

**Case Western Reserve University
Department of Physiology and Biophysics
American Heart Association Summer Training Program**

Cardiovascular diseases still remain the number 1 cause of death in Western industrialized Countries. Thus, interest is still high in better understanding the underlying causes of heart and vascular diseases to improve therapy and management of the pathologies.

To provide undergraduates interested in a career in Cardiovascular Research with an opportunity to test new hypotheses and work in *avant-garde* research laboratories at Case Western Reserve University, the Department of Physiology and Biophysics offers **5 summer research traineeships** supported by a recently awarded American Heart Summer Training Grant. The enrolled students are encouraged to select a laboratory and work together with a faculty member of their choice to obtain hands-on research experience in cardiovascular sciences.

The program is designed for outstanding students with majors in biology, chemistry, physics or related disciplines. Students will carry out a research project under the close guidance of a faculty member for 10 weeks during the summer months (*May 26 through July 31, 2015*). In general, the program accepts students who have finished their junior year. Exceptions are possible for advanced and talented sophomores.

Application Deadline: March 31, 2014

Decisions on acceptance into the program are made on a continuous basis, with the bulk of acceptances being made by **April 15, 2015**. Pending withdrawal from the program, applications are accepted and decisions on acceptance are still possible after this date.

Letters of inquiry should be directed to:

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The following is a list of faculty mentoring in the program, and their areas of research:

Walter Boron, MD: Regulation of gas and acid/base transport across membranes. The Boron laboratory investigates the transporters and channels responsible for regulating gas and acid/base transport across cellular membrane and how these mechanisms are controlled by factors such as cell volume, hormones and signaling proteins. One important focus of the Boron laboratory is the study of how gas and water channel function is altered by stroke. The Boron's laboratory utilized a broad variety of techniques spanning from single cell measurements and imaging to molecular and cellular biology approaches, to x-ray crystallography, to computational modeling.

Matthias Buck, DPhil: Plexin and Eph Receptors in CV development and disease. The Buck laboratory studies two receptor families responsible for cell guidance and positional maintenance (Plexins and Ephrins), both with key involvement in CV development and disease. A wide range of tools are used for structural biology (solution NMR / x-ray crystallography), and protein biophysical studies (CD, fluorescence spectroscopy, ITC and SPR). Part of the laboratory also pursues computational modeling and molecular dynamics to provide new insights into the experimental data and to suggest further studies.

Sudha Chakrapani, PhD: Structural dynamics underlying ion channel function. The Chakrapani laboratory focuses on elucidating the conformational dynamics underlying allosteric mechanisms in ligand- and voltage-gated channels, and to determine how these processes control basic features of channel function namely, gating and modulation. Mutations in these channels underlie a number of genetically inherited pathological conditions in cardiovascular disease. A multidisciplinary approach is used that combines structural techniques (EPR, Fluorescence spectroscopy, and X-ray crystallography), functional measurements (patch-clamp recordings, two electrode voltage-clamp recordings in oocytes) and biophysical tools (ITC) to elucidate the dynamics that govern of channel function.

Isabelle Deschênes, PhD: Molecular Mechanisms of Arrhythmias. The Deschênes laboratory focuses on the molecular basis of cardiac arrhythmias, and the fundamental basis of the electrical function of the heart, which is critical for the much-needed design of novel cardiac therapies for cardiac arrhythmias. Molecular and electrophysiological techniques are used to study the structure-function of mutant ion channels. Genetic tools are used to further investigate the source of incomplete penetrance in channelopathies. Insights from these fundamental studies are applied to develop translational approaches to treat patients with ion channels dysfunction susceptible to cardiac arrhythmias.

George Dubyak, PhD: Inflammatory Signal Transduction in Vascular Disease. The Dubyak laboratory investigates signal transduction in inflammation, anti-tumor immunity, and cardiovascular disease. A major focus is to understand how ion channels, such as the P2X7 ATP-gated ion channel receptor, trigger the caspase-1-based inflammasome signaling pathways in macrophages and dendritic cells (DCs) which mediate interleukin-1 β -based innate and adaptive immune responses. Inflammasome signaling is involved in inflammatory and immune responses in atherosclerosis. Another research area is characterization of autocrine, paracrine, and endocrine signaling pathways that contribute to the dysregulation of arterial calcification which is a major cardiovascular complication in kidney failure, diabetes, and aging.

