Table of Contents

Research Capabilities

Department of Ophthalmology .................................................. 3
Principal Investigators
    James Funderburgh, PhD .................................................. 3
    Jerold Gordon, MD .......................................................... 4
    Robert Hendricks, PhD .................................................... 4
    Hiroshi Ichikawa, MD ...................................................... 5
    Paul Kinchington, PhD .................................................... 5
    Jes Klarlund, PhD .......................................................... 6
    Kyle McKenna, PhD ......................................................... 6
    Joel Schuman, MD .......................................................... 7
    Robert Shanks, PhD ......................................................... 7
    Nirmala SundarRaj, PhD ................................................... 8
    Shiva Swamynathan, PhD ................................................... 8
    Xiangyun Wei, PhD .......................................................... 9
    Gadi Wollstein, MD ........................................................ 9

The Louis J. Fox Center for Vision Restoration ............................ 10
Research Capabilities

Department of Ophthalmology
http://ophthalmology.medicine.pitt.edu/default.asp
Joel S. Schuman, MD, FACS – Department Chair

The Department of Ophthalmology at the University of Pittsburgh School of Medicine recently ranked eighth in the country for National Institutes of Health funding for departments of ophthalmology and has one of the top basic and clinical research programs in the country. Research focuses on ocular immunology, infectious disease, molecular genetics, molecular biology of retinal disease and glaucoma, and advanced diagnostic imaging technology development. The UPMC Eye Center is rated among the top 10 ophthalmology programs in the United States in the delivery of patient care.

The Ophthalmology and Visual Sciences Research Center (OVSRC) is the research arm of the Department of Ophthalmology. The OVSRC is directed by Robert Hendricks and comprised of scientists representing distinct basic science and clinical disciplines who are engaged in research with the common goal of understanding the visual system and the diseases that compromise its function. These scientists work side by side with departmental Ophthalmologists who are conducting clinical trials. The mission of the OVSRC is to

- Apply state-of-the-art basic science to the advancement of vision research
- Use ocular models of normal and diseased states to elucidate basic scientific concepts
- Train the next generation of scientists and physicians through involvement in mentoring of graduate and medical students and residents.

Principal Investigators within the Department

James Funderburgh, PhD
Professor of Ophthalmology
Professor, Cell Biology & Physiology

Research Interests:

- **Corneal Cell Biology**
  - Using cultured corneal cells to investigate the biology of the wound healing response
    - Identified three distinct phenotypes of cultured cells that represent the quiescent keratocytes of the normal cornea, the motile fibroblasts, that repopulate healing wounds, and myofibroblasts that secrete opaque scar tissue
  - Identifying genes involved in the biosynthesis of proteoglycans, and characterizing transcription and promoter functions
- **Tissue engineering - development of a bioprosthetic cornea.**
  - Embedding keratocytes in a three dimensional scaffolding surrounded by the other cellular components of cornea to generate connective tissue similar to that made in vivo.
  - Examining means of expanding cultured corneal cells and means of adapting stem cells to assume corneal phenotypes.
Selected Recent Publications:

- Guo N, et al., Hyaluronan synthesis mediates the fibrotic response of keratocytes to transforming growth factor beta., J Biol Chem. 2010 Aug 4

Jerold Gordon, MD
Professor of Ophthalmology
Director, Charles T. Campbell Ophthalmic Microbiology Laboratory

Research Interests:

- Providing information on the best testing methods for detecting ocular pathogens, current antibiotic susceptibility data, and standard antibiotic therapies of ocular infections.
- Laboratory consists of a fully certified clinical diagnostic ophthalmic microbiology laboratory and a research laboratory that focuses on infectious diseases (adenovirus, HSV-1, bacteria) of the anterior segment of the eye and their treatment.

Selected Recent Publications:


Robert Hendricks, PhD
Joseph F. Novak Professor and Vice-Chair for Research
Director, Ophthalmology & Visual Sciences Research Center
Professor of Ophthalmology, Molecular Genetics & Biochemistry, Immunology

Research Interests:

- Recurrent herpes stromal keratitis (HSK) due to reactivation of herpes simplex virus type 1 (HSV-1) from a latent state in sensory neurons and anterograde transport to the cornea.
- Investigating the immunosurveillance by CD8+ T cells of latently infected neurons within the trigeminal ganglion and the immunopathology mediated by HSV-specific CD4+ T cells within infected corneas.
  - Identifying and characterizing the effector mechanism used by CD8+ T cells to inhibit HSV-1 reactivation in neurons that are refractory to IFN-γ
  - Identifying and characterizing the factors responsible for maintaining the HSV-specific memory CD8+ population within the latently infected TG.
  - Clarifying the role of Dendritic cells in HSK
  - Exploring the role of Th17 subpopulation of CD4+ T
  - Utilizing HSV-specific Th1 and Th17 CD4+ T cell clones to investigate the contribution of HSV-specific and bystander activated CD4+ T cells to HSK severity
**Selected Recent Publications:**

- Ramachandran S, et al., Delaying the expression of herpes simplex virus type 1 glycoprotein B (gB) to a true late gene alters neurovirulence and inhibits the gB-CD8+ T-cell response in the trigeminal ganglion., J Virol. 2010 Sep;84(17):8811-20.

