macular edema secondary to central retinal vein occlusion (CRVO).

The trial is called CRUISE (A Study of the Efficacy and Safety of Ranibizumab Injection in Patients With Macular Edema Secondary to Central Retinal Vein Occlusion). The trial has enrolled about 390 patients at 100 centers in the United States.

The CRUISE trial is a 12-month study that will randomly assign patients during the first six months to two concentrations of the drug, 0.3 mg and 0.5 mg, and placebo. After six months, all patients will receive either of the two doses of ranibizumab. A 24-month extension study is provided for those patients who would like to participate and will cover the costs of visits and injections until U.S. FDA approval occurs for this new indication.

“Currently, this is a group of patients in which there is a medical necessity for treatment, but there are no approved drugs. So, for a lot of patients, it’s a diagnosis that means basically no improvement in their vision is possible.”

The trial, which began in May 2008, will primarily measure the mean change from baseline in BCVA score.

In a recent study reported during the Retina Society Meeting in September 2008, patients who received ranibizumab gained on average six letters of vision with monthly therapy over placebo-treated patients.

“This is an exciting result and we think that many of these benefits will be seen in this larger trial as well,” Dr. Singh says.

For more information on Cole Eye Institute’s involvement in the CRUISE trial or to enroll a patient, please email Dr. Singh at singhr@ccf.org.
Study Seeks New Prognostic Tools and Treatment For Patients with Uveal Melanoma

Uveal melanoma is a primary intraocular malignancy in adults, which typically occurs in Caucasian men and women age 55 to 60. The cause of uveal melanoma remains unknown. Some patients have no symptoms, while others present with blurred vision or other visual distortions, such as floaters, shadows or flashing lights. In about half of patients, this rare and incurable cancer spreads to other organs, primarily the liver. Because there are no effective treatments for metastatic uveal melanoma, the median survival is less than six months. Despite advancements in diagnosis and treatments for local tumor control, this poor survival rate has remained constant for more than 30 years.

A Cleveland Clinic multidisciplinary team of physicians and investigators, however, is working to bring new hope to patients with uveal melanoma through cutting-edge translational research.

Arun D. Singh, MD, director of Ophthalmic Oncology at Cleveland Clinic Cole Eye Institute and Pierre Triozzi, MD, Solid Tumor Oncology and Hematologic Oncology and Blood Disorders at Cleveland Clinic’s Taussig Cancer Institute, lead the research team. Working with them are Raymond Tubbs, MD, Section Head, Morphologic Molecular Pathology, and Charles Biscotti, MD, Anatomic Pathology.

Previously published uveal melanoma studies, as well as Cleveland Clinic research, have revealed the presence of aberrations in chromosomes 3 and 8 within uveal melanoma patients. This means genetic analysis can prognosticate, within 90 percent to 95 percent accuracy, whether the disease will spread to other organs. What’s more, preclinical studies conducted at Cleveland Clinic suggest that combining interferon-alfa-2b with temozolomide can produce greater anti-tumor activity for uveal melanoma.

Based on these findings, Cleveland Clinic has launched a new study, “Prognostication and Adjuvant Treatment for Uveal Melanoma.” Patients with a clinical diagnosis of uveal melanoma, who have not had any prior therapy, are eligible for this single-site study. Drs. Singh and Triozzi expect to recruit up to 60 patients. The study is being underwritten by a three-year $698,000 grant from the Ralph and Marian Falk Trust for Medical Research.
“We want to validate our prognostication model that will allow us to identify patients who are at the highest risk of developing metastatic uveal melanoma,” says Dr. Singh. “There is no other research study like this in the U.S. because, in addition to exploring the prognostication model, we will be exploring an adjuvant treatment about which we are optimistic.”

So far, prognostication has been based on data obtained from enucleated eyes or resected tumors, which are obtained only in a minority of patients. However, fluorescence in situ hybridization (FISH) analysis on trans-scleral fine needle aspirate (FNA) can yield enough material for molecular cytogenetic analysis. These procedures are expected to expand the number of patients for whom a molecular cytogenetic analysis can be performed, enabling researchers to predict the development of metastatic disease for uveal melanoma.

