

## IBS Lab Rotation List

Fall 2009 [September 21<sup>st</sup> – December 11<sup>th</sup>]

Spring 2010 [January 4<sup>th</sup> – March 12<sup>th</sup>]

Summer 2010 [March 22<sup>nd</sup> – June 4<sup>th</sup>]

### **Dr. Brindley:**

**Availability:**  Spring 10  Summer 10

Molecular genetics studies on neglected tropical diseases, in particular schistosomiasis and food-borne liver fluke infections.

Specific projects involve vector-based RNA interference of parasite genes of the human blood fluke *Schistosoma mansoni*.

The research involves biohazards – schistosomes and retroviruses - and rodent models of human schistosomiasis.

Contact:

Department of Microbiology, Immunology & Tropical Medicine

Ross Hall, Room 448,

(202) 994-7499

[mtmpjb@gwumc.edu](mailto:mtmpjb@gwumc.edu)

### **Dr. Bukrinsky:**

**Availability:**  Fall 09  Spring 10

HIV infection has been shown to inhibit reverse cholesterol transport and modulate ABCA1 activity and HDL formation. We are investigating mechanisms of these activities.

Contact:

Ross Hall 734

(202) 994-2036

[mtmmib@gwumc.edu](mailto:mtmmib@gwumc.edu)

### **Dr. Caldovic:**

**Availability:**  Summer 10

I am interested in mechanisms that the body uses to sense its environment and regulate its metabolism. I am studying regulation of the urea cycle, a metabolic pathway responsible for disposal of neurotoxic ammonia from the body and trying to understand how the body senses changes in the ammonia load and adjusts levels of urea cycle enzymes and urea production. Several approaches are being used to address this problem: examination of proteins that interact with the urea cycle enzymes and have potential to regulate their levels or activity, transcriptional and proteomic profiling to examine global changes that accompany changes in ammonia load, and study of the function of the cycle throughout evolution.

Contact:

Center for Genetic Medicine Research

Children's National Medical Center  
(202) 476-5819  
[ljubica@cnmcresearch.org](mailto:ljubica@cnmcresearch.org)

**Dr. Constant:**                      **Availability:**    **Fall 09**     **Spring 10**     **Summer 10**

My laboratory currently has two major focuses:

1. How leukocyte recruitment is regulated during inflammatory diseases: Using several different mouse models of inflammation, including models of asthma and arthritis, we have found that a class of proteins called extracellular cyclophilins are important regulators of leukocyte recruitment into inflamed tissues. We are currently testing different antibodies and drug compounds known to block the function of cyclophilins to test whether these can be used to reduce ongoing tissue inflammation.
2. The contribution of chronic inflammation on the development of lung cancer: This project is done in collaboration with Drs. Steven Patierno and Susan Ceryak. My lab recently established a new mouse model of hexavalent chromium particle inhalation that induces chronic lung inflammation and ultimately lung cancer. We are currently testing the impact of altering the type of chronic inflammation induced during chromium exposure on oncogenic events associated with lung tumor development.

Rotation projects will primarily involve the use of immunology-based techniques. Handling of live animals will be required (training will be given if no prior experience).

Contact:  
Ross Hall 738  
(202) 994-1138  
[mtmslc@gwumc.edu](mailto:mtmslc@gwumc.edu)

**Dr. Corbin:**                      **Availability:**    **Spring 10**     **Summer 10**

Using the mouse as model, our lab studies development and dysfunction of the mammalian amygdala, a central structure of the brain's limbic system whose dysfunction is associated with autism spectrum disorders.

