Research Summaries for Faculty Trainers

Drew Adams, Ph.D., Genetics

The Adams lab uses chemical biology approaches to address problems at the interface of chemistry, biology, and medicine. A special emphasis is on the use of high-throughput screening to identify new small-molecule probes targeting proteins involved in disease, including diseases of the eye. An initial protein target for small-molecule inhibitor development is glutaredoxin 1, which has been characterized by Prof. John J. Mieyal of the CWRU School of Medicine Department of Pharmacology to promote diabetic retinopathy through its regulation of NFkB signaling.

Matthias Buck, Ph.D., Physiology & Biophysics

Dr. Buck's research program characterizes the structures and the dynamics of proteins involved in protein-protein interactions with a concentration on the plexin and the Eph-A1 and Eph-B1 transmembrane receptors. Protein interactions determine the basic mechanisms by which proteins transmit signals in cells and how signaling is disrupted by mutation in diseased states. Knowing at near-atomic resolution which residues interact in protein complex formation will allow them to rationalize their interaction affinity and specificity. Furthermore, it will provide an opportunity for them to alter the proteins for diagnostic or therapeutic purposes. Recently we have become interested in the role of Neuropilin and its co-receptors (incl. plexins) in the visual system, specifically in angiogenesis in the retina. An R21 was awarded for pilot work from the Eye Institute (2014-15).

William Bush, Ph.D., Epidemiology & Biostatistics

My research program applies statistical and bioinformatics approaches toward the analysis of genomic data for age-related macular degeneration (AMD). Specifically, we have developed an approach for looking at cumulative genetic effects and genetic interactions among disease pathways relevant to AMD.

Sudha Chakrapani, Ph.D., Physiology & Biophysics

My research focus over the last 15 years has been to understand the structure and function of ion channels, particularly the members of voltage- and ligand-gated channel family that are critical for the function of retinal ganglion cells and rod photoreceptors. I have expertise in membrane protein expression and purification, site-directed labeling and spectroscopy (electron paramagnetic resonance and fluorescence), X-ray crystallography, single-channel and macroscopic current measurements in reconstituted liposomes and heterologous expression systems. M

George Dubyak, Ph.D., Physiology & Biophysics

The Dubyak lab studies innate immune signaling pathways in different models of tissue infection or injury. A current emphasis is on how caspase-1 inflammasome signaling platforms are regulated to mediate production of inflammatory cytokines and pyroptotic cell death. Our recent studies have characterized roles for these signaling pathways during corneal infection by bacteria and in diabetic retinopathy.

David Friel, Ph.D., Neurosciences

My areas of expertise are: electrophysiology, calcium signaling, P/Q Ca^{2+} channelopathies, and mathematical modeling. Dysfunction of the P/Q-type voltage dependent calcium channels is associated with ocular motor abnormalities; *e.g*., involuntary eye movements (nystagmus).

Marcin Golczak, Ph.D., Pharmacology

My lab focuses on the role of Vitamin A in blinding eye diseases, focused on the elucidation of biochemical principles governing vitamin A metabolism in the eye. Our work has contributed substantially to understanding the mechanistic principles of RPE65-dependent 11-*cis*-retinal regeneration with special emphasis on the function of lecitihin:retinol acyltransferase (LRAT). Applying organic chemistry, protein biochemistry, cell biology, and analytical techniques we have developed and tested novel pharmacological strategies for the treatment of progressive retinal diseases.

Beata Jastrzebska, Ph.D., Pharmacology

The focus of my research is to address the functional implications of rhodopsin dimerization and its role in signal propagation and termination by studying complexes of rhodopsin with its partner proteins.

Jonathan Haines, Epidemiology & Biostatistics

My lab has developed and applied computational methods to big data with a focus on data reduction and integration of different data types. These methods involve the use of genomic and computational approaches to understand the pathophysiology of human disease, including disorders of the eye which is the focus of the Visual Sciences Training Program.

Yoshikazu Imanishi, Ph.D., Pharmacology

My research program has been focused on the process of photoreceptor membrane morphogenesis and organization of the rhodopsin-mediated signaling cascade. The research is relevant to the pathogenic mechanisms of blinding disorders.

Sudha Iyengar, Ph.D., Epidemiology & Biostatistics

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(patient) samples with a focus on genomic technology. These technologies are creating large volumes of data, quickly adding up from terabytes to petabytes and more. Analyses are performed with high density genome-wide linkage, genome-wide association, and next

addition, she has generated mice with mutations in visual cycle enzymes, resulting in delayed clearance of all-trans-retinal from the retina; and these mice develop cone-rod dystrophy.

Danny Manor, Ph.D., Nutrition

A number of projects in the Manor lab directly relate to the mission of the Visual Sciences Training Program. In particular, we are studying the molecular mechanisms and pathological outcomes of heritable defects in regulators of vitamin E status. Specifically, we are studying the outcomes of mutations in the tocopherol transfer protein (TTP), manifesting in CNS deficits especially in the cerebellum and the retina. Using genetic mouse models we are studying how alpha-tocopherol protects these tissues from functional deficits presented by affected humans, namely cerebellar ataxia and retinitis pigmentosis.

Jason Mears, Ph.D., Pharmacology

Within eukaryotic cells, mitochondria continually divide and fuse. Defects in these processes are associated with an increasing number of human diseases, including cancer, neurodegeneration and aging. Research in the Mears lab is focused on understanding of the cellular machinery that regulates mitochondrial dynamics in yeast and mammalian cells. Cryo-electron microscopy along with biochemical and computational methods are used to elucidate the structural and mechanistic roles of proteins in the eukaryotic fission machinery. Mitochondrial dysfunction has recently been associated with age related retinal disease including macular degeneration and glaucoma. Therefore, understanding how changes in mitochondrial dynamics contribute to these diseases is an important priority.

Vincent Monnier, Ph.D., Pathology

My lab is currently involved in research to decipher the role of the Maillard reaction *in vivo* on the destabilization of lens crystallins in the aging lens and the formation of age-related nuclear cataracts. In addition we are characterizing the basis for selective uptake of glutathione into the lens and how this process changes with aging, likely serving as a contributing factor to cataract formation.

Tingwei Mu, Physiology & Biophysics

My research focuses on studying the protein biogenesis and function of GABAes6a 0 0 1 2531 Tm[(m)-3(ech

assays of the retina;