Patients will be treated either with enucleation, plaque radiotherapy or tumor resection based on the standard-of-care guidelines. Fresh tumor obtained from the enucleated globe, resected tumors or FNA biopsy from tumors undergoing plaque radiotherapy will be processed for FISH analysis. Previously published methods for whole cell using cytopathology preparations and formalin-fixed paraffin sections will be performed for assessment of chromosomes 3 and 8. Chromosome 3 and 8 abnormalities are known predictors of survival. Additionally, disease-free survival rates will be estimated in patients whose tumors do or do not manifest these genotypes. Rates of successful FNA and complications also will be evaluated.

Patients identified as having a high risk of developing metastatic uveal melanoma are ideal candidates for systemic adjuvant treatment, says Dr. Singh.

The objective of the adjuvant treatment phase is to prevent micro-metastases from developing into metastatic disease. Furthermore, systemic therapy may be more active in treating a microscopic rather than a macroscopic metastatic tumor where multiple mechanisms of resistance can develop.

Interferon-alfa-2b and temozolomide have anti-angiogenic activity. The combination of daily oral temozolomide plus the concurrent weekly peginterferon-alfa-2b is well tolerated. This regimen also has advantages over existing treatment in terms of both ease of administration and quality of life. Patients will be treated for 24 weeks, unless disease progression or a dose-limiting toxicity supervenes. Disease-free survival rates will be estimated and compared to that reported for this population. The safety and tolerability also will be evaluated.

Data from this study also are expected to help Cleveland Clinic researchers develop a blood test to detect a biological marker for metastatic uveal melanoma. Because tumor angiogenesis is dependent on the action of several inhibitory and stimulatory molecules, plasma levels of angioregulatory biomarkers also will be evaluated in study patients.

For more information, please contact Dr. Singh at 216.445.9479 or at singha@ccf.org

More than 90 percent of patients with metastatic disease have liver involvement. There are no effective treatments for metastatic uveal melanoma, and the median survival is less than six months.

Fluorescence in situ hybridization (FISH) analysis on trans-scleral fine needle aspirate (FNA) can yield sufficient material for molecular cytogenetic analysis, thus expanding the number of patients for which this information can now be obtained.
Staged Intrastromal Riboflavin Delivery in UVA Corneal Cross-linking Used in Advanced Bullous Keratopathy

Staged UVA cross-linking with femtosecond laser-facilitated intrastromal 0.1 percent riboflavin administration may be a safe and effective temporizing alternative method for managing bullous keratopathy, according to a study involving Cleveland Clinic Cole Eye Institute refractive surgeons.

The procedure, done in Greece, resulted in a marked reduction of edema with no corneal scarring in an 84-year-old patient who decided she did not need to go through with a planned corneal transplant after this procedure, says Ronald R. Krueger, MD, Medical Director of Refractive Surgery at Cleveland Clinic’s Cole Eye Institute and lead author on the study, which was published in September 2008 in *Journal of Refractive Surgery*.

The study was a collaborative effort between Dr. Krueger with Jerome Ramos-Esteban, MD, at the Cole Eye Institute and A. John Kanellopoulos, MD, who practices in Athens, Greece. Dr. Kanellopoulos has performed many cross-linking procedures and decided to use this procedure to provide short-term pain relief to this patient.

Prior to the procedure, the patient’s vision was count fingers only. One month afterward, it was 20/80 with improved clarity and a reduction of central corneal thickness from 696 to 571 µm (by Scheimpflug). Today, about a year and a half later, the vision is stable at about 20/50 and the patient reports having no pain since the procedure.

“When I first saw the early results of this concept, I was impressed with it as a whole new indication for cross-linking,” says Dr. Krueger, who collaborated with Dr. Kanellopoulos in dissecting and interpreting the data.

He explains that the cross-linking procedure removes extracellular water from the fibers of the cornea, which makes it thinner, more compact and clearer. Although it is not approved for use in the United States, it is often used to treat keratoconus patients in other countries. It results in weak corneas becoming biomechanically stronger, with increasing sphericity of the corneal dimensions as surface tension equalizes.

