CELL BIOLOGY

Jon Morrow, M.D., Ph.D.

Research in the Morrow lab focuses generally on understanding the mechanisms by which the cytoskeleton of the cell contributes to the organization of cell polarity, receptor sorting, and signal transduction, and on the diseases that result from hereditary or acquired disorders of the cytoskeleton. Current research focuses on the spectrin-ankyrin membrane skeleton, which participates in a variety of cellular processes. This work has identified the molecular basis of several blood diseases involving fragile erythrocytes; disorders of renal function that follow ischemic injury; a role in certain forms of cancer; and hereditary neurological diseases including cerebellar ataxia and certain seizure disorders. In-progress studies suggest that cytoskeletal dysfunction may even play a role in the genesis of behavioral diseases such as anxiety-spectrum disorders and autism.

Gerald Shadel, Ph.D.

In humans, as in most animal cells, genetic information is housed not only in the nucleus, but also in mitochondria. Mitochondrial DNA (mtDNA) encodes thirteen essential proteins of the ATP-producing oxidative phosphorylation complexes as well as 22 tRNAs and 2 rRNAs required to translate these thirteen mRNAs in the mitochondrial matrix. Mutations in mtDNA cause maternally inherited disease syndromes that involve complex pathology, including neuromuscular and cardiac pathology, deafness, and blindness. In addition, mtDNA mutations accumulate in normal aging tissues, certain tumors, and have been implicated in late-onset diseases such as Alzheimer's, Parkinson's, diabetes, and cancer, indicating that the pathology of dysfunctional mitochondria is only beginning to be unraveled. The research in the Shadel laboratory is directed toward understanding the mechanism of gene expression in human mitochondria and its impact on human disease and aging. The ultimate goal is to understand the full impact of dysfunctional mitochondrial gene expression on human health and use this information to design specific interventions to treat mitochondria-based disease and age-related pathology.

Gilbert Moeckel, M.D., Ph.D.

The research focus areas in the Moeckel lab are centered on understanding the molecular biology of interstitial fibrosis and progression of chronic kidney disease. Renal fibroblasts play an important role in the development of interstitial fibrosis and progression of CKD. Our lab is currently investigating the mechanisms that lead to increased synthesis of fibrogenic molecules such as fibronectin and collagen in renal fibroblasts under hyperphosphatemic and hyperglycemic conditions. We have generated primary and immortalized fibroblast cell lines from renal cortex and medulla, which we employ to study signaling pathways and the regulation of transcription factors that drive progression of fibrosis. Moreover, we are investigating the role of endothelial cell injury in progression of renal fibrosis using diabetic mouse models.

GENETICS / GENOMICS

S. David Hudnall, M.D.

The Hudnall laboratory is involved in elucidating the contributory roles of genetic mutation, herpes virus infection, and tumor-infiltrating inflammatory cells in the pathogenesis of human lymphoproliferative disorders, including Hodgkin lymphoma.

Pei Hui, M.D., Ph.D.

Gestational trophoblastic disease (GTD) encompasses a group of human disorders of reproduction resulting in significant morbidities in women, and is remarkable for its geographical distributions and varying frequencies in the different age and ethnic groups. In human pathology, these disorders are unique proliferative conditions with regard to their clinical setting, genetic compositions, and varying biological behaviors. Although it is one of the earliest recognized human disorders in history, the biology, pathogenesis, diagnosis, and clinical management of the disease are still fascinating diagnosticians and scientific investigators alike. Genomic imprinting and preferential X inactivation in placental trophoblasts likely regulate many of the complex biological interactions and play important roles in the pathogenesis of GTDs. Moreover, practical and timely translation of our growing knowledge of molecular pathogenesis of GTD into diagnostic and therapeutic applications in patient care has drawn greater attention. Recently, chorionic villous DNA genotyping has been validated at Yale Pathology as a highly practical and cost-effective method for the routine diagnosis and sub-typing of hydatidiform mole, the most common subtype of GTD.

NEUROSCIENCE

Alexander Vortmeyer, M.D., Ph.D.

Dr. Vortmeyer's research interests are hereditary tumorigenesis, tissue microdissection, and tissue proteomics. His research has studied in detail tumor precursor structures arising in the context of different tumor suppressor gene syndromes. At NINDS, he developed and promoted human tissue-based research in collaboration with numerous basic and clinical laboratories within NINDS departments, NCI, and the National Human Genome Research Institute (NHGRI).

Anita Huttner, M.D.

The Huttner lab is focused on somatic cell reprogramming, particularly the isolation and characterization of human induced pluripotent stem cells (iPSCs), which are derived from skin fibroblasts and closely resemble conventional embryonic stem cells. These cells provide an unparalleled opportunity to model human pathologic disease processes, since patient derived iPSCs retain the donor's complex genetic background. Our goals are to establish and validate in vitro and in vivo model systems, which allow the recapitulation of disease-specific pathological changes and provide insight into disease mechanisms of neurodevelopmental and neuromuscular disorders. The Huttner lab hosts a national bio-repository for neurodevelopmental/neuromuscular disorders and tumors, supported by CURE CMD, an international registry for congenital muscle disease.