

John T. Milliken

Department of Medicine

Website: <https://internalmedicine.wustl.edu>

Research Electives

Medicine Research Electives

During the fourth year, opportunities exist for many varieties of advanced clinical or research experiences.

For information about Primary Care Summer Preceptorships (p. 4), please refer to the information at the bottom of this section.

John P. Atkinson, MD

Clinical Sciences Research Building, 10th Floor
Phone: 314-362-8391

A clinical research elective is offered in the evaluation of patients with complement deficiency or overactivity states and with undiagnosed rheumatic disease syndromes.

Roberto Civitelli, MD

BJC Institute of Health, 11th Floor, Musculoskeletal Research Center
Phone: 314-454-8408

Biology of cell-cell interactions and communication in bone via gap junctions and cell adhesion molecules; function of connexins and cadherins in transcriptional control of osteoblast differentiation, osteoclastogenesis, and mechanotransduction; modulation of mesenchymal lineage allocation and osteogenic differentiation by cadherins and beta-catenin signaling.

Nicholas O. Davidson, MD

910 Clinical Sciences Research Building, North Tower
Phone: 314-362-2027

Our focus is on the genetic pathways of nonalcoholic fatty liver disease (NAFLD) and colorectal cancer development. We have two major areas of research interest. Our laboratory is interested, first, in the molecular mechanisms of hepatic steatosis and the pathogenesis of NAFLD. This is the most prevalent liver disease in the United States, likely affecting a quarter of the population. We have generated genetically manipulated mouse strains that offer insights into the mechanisms of hepatic steatosis. The student would work as part of a team, designing and conducting experiments that will test hypotheses concerning the mechanisms and consequences of hepatic steatosis. These studies will primarily involve mouse genetics, examining the expression of candidate genes under a variety of nutritional and pharmacologic settings that modulate hepatic lipid metabolism. In addition, we are using microarrays to study the spectrum of genetic changes that

may predict the extent of hepatic lipid accumulation in patients with steatohepatitis. Our goal is to test hypotheses using mouse genetics and to extend these studies to examine the same pathways in humans with NAFLD. Our second area of interest concerns the genetic pathways involved in colorectal cancer, the second leading cause of cancer-related deaths. We have developed a novel strain of mice in which the dominant effects of mutations in the APC tumor suppressor gene have been abrogated through deletion of an RNA binding protein, apobec-1. This deletion has a major effect on the expression of cox-2, abrogating the increase in expression seen in human colonic adenomas and wild-type mouse intestinal adenomas. These findings suggest that apobec-1 is a genetic modifier of colon cancer development. We will study the importance of apobec-1 expression in human colon cancer specimens and continue our murine genetic studies of this novel pathway for modulating colon cancer development and progression.

Bradley Evanoff, MD, MPH

Phone: 314-454-8638

Our primary interest is on occupational medicine epidemiology and intervention research. Our research involves the use of epidemiology methods to characterize associations between diseases and work-related exposures. We are also doing workplace intervention studies to prevent injuries and illnesses and to improve healthy diet and physical activity among working populations. During an elective in occupational medicine epidemiology research, students will learn how to use epidemiologic methods to investigate disease processes by working on a mutually agreed-on topic of interest related to occupational diseases. Other activities can include worksite visits and intervention projects as well as involvement with worksite health promotion and policy making. Elective length is variable, depending on individual circumstances. Please contact Dr. Evanoff to discuss this research.

Gregory I. Goldberg, PhD

Wohl Clinic, 4th Floor
Phone: 314-362-8172

Role of secreted extracellular matrix metalloproteases in tissue remodeling; structure and function of the metalloproteases.

Richard W. Gross, MD, PhD

4525 Scott Avenue, East Building
Phone: 314-362-2690

Lipid mediators of signal transduction in the cardiovascular system; characterization of regulatory mechanisms responsible for the liberation of lipid second messengers during cellular activation; roles of phospholipases in mediating the metabolic syndrome and end-organ tissue damage.