_Hiroshi Ichikawa, MD_  
**Assistant Professor of Ophthalmology and Bioengineering**  
**Director, Ocular Imaging Center**

**Research Interest:**

- Ocular Imaging and Software Development
- Examine the structure and function of glaucoma and other diseases of the eye
- Developing new methods for glaucoma diagnosis and monitoring

**Selected Recent Publications:**


_Paul Kinchington, PhD_  
**Associate Professor of Ophthalmology, Molecular Genetics & Biochemistry**  
**Director, Molecular Biology Facilities in Department of Ophthalmology**

**Research Interests:**

- Studying viruses that cause ocular infections, Varicella zoster virus (VZV), herpes simplex virus (HSV), and adenovirus
- Characterizing protein functions that could be targeted for antiviral strategy development
- Studying HSV and molecular aspects of its latency in the neuron to develop both therapeutic and preventative vaccines

**Selected Recent Publications:**

- Ramachandran S, et al., Delaying the expression of herpes simplex virus type 1 glycoprotein B (gB) to a true late gene alters neurovirulence and inhibits the gB-CD8+ T-cell response in the trigeminal ganglion., J Virol. 2010 Sep;84(17):8811-20.
Jes Klarlund, PhD  
Associate Professor of Ophthalmology, Molecular Genetics & Biochemistry

Research Interests:
- Corneal epithelial wound healing
- Understanding how cells recognize that a wound needs to be healed and how cells process the information
- Epithelial cell recruitment to a wound site
  - Understanding the immediate signals that lead to activation of phospholipase D, and identifying the targets for the messenger, phosphatidic acid, that is produced by the lipase.
  - Developing rational strategies to develop drugs to promote healing of wounds in the corneal and other epithelia.

Selected Recent Publications:

Kyle McKenna, PhD  
Assistant Professor of Ophthalmology, Immunology

Research Interests:
- Understanding mechanisms of immune evasion by eye tumors.
- Understanding mechanisms of CD8+ cytolytic T lymphocyte (CTL) inhibition within the tumor utilizing a transplantable tumor mouse model
- Understanding the requirements for migration of CD11b+ cells into the tumor microenvironment
- Improving the efficacy of immunotherapies which target immunosuppressive myeloid cells to promote tumor elimination.

Selected Recent Publications:
- McKenna KC, et al., Activated CD11b+ CD15+ granulocytes increase in the blood of patients with uveal melanoma., Invest Ophthalmol Vis Sci. 2009 Sep;50(9):4295-303
Joel Schuman, MD
Eye & Ear Foundation Professor and Chairman, Department of Ophthalmology
Director of UPMC Eye Center
Professor of Bioengineering

Research Interests:
• Imaging of the eye
  o Ocular Imaging and Software Development
  o Examine the structure and function of glaucoma and other diseases of the eye
  o Developing new methods for glaucoma diagnosis and monitoring
• Laser-tissue interactions
• Aqueous outflow
• Clinical pharmacology.

Selected Recent Publications:
• Feuer WJ, et al., Topographic Differences in the Age-related Changes in the Retinal Nerve Fiber Layer of Normal Eyes Measured by Stratus Optical Coherence Tomography., J Glaucoma. 2010 Jun 23

Robert Shanks, PhD
Associate Professor of Ophthalmology

Research Interests:
• Elucidating the molecular mechanisms behind Serratia marcescens biofilm formation and pathogenesis.
  o Screened over 14,000 transposon mutants of S. marcescens for mutations that confer biofilm-defective or hyper-biofilm phenotypes and mapped the genes
• Have determined that an OxyR homolog is required for biofilm formation and that the second messenger cAMP plays a significant role in regulation of S. marcescens biofilm formation and motility
• Exoenzyme production by S. marcescens.
• Exploring the role of surface adhesins of Pseudomonas aeruginosa and Staphylococcus aureus in corneal infection and biofilm formation.

Selected Recent Publications:
Research Interests:

- Understanding the mechanisms of homeostasis in corneal epithelium and the activation of corneal stromal cells during wound healing.
- Characterizing the mechanisms of involvement of Rho signaling pathway(s) in corneal epithelial cell cycle, cell-cell communication via gap junctions, and cell-cell adhesion through adherence junctions.
- Investigating the mechanisms of involvement of ROCK and mDia in the assembly of the actin filament network in the corneal fibroblasts and myofibroblasts.
- Testing the hypothesis that type XII collagen gene is mutated in some keratoconus patients and the mutated forms of type XII collagen are responsible for the assembly of altered ECM which is prone to break-down by specific proteases.