“Since it is simple and successful with keratoconus, many other uses are being developed,” Dr. Krueger says, citing infectious keratitis/scleritis, progressive axial myopia and post-LASIK ectasia as examples.

In each of these applications, the formation of interfiber collagen cross-links, through singlet oxygen reactivity, leads to a stiffer, tougher collagen matrix that maintains its rigidity over several years.

In the 84-year-old patient, the doctors wanted to achieve deeper riboflavin penetration than surface delivery allows, so they decided to leave the epithelium intact and instead make an intrastromal pocket with the femtosecond laser.

<table>
<thead>
<tr>
<th>Staged Intrastromal Delivery of Riboflavin/UVA in Bullous Keratopathy</th>
<th>PreOp</th>
<th>Day 1</th>
<th>Week 1</th>
<th>Month 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best Spectacle-Corrected Visual Acuity (BSCVA)</td>
<td>CF</td>
<td>20/100</td>
<td>20/80</td>
<td>20/80</td>
</tr>
<tr>
<td>Central Clarity Score</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Ultrasound and Scheimpflug Corneal Thickness</td>
<td>675/696</td>
<td>516/520</td>
<td>545/549</td>
<td>550/571</td>
</tr>
</tbody>
</table>
Previously, this technique was tested on 10 eye bank corneas divided into two groups of five that were placed on a pressurized artificial anterior chamber following Descemet’s membrane stripping, which resulted in the formation of corneal edema. Two consecutive corneal pockets (350- and 150-µm depth) were sequentially created using a femtosecond laser. Sequential intrastromal injections of 0.1 percent riboflavin (0.2 mL) followed by either UVA irradiation (15 mW/cm²) for seven minutes or exposure to air were performed for each pocket. Corneal clarity and central thickness were measured before and after the two UVA cross-linking steps.

Corneal clarity improved in the treated but not the control eyes. The mean central corneal thickness was significantly reduced by 256 µm (ultrasound, \(P=.0002\)) and 273 µm (Scheimpflug, \(P=.0004\)) in treated eyes, but only 100 µm (ultrasound, \(P=.048\)) and 107 µm (Scheimpflug, \(P=.075\)) in the control eyes. The clinical treatment of corneal edema showed improved clarity and reduced central corneal thickness from 675 to 550 µm (ultrasound) and 696 to 571 µm (Scheimpflug) at one month.

Dr. Krueger says he and Dr. Kanellopoulos observed that using a higher exposure level of UV light shortens the procedure time with the same safety and efficacy of cross-linking effect.

“In both the experimental and clinical application of staged intrastromal cross-linking, we used a high UVA irradiance of 15 mW/cm² for seven minutes, rather than the standard dose of 3 mW/cm² for 30 minutes, because of the diminished practicality of intrastromally reapplying the riboflavin every five minutes,” Dr. Krueger says.

“This is the first study to look at high radiance, shorter duration exposure in crosslinking,” he adds.

Dr. Krueger notes that some of these results were presented at the International Congress of Corneal Cross-Linking in December 2007 in Zurich, Switzerland; the American Society of Cataract and Refractive Surgery annual meeting in April 2008 in Chicago; and the World Ophthalmic Congress in June 2008 in Hong Kong.

For more information, contact Dr. Krueger at ophthalmologyupdate@ccf.org.
Daniel F. Martin, MD, a distinguished ophthalmologist and established leader in the development of new therapies for retinal disease, has been appointed Chairman of the Cleveland Clinic Cole Eye Institute.

Officially joining Cole Eye Institute on Dec. 1, 2008, Dr. Martin came to Cleveland Clinic from Emory University in Atlanta, where he most recently served as the Thomas M. Aaberg Professor of Ophthalmology and Director of the Retina Service.

“Over the past 15 years, Dr. Martin has established deep expertise in the treatment of age-related macular degeneration (AMD) and has become the foremost authority on the design and execution of clinical research in this area,” says Joseph Hahn, MD, Cleveland Clinic Chief of Staff. “His reputation, talent and energy will bring continued growth and ideas to Cleveland Clinic Cole Eye Institute and set the stage for new advanced research and continued clinical excellence.”