Details can also be found at: <http://www.childrensnational.org/research/faculty/bios/cnr/corbin.aspx>

Contact:  
6<sup>th</sup> Floor, Children's National Medical Center  
(202) 476-6281  
[JCorbin@cnmcresearch.org](mailto:JCorbin@cnmcresearch.org)

**Dr. Freishtat:**                      **Availability:**    **Fall 09**     **Spring 10**     **Summer 10**

Pharmacologic analogues of cortisol (e.g. prednisone, dexamethasone) have been the standard of anti-inflammation in asthma for decades. Ironically, the circadian peak (i.e. pre-waking hours) in endogenous cortisol corresponds to an asthmatic clinical trough: minimum lung function and maximum inflammation. We have evolved a novel model for the pharmacologic efficacy of GCs. Specifically, we used flow cytometry to determine the cell cycle characteristics of BrdU-labeled (i.e. regenerating) primary

respiratory epithelium. We show that scrape-wounded normal epithelia progress through the cell cycle synchronously and regenerate efficiently. However, scrape-wounded asthmatic epithelium regeneration is poorly synchronized and inefficient, but can be rescued by pulse treatment with dexamethasone. These data have led us to hypothesize that asthmatic respiratory epithelium lacks intrinsic circadian patterns of mitotic regeneration. The resulting asynchronous cell cycling and inappropriate fibrogenic and inflammatory intercellular crosstalk can be rescued with chronotherapeutic glucocorticoid dosing.

Contact:

Children's National Medical Center  
(202) 476-2971  
[rfreishtat@cnmcresearch.org](mailto:rfreishtat@cnmcresearch.org)

**Dr. Hathout:**

**Availability:**  **Spring 10**  **Summer 10**

The overall focus of our laboratory is proteomics and mass spectrometry applications to study and understand the molecular mechanisms of age related macular degeneration and other humane pathologies such as neurodegenerative diseases and brain tumors.

**Primary project:**

1/ Understanding the molecular mechanism of age related macular degeneration (e.g. drusen formation and angiogenesis). The methods currently used in this project are:

- a) Primary culture of human retinal pigment epithelial cells isolated from autopsy eyes.
- b) Metabolic labeling by stable isotope amino acids for quantitative proteomics especially secreted proteins
- c) Protein-protein interaction studies
- d) Bioinformatics

**Secondary projects:**

2/ Detection of disease associated biomarkers:

Test and develop new comparative proteomics methods to detect and characterize disease associated biomarkers in peripheral and central nervous system

- a) Detection of biomarkers associated with malignant peripheral nerve sheath tumors affecting patients with neurofibromatosis type-1.
- b) Study of cell signaling in malignant schwannoma cells versus benign schwannoma cells using phosphoproteome profiling method.

*N.B. Specific student projects will be developed on an ad hoc basis, according to the student's interests and experience and the status of research projects*

Contact:

Children's National Medical Center  
(202) 476-3136  
[yhathout@cnmcresearch.org](mailto:yhathout@cnmcresearch.org)

**Dr. Hawdon:**                      **Availability:**    **Fall 09**     **Spring 10**     **Summer 10**

My lab is investigating the molecular biology of the hookworm infective process. Developmentally arrested stages encounter a host-specific signal during invasion of their host that initiates development in the host. We have identified components of this process, and have determined that insulin-like signaling (ILS) is involved. Currently we are focusing on the regulation of the forkhead transcription factor DAF-16 that negatively regulates development in the model nematode *C. elegans*. We are also interested in the role of other transcription factors, including the nuclear hormone receptor DAF-12 and heat shock factor 1 (HSF-1) that controls the heat shock response and development in *C. elegans*.

Contact:  
Ross Hall 705  
(202) 994-2652  
[mtmjmh@gwumc.edu](mailto:mtmjmh@gwumc.edu)

**Dr. Hoffman:**                      **Availability:**    **Fall 09**     **Spring 10**     **Summer 10**

The lab is interested in muscle, both in terms of muscular dystrophy, and muscle as an organ system in sports medicine, metabolic syndrome, obesity and type 2 diabetes. In muscular dystrophy, ongoing projects available for rotations include identification of primary gene defects in patients with undefined types of muscular dystrophy, understanding the downstream molecular pathophysiology of different types of muscular dystrophies using microarrays and proteomics approaches, and understanding genetic modifiers (SNPs) influencing of disease progression and drug responsiveness. We conduct extensive human clinical studies of normal volunteers, studying genetic predispositions to fitness, metabolic syndrome, strength and response to training. Health disparities in Washington DC African-Americans are also a major interest of the lab.