Selected Recent Publications:


Shiva Swamynathan, PhD
Assistant Professor of Ophthalmology

Research Interests:

- Regulation of gene expression during ocular surface development and maintenance.
- Understanding the role of Kruppel-like zinc-finger transcription factors in the ocular surface utilizing a conditional deletion of Klf4 gene in the surface ectoderm-derived tissues of the eye (lens, cornea, conjunctiva and eyelids) mouse model.
  - This model may be useful in investigating ocular surface pathologies such as dry eye, Meesmann’s dystrophy and Stevens-Johnson syndrome.
  - Using the Klf4CN mice to identify genes whose expression is required in the conjunctival epithelium for proper development of mucin secreting goblet cells.
- Generating Klf5-loxP mice to mate with Le-Cre mice to generate Klf5 conditional null mice so that Klf4 and Klf5 double conditional null mice can be made to identify overlapping or antagonistic effects of these factors.
- Regulation of mouse αB-crystallin and HspB2 genes

Selected Recent Publications:

- Swamynathan SK., Krüppel-like factors: three fingers in control,. Hum Genomics. 2010 Apr;4(4):263-70

Xiangyun Wei, PhD
Assistant Professor of Ophthalmology, Cell Biology and Physiology
Retinal Development Laboratory

Research Interests:
• Utilizing the zebrafish retina as a model system to study the molecular mechanisms underlying cellular pattern formation in the central nervous system.
• Studying how retinal epithelial polarity contributes to the formation of the layered cellular structure of the mature retina
• Investigating how cell-cell adhesion molecules play a role in retinal pattern formation
• Identifying novel mutations that affect retinal development through mutagenesis screens

Selected Recent Publications:
• Zou J, et al., Restricted localization of ponli, a novel zebrafish MAGUK-family protein, to the inner segment interface areas between green, red, and blue cones., Invest Ophthalmol Vis Sci. 2010 Mar;51(3):1738-46

Gadi Wollstein, MD
Associate Professor of Ophthalmology
Director, Ophthalmic Imaging Research Laboratories

Research Interests:
• Ocular Imaging and Software Development
• Examine the structure and function of glaucoma and other diseases of the eye
• Developing new methods for glaucoma diagnosis and monitoring

Selected Recent Publications:
• Kim JS, et al., Retinal nerve fiber layer thickness measurement comparability between time domain optical coherence tomography (OCT) and spectral domain OCT. Invest Ophthalmol Vis Sci. 2010 Feb;51(2):896-902.
The Louis J. Fox Center for Vision Restoration (Fox Center) of UPMC and the University of Pittsburgh
http://www.foxcenter.pitt.edu/
Joel S. Schuman, MD and Alan J. Russell, PhD, Interim Co-Directors

The Louis J. Fox Center for Vision Restoration of UPMC and the University of Pittsburgh is a multidisciplinary research and clinical program dedicated to discovering and delivering new cures for blindness and vision impairment. As the world’s first comprehensive program dedicated to ocular regenerative medicine, the center’s researchers and clinicians develop nontraditional therapies for the prevention and treatment of vision impairment and loss through the use of:

- Regenerative research and translation
- Tissue engineering
- Cell therapy
- Gene therapy
- Transplantation

Mission:

The Fox Center focuses on the restoration of sight through technology, tissue regeneration and transplantation. We optimize quality of life for those challenged by vision loss. We insure that individuals and their loved ones know they are not alone in addressing this challenge. We seek to maximize participation in work, community, and society of those who lose their sight for any reason. Finally, we educate the sighted community on the prevalence of vision loss in America and around the world.

Objectives:

Long term objective:

- To discover and develop new cures for blindness and impairment through basic and clinical research. We focus on problems affecting the retina, optic nerve, cornea, and lens.

Short-term objective:

- To restore hope and improve the quality of life for those currently suffering from vision loss. The Fox Center will provide vision restoration through the augmentation of existing visual pathways or by providing vision through sensory substitution.

Areas of specialization:

The Fox Center specializes in the five most common and important disease areas associated with vision loss:

- Macular disease (retinal degenerations including macular degeneration, retinal vein and artery occlusion)
- Diabetic retinopathy
- Optic nerve disorders (glaucoma, other optic neuropathies)
- Corneal scarring
- Ocular trauma
Strategies to achieve objectives:

- Identifying new methods to stabilize active eye disease
- Improving vision in patients in whom active eye disease has been stabilized, but vision remains poor
- Providing the best possible care for patients suffering from vision impairment
- Performing innovative research in ocular regeneration and vision rehabilitation
- Discovering new treatments to maximize vision recovery and function
- Educating health care professionals and patients on issues related to vision loss