Dr. Martin is a graduate of the Johns Hopkins University School of Medicine. He completed his ophthalmology residency at Emory University School of Medicine, where he also served as Chief Resident. He completed a fellowship in vitreoretinal surgery and diseases at Duke University Medical Center and a fellowship in ocular immunology and uveitis at the National Institutes of Health (NIH).

For the past 15 years, Dr. Martin’s research has primarily focused on the design, development and implementation of clinical trials. Dr. Martin currently serves as the Study Chair for the Comparison of AMD Treatments Trials (CATT). This multi-center randomized clinical trial, funded by the NIH, is a head-to-head comparison of two leading drugs used to treat neovascular AMD – Lucentis® (ranibizumab) and Avastin® (bevacizumab). It is hoped that the results of this highly publicized study, now under way at 46 sites, will improve the treatment of neovascular AMD. Results are expected in 2011.

He also has served as the study chairman for six other multi-center randomized trials, including the studies that led to FDA approval of the ganciclovir implant and valganciclovir for the treatment of CMV retinitis in patients with AIDS. Both of these drugs remain the standard of care today. Finally, Dr. Martin has served on many clinical trial steering committees and data and safety monitoring boards and as principal investigator for more than 25 clinical trials.

Dr. Martin will now lead one of the premier dedicated, comprehensive eye institutes in the world. Cole Eye Institute has long had a reputation for innovation and superior outcomes. It is ranked by U.S. News & World Report as one of “America’s Best” ophthalmology programs, making it the No. 1 program in Ohio.

Dr. Martin’s vision for the Cole Eye Institute includes increasing the number of clinicians and researchers, increasing the department’s academic contributions, enhancing its residency training program and expanding its regional presence.

“It is the tradition of academic and clinical excellence as well as the people who make up this department that influenced my decision to accept this position,” says Dr. Martin. “Dr. Hilel Lewis did a terrific job building a great institute. I look forward to working with this highly acclaimed staff to take the Cole Eye Institute to the next level.”

Dr. Martin has published more than 80 peer-reviewed articles and delivered more than 170 invited lectures. He has been the recipient of numerous awards, including the 2004 Rosenthal Award from the Macula Society for outstanding contributions to the field, a 2007 Honor Award from the American Society of Retina Specialists, and a 2007 Senior Honor Award from the American Academy of Ophthalmology.
Age-Related Macular Degeneration

A Phase I Open-Label, Dose Escalation Trial of REDD14NP Delivered by a Single Intravitreal Injection to Patients with Choroidal Neovascularization Secondary to Exudative Age-Related Macular Degeneration (QUARK)

Objective: This is an open-label, dose escalation study in which patients will receive a single intravitreal injection of REDD14NP. The primary objective of the study is to determine the safety and pharmacokinetics of REDD14NP when administered as a single intravitreal injection.

Contact: Peter K. Kaiser, MD, 216.444.6702 or Lynn Bartko, RN, 216.444.7137

Diabetic Retinopathy

Vascular Remodeling and Effects of Angiogenic Inhibition in Diabetic Retinopathy (NIH)

Objective: This study will test whether the pattern of the retinal vasculature changes in patients with different levels of diabetic retinopathy can be quantified using computerized image analysis. In addition, the study will evaluate whether new drugs to treat diabetic retinopathy will be able to reverse these vascular changes.

Contact: Peter K. Kaiser, MD, 216.444.6702 or Ly Pung, RN, 216.445.6497

Pediatric Eye Disease

Infant Aphakia Treatment Study (IATS)

Objective: The primary purpose of this study is to determine whether infants with a unilateral congenital cataract are more likely to develop better vision following cataract extraction surgery if they undergo primary implantation of an intraocular lens or if they are treated primarily with a contact lens. In addition, the study will compare the occurrence of postoperative complications and the degree of parental stress between the two treatments.