Stacey House, MD, PhD

Phone: 314-362-8070
houses@wustl.edu

Lisa Hayes

Phone: 314-362-4362
hayesl@wustl.edu

Emergency medicine clinical research is the primary focus of this lab. This type of research involves the gamut of research designs, from retrospective cohort studies ("The Use of B Hydroxy Butyrate Point-of-Care Testing in Diabetic Ketoacidosis") to prospective clinical trials ("Biomarkers in Traumatic Brain Injury") to the evaluation of health care systems and emergency department processes ("Effects of a Triage Process Conversion on the Triage of High Risk Presentations") to the analysis of health policy issues ("Rate of Follow-up to a Primary Care Clinic and Subsequent Emergency Department Utilization among an Urban ED Population"). Students will learn the basic clinical research designs and will be able to articulate the benefits and drawbacks of each. They will be involved in hypothesis generation and study design for projects that are at that stage. For ongoing projects, they will learn about the informed consent process and be involved in screening for study subjects and subject selection and enrollment. They will be allowed to consent for studies judged to be of minimal risk. Students will be taught important rules regarding data acquisition and entry, particularly as these relate to standards that have been set forth in the medical literature. They will learn about bias and inter-rater reliability. Students will participate in data entry, data analysis, and subsequent abstract/manuscript preparation based on their level of interest and time commitment. Students will meet weekly with one of the course directors to discuss study progress and to identify any roadblocks to study completion. These meetings will also serve as a forum for one-on-one education of the student regarding study methodology, ethical issues in research, and various resources available to the clinical researcher at Washington University.

Sandor J. Kovacs, MD, PhD

9965 Clinical Sciences Research Building
Phone: 314-362-8901

This experience is geared toward students with math, physics and engineering backgrounds. The cardiovascular biophysics research elective concentrates on physiologic modeling and the comparison of model predictions to in vivo human data. The minimum elective time is eight weeks.

Marc S. Levin, MD, and Deborah C. Rubin, MD

922/924 Clinical Sciences Research Building
Phone: 314-362-8933 or 314-362-8935

Students will be members of a collaborative research team headed by Drs. Levin and Rubin (Department of Medicine) investigating the mechanisms underlying the intestinal adaptive response that occurs to compensate for the loss of functional small intestine. A second project focuses on epithelial-mesenchymal interactions and their role in regulating gut epithelial proliferation carcinogenesis and the normal and cancer stem cell niche. Specific mechanisms under investigation include the function of an immediate early gene *Tis7* on gut adaptation after resection or injury. The role of myofibroblast protein epimorphin in regulating cell proliferation and colon carcinogenesis is being explored. The student will have

the opportunity to learn basic molecular biology and physiology as they relate to small intestinal growth and function. Examples of techniques that are used in these studies include small animal surgery and colitis and cancer models (mice and rats), molecular biological techniques including PCR, Northern blotting, vector construction for the production of transgenic and knockout mouse models, in situ hybridization and immunohistochemistry.

Jason C. Mills, MD, PhD

Clinical Sciences Research Building, North Tower, Room 1030
Phone: 314-362-4213

We investigate the differentiation of epithelial stem cells in the upper gastrointestinal tract. We study how genes regulate differentiation in mouse models and in vitro in tissue culture, and we correlate our findings with human tissue specimens. Specific projects include the following: (1) understanding how inflammation leads to aberrant differentiation (metaplasia), which is a precursor for cancer; (2) elucidating how master regulatory transcription factors like *Xbp1* and *Mist1* coordinate the massive cytoskeletal and organellar expansion of specialized secretory cells as they differentiate from stem cells; and (3) understanding the mechanisms that regulate how differentiated cells can be reprogrammed into stem cells in gastrointestinal organs like the stomach and the pancreas.

Richard E. Ostlund, MD

8804 Wohl Hospital
Phone: 314-362-8286

Our laboratory focuses on the prevention and treatment of coronary heart disease by studying cholesterol absorption, detoxification and elimination from the body. Direct patient studies that use new stable isotopic cholesterol tracers and mass spectrometry techniques complement in vitro work on the biochemistry of cholesterol transport in cultured cells.

Russell Pachynski, MD

BJC Institute of Health, 7th Floor
Phone: 314-286-2341

Our lab focuses on several aspects of tumor immunology and translational immunotherapy. We utilize mouse tumor models, human tissues and samples, and advanced molecular and immunologic techniques to study leukocyte trafficking in the setting of tumor development and progression. We also have projects focusing on developing novel immunotherapeutics aimed at augmenting the recruitment of beneficial leukocyte subsets into the tumor microenvironment in order to suppress tumor growth. We are utilizing several approaches, such as nanoparticles, fusion proteins and viruses.

Katherine Ponder, MD

8818 Cancer Science Research Building
Phone: 314-362-5188
kponder@wustl.edu

The focus of this lab is on gene therapy for lysosomal storage diseases such as mucopolysaccharidosis (MPS). We have developed a retroviral vector that can be efficiently delivered to the liver of mice and dogs and that results in expression sufficient to reduce many of the clinical manifestations of these genetic diseases. Current studies focus on assessing the therapeutic effect of gene therapy on sites that are affected in MPS (e.g., heart, aorta, bones, joints) and on developing vectors that might be translated into human patients. In addition, we are evaluating the pathogenesis of disease in MPS, which appears to involve the upregulation of destructive proteases in the aorta and possibly other sites. A better understanding of the pathogenesis of disease might result in additional therapies for MPS.