Contact:  
Children's National Medical Center  
(202) 476-6011  
[ehoffman@cnmcresearch.org](mailto:ehoffman@cnmcresearch.org)

**Dr. Hu:**                                      **Availability:**    **Fall 09?**     **Spring 10**     **Summer 10**

We are studying the biological/genetic bases of autism spectrum disorders using a combination of genomics, epigenetics, and bioinformatic tools. Goals are to better understand the pathobiology underlying ASD as well as to identify genes that may serve as biomarkers and therapeutic targets of ASD. [See website for related references]

Contact:  
Ross Hall 526  
(202) 994-8431  
[bcmvwh@gwumc.edu](mailto:bcmvwh@gwumc.edu)

**Dr. Khan:**            **Availability:**    **Fall 09**     **Spring 10**

To study the generation and maintenance of CD8+ T cell memory against *Toxoplasma gondii*, which is an intracellular parasite causing morbidity or mortality in immuno-compromised individuals. My laboratory has demonstrated that *T.gondii* infection induces a strong CD8+ T cell response in the infected host. However, this response starts to exhaust with the passage of time. We are interested to determine the factors which lead to the down-regulation of CD8+ T cell immunity. The possible mechanism could be due to lack of CD4+ T cell help which has been shown to be essential for the maintenance of CD8+ T cell memory. Also non-availability of cytokines like IL-15, IL-7 or IL-21 could be the reason for poor immunological memory in the host. The project will move along these lines.

Contact:  
Ross Hall 745C  
Department of Microbiology, Immunology, and Tropical Medicine  
(202) 994-2863

**Dr. Mendelowitz:**            **Availability:**    **Fall 09**     **Spring 10**     **Summer 10**

Neurobiology of cardiorespiratory networks in the brainstem. Techniques include patch clamp electrophysiology using *in vitro* slices.

Contact:  
Ross Hall 656  
(202) 994-3466  
[dmendel@gwu.edu](mailto:dmendel@gwu.edu)

**Dr. Morizono:**            **Availability:**    **Fall 09**     **Spring 10**     **Summer 10**

The focus in our group is the treatment of urea cycle disorders, with emphasis on gaining a better understanding of the metabolic pathways that feed in and out of the pathway. As part of this work, we also are interested in learning how the urea cycle evolved from the bacterial arginine biosynthetic pathway. We have been measuring the effectiveness and rapidity of AAV mediated gene therapy in treating ornithine transcarbamylase deficiency, the most common inherited urea cycle disorder. A combination of biochemical, mass spectrometric, biophysical and computational methods are used to tackle these problems.

Contact:  
Research Center for Genetic Medicine  
Children's National Medical Center  
(202) 476-4862  
[hmorizono@cnmcresearch.org](mailto:hmorizono@cnmcresearch.org)

**Dr. Nagaraju:**            **Availability:**    **Fall 09**     **Spring 10**     **Summer 10**

Our laboratory research interests include:

- 1) To define mechanisms of initiation and perpetuation of autoimmune and inflammatory responses in systemic autoimmune rheumatic diseases.
- 2) To investigate immune and non-immune mechanisms of tissue damage in autoimmune and genetic muscle diseases.
- 3) To define sex-based differences in immune response genes and their effect on disease phenotypes.
- 4) To investigate experimental therapeutics and pre-clinical drug trials in various mouse models of human disease.

