Current Research in Pathology

VASCULAR BIOLOGY and CELL BIOLOGY

Joe Madri, Ph.D., M.D.

The interests of the Madri laboratory center around investigations of signaling pathways stimulated following endothelial–immune cell and endothelial–neural cell interactions, and endothelial cell–extracellular interactions and how they influence the processes of vasculogenesis, angiogenesis, neurogenesis, and transendothelial migration. Endothelial cells play central roles in the development, growth and maintenance of the vascular system as well as in the processes of inflammation, repair, and metastasis. Interactions of vascular cells with other cells (homotypic and heterotypic), surrounding matrix, and soluble factors influence vascular cell responses.

We are currently investigating the roles of selected homotypic and heterotypic cell adhesion molecules (PECAM-1), integrins (selected beta 1, beta 2, and beta 3 integrins), junction associated molecules and extracellular matrix components in modulating vascular cell and T cell behavior (attachment, spreading, proliferation, migration, interactions with mononuclear (T) cells, and angiogenesis). Specific projects in the laboratory currently include: elucidation of the role of CD44 in modulating endothelial and T cell behavior in neuro-inflammation and elucidation of the mechanisms of hypoxia-driven cerebral angiogenic responses noted in the premature infant population and their association with neurodevelopmental handicaps.

Themis Kyriakides, Ph.D.

The Kyriakides laboratory is investigating the interactions between synthetic biomaterials and tissues. In general, insertion of biomaterials into the body elicits a rejection-like response and our research focuses on identifying the cells and molecules that regulate this response. A major goal of our research is to identify molecular targets that can limit inflammatory responses and enhance blood vessel formation. In addition, in translational approaches we aim to generate novel modified synthetic blood vessels and networks of vessels for tissue engineering applications.

Wang Min, Ph.D.

Understanding of the fundamental molecular mechanisms for vasculogenesis, arteriogenesis, and angiogenesis may lead to improved therapeutic strategies for treatment of vascular diseases. The vascular cells that primarily respond to inflammatory stimuli are the vascular endothelial cells (EC). The goal in the Min lab is to dissect the signaling pathways in EC involved in vascular development, remodeling and disease progression. We have used biochemical, cell biological, and mouse genetic approaches to define the critical molecules mediating vascular development, remodeling, and vascular disease progression.

COMPUTATIONAL BIOLOGY

John Sinard, M.D., Ph.D.

John Sinard's research focuses on designing and developing informatics solutions which can be deployed into the day-to-day practice of pathology and medicine. Dr. Sinard has led the development of several custom software solutions addressing workflow issues in the Department. At the institutional level, he is interested in the design and building of data repositories that can deliver clinical data directly to faculty investigators, enabling clinical research. He also has an interest in the use of computers in medical education.

Michael Krauthammer, M.D., Ph.D.

The Krauthammer lab focuses on research in biomedical informatics and computational biology. Our research centers around the development and use of computational techniques to analyze molecular networks for the purpose of identifying disease pathways and drug effector pathways for toxicity prediction. Our lab is also pursuing the use of natural language processing (NLP) techniques to extract problem-specific information from scientific articles or medical reports.

Yuval Kluger, Ph.D.

The research in the Kluger computational biology and bioinformatics laboratory involves analysis of genomics and proteomics experiments. This includes computational analysis of output from high-throughput datasets generated from experiments involving melanoma, breast cancer, hematopoiesis, cell cycle genomics, and protein-protein interactions. The computational activities in our laboratory currently include the following areas: 1) application of signal processing approaches for identification of relevant biological signals in high-throughput experiments, such as identification of aberrations in multi-subclonal cancer samples, signal denoising in next generation platforms, and de-mixing of cell types in heterogeneous samples; 2) developing approaches to analyze high dimensional data from genomics platforms for biomarker discovery and personalized medicine. In particular, we use advanced applied mathematical methods to search complex local and non-local genomic patterns across the genome that may discriminate cancer patients with good vs. poor outcomes in CNA studies employing next generation sequencing or SNP platforms; and 3) uncovering direct and collective regulatory relationships between regulators (TFs, epigenomic factors, and miRNAs) and their target genes by integration of heterogeneous Omics datasets and DNA sequences.

Steven Kleinstein, Ph.D.

The Kleinstein group integrates techniques from dynamic modeling, systems biology, and bioinformatics to gain insights into the immune response. We are particularly interested in the generation and selection of high affinity B lymphocytes. Our group has developed widely-used methods to detect and quantify immune selection based on the analysis of somatic mutation patterns from B cell receptor sequences. These methods are being applied to understand the adaptive response to pathogens as well as to determine the role of antigen-driven selection in autoimmunity and B cell cancers. Another major area of focus is the response to influenza infection and vaccination. Our group is developing mathematical models to understand how pathogen and host variation, cytokine environment, and genetics shape the human response to the influenza virus.