Clay F. Semenkovich, MD

Southwest Tower, 8th Floor
Phone: 314-362-4454

Fatty acid metabolism and its role in atherosclerosis, diabetes, hypertension and obesity; modulation of respiratory uncoupling for the treatment of aging, obesity and vascular disease.

Phyllis K. Stein, PhD

Northwest Tower, Room 13116
Phone: 314-286-1350
pstein@wustl.edu

This lab's main focus is on the clinical significance of heart rate variability and ECG-derived waveform parameters obtained from continuous ambulatory monitoring. This elective affords the student the opportunity to perform research in heart rate variability or in other measurements, like QT variability or T-wave alternans that can be derived from continuous ECG monitoring from Holter recordings or polysomnography recordings in the sleep lab. One area of active research is the identification of heart rate patterns associated with obstructive and central sleep apneas and hypopneas and the relationship of previously unappreciated cycling heart rate patterns and outcomes. Data are also available from mice. Many possible projects are available using our many large existing datasets, using the thousands of stored studies in the sleep lab, or using de novo data collection in a clinical or animal population and in infants. Also, many possible directions for this research are available, from applying traditional and nonlinear HRV to different populations to developing methods to quantify ultradian heart rate variability patterns to developing novel ECG analysis techniques, among others. Also, we are involved with the Cardiovascular Health Study (CHS), a large population-based longitudinal study of risk factors for heart disease and stroke among community-dwelling people more than 65 years old. There is a subset of this population who had Holter recordings (~1400 at baseline, ~800 of the same people five years later, and ~370 minority subjects recorded at the same time as the second CHS recording). These recordings have already been analyzed by us, so there is a large amount of heart rate variability and heart rate pattern data available. There are also subsets of patients from the CHS and from another study (EPHESUS) who are known to have died suddenly, and we have developed a matched control group in order to examine ECG-based differences in those who died suddenly. We also have

electronic sleep studies at two time points for about 300 of the CHS Holter participants who also participated in the Sleep Heart Health Study. We have analyzed an additional ~1500 sleep studies from CHS participants who did not have Holter recordings. Thus, there is also an opportunity in the CHS dataset for studies of the relationship of heart rate variability with changes in heart rate variability over time and with a huge number of clinical and demographic factors among the elderly. We also have data on the relationship of Holter-based HRV and sleep apnea patterns to the development of atrial fibrillation after cardiac surgery as well as data from a study of the treatment of depression in treatment-resistant depressed post-MI patients, a study of sickle cell patients, and a study of heart rate variability and echo parameters in elderly African Americans. Currently, we are also analyzing HRV in premature infants as they mature and HRV as a predictor of response to treatment in babies in the NICU and PICU, using stored 24-hour bedside ECGs.

Heart rate variability and clinical outcomes: The student will be learning about HRV methods and will investigate the relationship of HRV and outcomes in one of our datasets. Because we have clinical and demographic data for about 20,000 subjects for whom continuous ECGs from Holter recordings, sleep studies, and ICU studies are available, as well as some mouse data, the student will be able to choose a project that may lead to a publishable result in an area of interest. The HRV Lab has enough computers and software to accommodate the needs of any interested students.

John Turk, MD, PhD

Southwest Tower, 8th Floor
Phone: 314-362-8190

Phospholipid signaling mechanisms in pancreatic islets is the main focus of this lab. Experience with the mass spectrometric analysis of complex lipids is available.

H.J. Wedner, MD

5002 Steinberg Pavilion, Barnes-Jewish Hospital, North Campus
Phone: 314-454-7937 or 314-454-7377

Asthma care in the inner city: Students will participate in ongoing studies of the delivery of asthma care to inner-city children and adults. The emphasis will be on direct contact between the asthmatic patients and the student, along with an asthma counselor.

Biology of pollen and fungal allergens: Our laboratory has been characterizing the important allergenic proteins from molds and pollen. The allergens are identified using skin-test-sensitive individuals, and the proteins are isolated and characterized by a combination of physicochemical and molecular biological techniques. These studies should lead to better forms of allergy immunotherapy. Students will participate in the isolation, characterization and modification of major allergens from a number of molds, including *Stachybotrys atra* and *Epicoccum nigrum*, and from several pollens, including those from white oak and *Parthenium hysterophoros*, a newly recognized allergen.

Primary Care Summer Preceptorships

Since 1996, the School of Medicine has sponsored a primary care preceptorship program for medical students during the summer between their first and second years of classes. Students select a preceptor in internal medicine, pediatrics or family practice and spend up to eight weeks observing that physician's clinical practice. A stipend is provided to the student. Although many of the preceptors are in St. Louis, others — particularly alumni — are located in cities throughout the country.