Contact:  
Research Center for Genetic Medicine  
Children's National Medical Center  
(202) 884-6220  
[knagaraju@cnmcresearch.org](mailto:knagaraju@cnmcresearch.org)

**Dr. Partridge:**                      **Availability:**     **Fall 09**     **Spring 10**     **Summer 10**

My laboratory is interested in gaining an understanding of the mechanisms that maintain skeletal muscle in healthy individuals and the factors that account for failure of this maintenance in inherited myopathic diseases such as the muscular dystrophies as well as in acquired muscle conditions such as the atrophies associated with old age, with cancer and with bed-rest. These investigations involve analysis of cell behaviour in a variety of tissue culture systems in parallel with in vivo studies in mice, run partly in collaboration with Dr Nagaraju. We aim to study both the mechanisms that operate in these various disease conditions and the effects of know agents that promote or inhibit the growth of skeletal muscle.

Contact:  
Research Center for Genetic Medicine  
Children's National Medical Center  
(202) 476-2192  
[tpartridge@cnmcresearch.org](mailto:tpartridge@cnmcresearch.org)

**Dr. Sorenson:**                      **Availability:**     **Fall 09**     **Spring 10**     **Summer 10**

I am interested in the functional role of nicotinic receptors within neuronal circuitry. Nicotinic receptors modulate neuronal activity indirectly, by modulating neurotransmitter release, or indirectly, by mediating fast synaptic transmission. Our laboratory has established two chick brain slice preparations that make it possible to study both types of nicotinic receptor function. The first model is the ventral lateral geniculate, a nucleus that receives direct retinal ganglion cell afferents. Nicotinic agonists have been found to modulate the strength of the retinal signal to the lateral geniculate by modulating release of glutamate from the retinal axons. The second model system centers on the lateral spiriform nucleus, a component of the avian basal ganglion system. The lateral spiriform neurons receive direct cholinergic innervation on their dendrites and express several different nicotinic receptor subunits.

Rotation projects can be designed to fit the individual needs of the student and include immunohistochemical, anatomical, imaging, and patch clamp recording techniques.

In addition to my studies in the chick, I am working with Dr. Perry to understand the effects of exogenous nicotine on development and neuronal activity. In these studies the morphology of nu. accumbens medium spiny neurons is compared between nicotine and saline treated animals. Specifically, the number and morphology of spines will be compared, as well as the number of dopaminergic synapses on the spines. This study hopes to address the question of whether increased

nicotinic receptor expression after nicotine treatment increases the number of nicotinic receptors on dopaminergic terminals or whether the number of terminals themselves is increased.

Contact:  
Ross Hall 636  
(202) 994-2926  
[phmems@gwumc.edu](mailto:phmems@gwumc.edu)

**Dr Perry:**                      **Availability:**    **Spring 10**    **Summer 10**

Studies in my lab center on the neurobiology of nicotine and nicotine addiction. Chronic nicotine exposure causes a variety of important neurobiological changes, including receptor regulation and desensitization, changes in gene expression and behavior, dependence, and altered neural development. Furthermore, the effects of nicotine vary according to age: exposure during adolescence and *in utero* are associated with unique patterns of responses. The sheer numbers of people who are chronically exposed to nicotine, either as smokers or users of NRT products, or indirectly by second-hand smoke or in utero, makes this a major public health problem.

We will be studying the effects of chronic nicotine using multiple experimental approaches, including receptor binding (including autoradiography), receptor function (including <sup>86</sup>Rb efflux and neurotransmitter release), gene expression (including microarray analysis and rtPCR), behavior (including locomotor activity and conditioned place preference), and morphology (including dendritic length and spine density). Our animal models will be focused on unique effects of nicotine exposure *in utero* and in adolescents. I collaborate with Drs. Norm Lee and Eva Sorenson on these studies, so some rotation projects may be based in one or the other of those labs as well as in my lab.

If you are interested in this research, please come and talk so we can explore more specifically what projects might be a good fit for a rotation project.