Contact: Elias Traboulsi, MD, 216.444.4363 or Sue Crowe, RN, 216.445.3840

Retinal Vein Occlusion

An Open-Label, Multi-Center Extension Study To Evaluate the Safety and Tolerability of Ranibizumab in Subjects with Macular Edema Secondary to Retinal Vein Occlusion (RVO) Who Have Completed a Genentech-Sponsored Ranibizumab Study (HORIZON 2)

Objective: This is an open-label, multi-center, extension study of intravitreally administered ranibizumab in subjects with macular edema secondary to RVO who have completed the six-month treatment and six-month observation phases (12 months total) of a Genentech-sponsored study (FVF4165g or FVF4166g).

Contact: Rishi P. Singh, MD, 216.445.9497 or Gail Kolin, RN, 216.445.4086

The following studies have completed patient enrollment in the last year at Cole Eye Institute and are in follow up:

A 24-month Randomized, Double-masked, Controlled, Multi-center, Phase IIIB Study Assessing Safety and Efficacy of Verteporfin (Visudyne®) Photodynamic Therapy Administered in Conjunction with Ranibizumab (Lucentis™) versus Ranibizumab (Lucentis™) Monotherapy in Patients with Subfoveal Choroidal Neovascularization Secondary to Age-related Macular Degeneration (DENALI)

A Phase III, Multi-center, Randomized, Sham-Controlled Study of the Efficacy and Safety of Ranibizumab Compared with Sham in Subjects with Macular Edema Secondary to Central Retinal Vein Occlusion (CRVO)

A Phase III, Double-Masked, Multi-center, Randomized, Sham-Controlled Study of the Efficacy and Safety of Ranibizumab Injection in Subjects with Clinically Significant Macular Edema with Center Involvement Secondary to Diabetes Mellitus (DME)

An 8-Week, Multi-center, Masked, Randomized Trial to Assess the Safety and Efficacy of 700 µg and 350 µg Dexamethasone Posterior Segment Drug Delivery System Applicator System Compared with Sham
Physicians are invited to attend the following ophthalmic continuing medical education courses at Cleveland Clinic’s Cole Eye Institute. All courses will be held in the James P. Storer Conference Center on the first floor of the Cole Eye Institute. For more information, contact Jane Sardelle, program coordinator, at 216.444.2010 or 800.223.2273, ext. 42010, or at sardelj@ccf.org.

**Innovations in Glaucoma**
Saturday, March 14, 2009

*Course Director:*
Edward J. Rockwood, MD
Adult and Pediatric Glaucoma and Cataract
Cole Eye Institute

*Guest Faculty:*
Marlene R. Moster, MD
Professor of Ophthalmology
Glucoma Service
Wills Eye Hospital

**Location:**
Cleveland Clinic Cole Eye Institute,

**Description:**
The course will feature discussion on current diagnostic tools and the newest strategies for the clinical practice of glaucoma.

**Annual Research, Residents & Alumni Meeting**
June 19, 2009

*Course Director:*
Andrew P. Schachat, MD
Vitreoretinal Department
Vice Chairman, Clinical Affairs
Cole Eye Institute

*Cole Eye Institute Faculty:*
Peter K. Kaiser, MD, Ronald R. Krueger, MD, Daniel F. Martin, MD, Steven E. Wilson, MD

*Invited Faculty:*
Andrew J. W. Huang, MD, MPH
Professor of Ophthalmology & Visual Sciences
Washington University in St. Louis School of Medicine

Robert H. Osher, MD
Medical Director, Cincinnati Eye Institute
Professor of Ophthalmology
University of Cincinnati

Kirk Packo, MD, FACS
Rush University Medical Center
Illinois Retina Associates

Francis W. Price, Jr., MD
Medical Director
Cornea Research Foundation of America

J. Bradley Randleman, MD
Assistant Professor of Ophthalmology
Section of Cornea, External Disease and Refractive Surgery
Emory University School of Medicine

Philip J. Rosenfeld, MD, PhD
Professor of Ophthalmology
Bascom Palmer Eye Institute
University of Miami

**Description:**
The course will provide a comprehensive review of new developments in clinical practice and will highlight state-of-the-art management, problem-solving, case presentations and evaluation of new innovations, interventions and technologies. There will be ample time for questions and answers and the course faculty will be available throughout the course for informal discussion and consultation.