Jeffrey Garvin, PhD: Regulation of Blood Pressure. The Garvin laboratory investigates fundamental processes that mediate and regulate salt and water absorption by the kidney. A major interest is how changes in these processes can lead to hypertension, especially salt-sensitive increases in blood pressure. A wide range of techniques is employed from subcellular imaging of freshly isolated tissue to cell culture to measurements of physiological parameters in the whole animal.

Aaron Proweller, MD, PhD: Vascular development and signaling. The Proweller laboratory focuses on the molecular pathways regulating vascular development and post-natal blood vessel maturation. Current research addresses the influential role of Notch signaling in vascular smooth muscle for angiogenic patterning and physiologic function of the arterial vasculature. The laboratory utilizes mouse gene targeting in gain- and loss-of-function experiments and employs a wide array of cell, molecular and vascular imaging techniques to characterize the function of Notch signaling in vascular smooth muscle cells. The long-term goal is to determine how cellular derangements from Notch dysfunction play important roles in adult vascular diseases including hypertension and stroke.

Rajesh Ramachandran, PhD: Molecular biophysics of membrane remodeling. The Ramachandran laboratory studies the role of dynamin in membrane remodeling events in the cells of large organelles including the mitochondria and peroxisomes. Defects in intracellular membrane remodeling events have been implicated in various human conditions including neuromuscular disorders, cancer and cardiovascular disease. A major goal is to elucidate the various molecular mechanisms at play that ultimately effect membrane remodeling and fission. Cutting-edge, state-of-the-art tools are employed, including, fluorescence spectroscopic and microscopic techniques, single-molecule FRET, FCS.

Andrea Romani, MD, PhD: Protein Dynamics and Ion regulation in the heart. The Romani laboratory studies how mammalian cells tightly control cellular Mg²⁺ content by partitioning these ions within cellular compartments and by transporting this ion across the plasma membrane. Current studies investigate how cardiac cells regulate Mg²⁺ transport and homeostasis under physiological conditions and how changes in cellular Mg²⁺ content affect function of enzymes located in mitochondria and endoplasmic reticulum. Techniques employed include atomic absorbance spectrophotometry and fluorescence, as well as mass spectrometry for detection of post-translation modifications in cardiac cells.

Menachem Shoham, PhD: Drug screening for the treatment of infectious disease. The Shoham laboratory focuses on drug discovery and drug screening to combat infectious diseases. A major goal is to screen for drugs that will prevent the formation of virulence factors, such as toxins and biofilm, thereby neutralizing pathogens. The Shoham laboratory uses a longitudinal approach, moving from virtual screening to the testing of promising molecules in insect and rodent infection model. Recent studies have focused on screening inhibitors of *Staphylococcal* infections, a major cause of infective endocarditis.

Julian Stelzer, PhD: Regulation of cardiac contractile function. The Stelzer laboratory investigates the regulation and function of contractile proteins in the heart. Defects in contractile proteins are a major cause of heart failure and even sudden cardiac death. State-of the art biophysical approaches are utilized that allow measurement contractile force and cross-bridge kinetics in single myocytes and cardiac fibers, and transgenic animal models of cardiovascular disease are utilized for the study of in vivo cardiac function and to determine the functional consequences that defects in contractile proteins have on whole organ function and the development of cardiac disease.

Xin Qi, PhD: Mitochondrial dysfunction in stroke. The Qi laboratory investigates the role of mitochondria dysregulation in neurovascular disorders including stroke. Fusion and fission peptide regulators are used to determine whether manipulation of mitochondrial dynamics could provide therapeutics for treatment of these neurological injuries in stroke.

Xin Yu, ScD: Cardiac Mechanics and Metabolism. The Yu laboratory is devoted to the development of state-of-the-art magnetic resonance imaging (MRI) and spectroscopy (MRS) methods for multi-level, integrative understanding of the heart under normal and diseased conditions.