Contact:  
Ross Hall 618  
(202) 994-3544  
[phmdcp@gwumc.edu](mailto:phmdcp@gwumc.edu)

**Dr. Rose:**                      **Availability:**    **Fall 09**    **Spring 10**    **Summer 10**

The respiratory tract is protected from invasion by pathogens by secretions composed of an intricately regulated mixture of components. Research in our lab group focuses on chronic respiratory tract diseases that result from malfunctions in this system: cystic fibrosis, asthma, chronic rhinosinusitis, and otitis media. We utilize cell and molecular biological, biochemical, and genetic approaches to investigate the roles of mucin glycoproteins (mucins), especially *MUC5AC* and *MUC5B*, in the respiratory tract and mucosal innate immune system. Major projects currently focus on the role of chromatin remodeling in glucocorticoid-induced repression of the *MUC5AC* mucin gene and upregulation of *MUC5AC* gene by inflammatory mediators, post-transcriptional regulation of *MUC5AC* gene expression by IL8, and biochemical characterization of mucins.

Research projects with a sub-project that could be carried out by IBS student(s) during a 2.5-month rotation under the direct mentorship of a Visiting Scientist, Post Doc, or Research Associate are briefly described below.

- Dexamethasone repression of the *MUC5AC* gene in lung epithelial cells.

Project: Characterize role of candidate nuclear co-repressors identified by pull-down and proteomics in Dex-induced chromatin remodeling at the *MUC5AC* promoter.

- IL1 $\beta$  regulation of the *MUC5AC* gene at the transcriptional level.

Project: Identify transfection factors that bind to specific *cis*-sequences in the mucin-regulatory domain of the *MUC5AC* promoter using a 'pull-down' assay and proteomics.

- IL8 upregulates expression of the *MUC5AC* gene at the post-transcriptional level.

Project: Identify RNA Binding proteins that bind to specific *cis*-sequences in the 3'UTR of *MUC5AC* using affinity chromatography and proteomics. Evaluate role of miRNAs in post-transcriptional regulation.

• MUC7 mucin as an immunomodulator in the innate defense system. The MUC7 protein with 5 rather than 6 tandem repeats is expressed at a lower frequency in asthmatic patients and is thought to be protective for asthma.

Projects: Express recombinant MUC7 proteins that express 5 tandem repeats by mutagenesis of the 6 tandem repeat clone. Transfect the *MUC7* promoter into primary human bronchial epithelial cells and determine response to inflammatory mediators.

- Biochemical analyses and characterization of mucins.

Projects: Establish a method for solubilizing mucoid secretions in the middle ear that could be used *in vitro* or as a treatment (1<sup>st</sup> or 2<sup>nd</sup> semester). Ascertain whether a gastric mucin is a marker for lung exacerbations induced by gastric reflux aspiration (2<sup>nd</sup> or 3<sup>rd</sup> semester).

• Candidate master genes that mediate the IL13-induced goblet cell metaplasia in murine models of asthma have been identified by expression arrays and validated by RT-PCR.

Project: Clone candidate genes into luciferase reporter plasmids and perform functional studies (2<sup>nd</sup> or 3<sup>rd</sup> semester, 2010).

Contact:

Room 5726, 5R, Children's Research Institute, Children's National Medical Center  
(202) 476-4076

[mrose@cnmc.org](mailto:mrose@cnmc.org)

**Dr. Vukmanovic:**      **Availability:** ☒ **Fall 09**

Red blood cell (RBC) transfusion is a key component of comprehensive management in sickle cell disease (SCD). Transfusion treats anemia, improves oxygen carrying capacity, and alleviates the secondary pathophysiological consequences of SCD patients. Development of anti-RBC antibodies (alloimmunization) is a complication of RBC transfusion that leads to more complicated management of transfusion, and to development of potentially lethal delayed hemolytic transfusion reaction. Genetic component was proposed to determine which transfused subjects would develop anti-RBC antibodies. The goal of our study is to determine whether alloimmunization is associated with single nucleotide polymorphisms (SNPs) in genes located in the vicinity of Hemoglobin beta gene cluster. Our initial results have identified several candidate SNPs that could potentially serve as biomarkers of alloimmunization (and as such can be used to tailor transfusion therapy in SCD) and could reveal a molecular basis of alloimmunization.

Contact:

Children's National Medical Center  
(202) 476-3078

[svukmano@cnmc.org](mailto:svukmano@cnmc.org)