**Innovations in Optical Coherence Tomography: Spectral Domain and Beyond**
July 24-25, 2009

*Course Director:*
Peter K. Kaiser, MD
Director, OCT Reading Center

*Invited Faculty:*
Carmen A. Puliafito, MD, MBA
May S. and John Hooval Dean’s Chair in Medicine
Dean, Keck School of Medicine of University of Southern California

SriniVas R. Sadda, MD
Associate Professor of Ophthalmology
Doheny Eye Center, Los Angeles
University of Southern California

Joel S. Schuman, MD
Eye and Ear Foundation Professor
Chairman of Ophthalmology
University of Pittsburgh School of Medicine
Eye & Ear Institute

Jason S. Slakter, MD
Clinical Professor of Ophthalmology
New York University School of Medicine
Vitreous–Retina–Macula Consultants

Cynthia A. Toth, MD
Professor of Ophthalmology
Vitreoretinal Diseases and Surgery
Duke Eye Center, Duke Medical Center

**Description:**
This course will describe the new spectral domain OCT systems and how the device can aid in the diagnosis and management of retinal and glaucomatous diseases.

**Location:**
Ritz-Carlton, Cleveland, Ohio (downtown)
The Cleveland Clinic Cole Eye Institute is proud to present the 2009 Distinguished Lecture Series, which provides a forum for renowned researchers in the visual sciences to present their latest research findings. This series of lectures will feature advances in many areas of ophthalmic research presented by noted basic and clinical scientists from throughout the world. Ample opportunity for questions and answers will be provided.

Please join us for these insights into ophthalmic research and the promises they hold for patient care. No registration is required; call 216.444.5832 with any questions.

All programs will be held in the James P. Storer Conference Center of the Cole Eye Institute from 7 to 8 a.m. Attendees should park in the East 102nd Street parking lot (facing the front of the Cole Eye Institute) or the visitor’s parking garage at East 100th Street and Carnegie Avenue. We will validate your parking ticket.

**January 15, 2009**
**Glaucoma: An Axonopathy of the Visual System**
David J. Calkins, PhD
Associate Professor
Departments of Ophthalmology & Visual Sciences and Psychology
The Vanderbilt Eye Institute and The Vanderbilt Brain Institute
Vanderbilt University Medical Center
Nashville, Tenn.

**February 19, 2009**
**The Role of the Rb Family in Retinal Development and Retinoblastoma**
Michael A. Dyer, PhD
Associate Member
Department of Developmental Neurobiology
St. Jude Children’s Hospital
Memphis, Tenn.

**March 12, 2009**
**Functionalizing Cell Based Therapy for Age-Related Macular Degeneration**
Marco Zarbin, MD, PhD
Institute of Ophthalmology and Visual Science
New Jersey Medical School
University of Medicine and Dentistry of New Jersey
Newark, N.J.

**April 16, 2009**
**Retinal Stem Cells**
Derek van der Kooy, PhD
Professor
Department of Medical Genetics
University of Toronto
Toronto, Canada

**May 21, 2009**
**Chemokine Receptor CX3CR1 in Age-Related Macular Disease**
Florian Sennlaub, MD, PhD
Professor, Inserm
Centre de Recherche des Cordeliers
Paris, France

**June 4, 2009**
**Deciphering the Protein Interactome Related to the Human Usher Syndrome**
Uwe Wolfrum, PhD
Professor, Institute of Zoology, Cell and Matrix Biology
Johannes Gutenberg University of Mainz
Mainz, Germany
July 16, 2009
A Novel Class of Angiogenesis Inhibitors
Jayakrishna Ambati, MD
Dr. E. Vernon Smith & Eloise C. Smith Chair in Macular Degeneration
Professor of Ophthalmology & Visual Sciences and Physiology
Vice Chair of Ophthalmology & Visual Sciences
University of Kentucky College of Medicine
Lexington, Ky.

September 17, 2009
New Insights into the Molecular and Cellular Regulation of Corneal Immunity
Reza Dana, MD, MPH, MSc
Director of Cornea and Refractive Surgery Services
Massachusetts Eye & Ear Infirmary
Professor and Senior Scientist, Harvard Medical School
W. Clement Stone Scholar & Director of the Corneal Immunology Lab
Schepens Eye Research Institute
Director, Harvard-Vision Clinical Scientist Development Program
Boston

October 15, 2009
Role of VEGF in Blood Vessel Growth and Stability
Implications for Anti-Angiogenic Therapies
Patricia A. D’Amore, PhD
Senior Scientist
Ankeny Scholar of Retinal Molecular Biology
Professor, Harvard Medical School
The Schepens Eye Research Institute Boston

November 19, 2009
Emerging Concepts in Uveal Melanoma
Hans E. Grossniklaus, MD, MBA
F. Phinizy Calhoun Jr. Professor of Ophthalmology
Director, L.F. Montgomery Pathology Laboratory
Vice-Chairman, Department of Ophthalmology
Emory Eye Center
Emory University
Atlanta, Ga.
Daniel F. Martin, MD
Chairman, Cole Eye Institute
Chairman, Division of Ophthalmology
Specialty/Research Interests: Medical and surgical treatments of the retina, management of age-related macular degeneration, diabetic retinopathy, macular pucker, macular hole, retinal detachment, inflammatory and infectious diseases of the retina
Office Phone: 216.444.0430

Bela Anand-Apte, MBBS, PhD
Ophthalmic Research Department
Research Interest: Angiogenesis
Office Phone: 216.445.9739

Kathryn Bollinger, MD, PhD
Glaucoma Department
Specialty/Research Interests: Glaucoma, cataract
Office Phone: 216.444.5960

John W. Crabb, PhD
Ophthalmic Research Department
Research Interests: Age-related macular degeneration, inherited retinal diseases
Office Phone: 216.445.0425

William J. Dupps, Jr., MD, PhD
Cornea and External Disease Department
Specialty/Research Interests: Cornea, cataract and refractive surgery
Office Phone: 216.444.8396

Marc A. Feldman, MD
Ophthalmic Anesthesia
Research Interests: Ophthalmic surgery anesthesia, preoperative assessment, resident education
Office Phone: 216.444.9088

Richard E. Gans, MD, FACS
Comprehensive Ophthalmology Department
Specialty/Research Interests: Cataract, glaucoma, diabetes
Office Phone: 216.831.0120

Philip N. Goldberg, MD
Comprehensive Ophthalmology Department
Specialty Interests: Cataract, glaucoma
Office Phone: 216.831.0120

Froncie A. Gutman, MD
Vitreoretinal Department
Specialty/Research Interests: Retinal vascular diseases, laser therapy, diabetic retinopathy
Office Phone: 216.444.5888

Stephanie A. Hagstrom, PhD
Ophthalmic Research Department
Research Interests: Inherited forms of retinal degeneration, including macular degeneration and retinitis pigmentosa
Office Phone: 216.445.4133

Joe G. Hollyfield, PhD
Ophthalmic Research Department
Research Interests: Retinal degeneration, retinal diseases
Office Phone: 216.445.3252

Peter K. Kaiser, MD
Vitreoretinal Department
Specialty/Research Interests: Vitreoretinal diseases, age-related macular degeneration, retinal detachment, diabetic retinopathy, endophthalmitis, posterior segment complications of anterior segment surgery
Office Phone: 216.444.6702

Gregory S. Kosmorsky, DO
Neuro-Ophthalmology Department
Specialty Interests: Neuro-ophthalmology, cataract, refractive surgery
Office Phone: 216.444.2855

Ronald R. Krueger, MD, MSE
Refractive Surgery Department
Specialty/Research Interests: Refractive surgery, lasers, refractive corneal pathology, lamellar corneal transplants, investigational clinical trials
Office Phone: 216.444.8158

Lisa Kuttner-Kondo, PhD
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