

RESEARCH & EDUCATION

A publication of the Department of Microbiology & Immunology, Drexel University College of Medicine

Recent Faculty Highlights FY05/06



Dr. James Burns

Dr. James Burns, Jr. (Associate Professor) has continued his studies of blood-stage malaria and the immune-mediated mechanisms that contribute to protection against these protozoan parasites. During the past year, the work specifically focused on two lines of investigation. The first was the initiation of a project to identify mechanisms by which parasites with a tropism for reticulocytes, young red blood cells, can avoid neutralizing antibodies. The second project involved the design, production and testing of a chimeric malaria vaccine candidate to improve vaccine immunogenicity and protective efficacy over vaccines currently being tested. Publications and supporting data for both projects came from the thesis work of Qifang Shi in the Microbiology and Immunology Graduate Program, who received her Ph.D. degree in May, 2006. Dr. Burns also continues to collaborate with Dr. William Weidanz, University of Wisconsin, on cell-mediated mechanisms of immunity against malaria. In addition to serving as an ad hoc reviewer for NIH-NIAID, Dr. Burns was appointed Chair of the Malaria Vaccine Review Panel for the Military Infectious Diseases Research Program. Dr. Burns has continued to be actively involved in graduate and medical education programs and serves as the Assistant Director of the Microbiology and Immunology Graduate Program. In recognition of these efforts, he received the 2005 Graduate Student Association Teaching Award and was nominated for a Golden Apple Award by both the PIL and the IFM Medical School Classes of 2008. Throughout the year, Dr. Burns served on a number of committees in support of the research and educational activities of the Department, the College, and the University.

Dr. Sonia Navas-Martin (Assistant Professor) has completed her first year at the Drexel University College of Medicine. Dr. Navas-Martin continues to establish her research, education and service responsibilities in the Department. In addition to her ongoing research on coronavirus, pathogenesis, and evolution, she is also developing studies on hepatitis C virus tropism. Dr. Navas-Martin has been awarded a 2006 Professional Enrichment and Growth (PEG) Grant provided

Brian Wigdahl, Ph.D. • Professor and Chair

by the Drexel College of Medicine for the study entitled "Hepatitis C virus neurotropism." Dr. Navas-Martin is a Lecturer in Molecular Pathogenesis I and the second year course in Molecular Virology, within the multidisciplinary Microbiology and Immunology Graduate Program, actively contributing to the teaching and training of first and second year graduate students, both in the classroom and in laboratory rotations. Dr. Navas-Martin is also serving as Scientific Coordinator of the Institute for Molecular Medicine and Infectious Disease Seminar Series.



Dr. Sonia Navas-Martin

Dr. Thomas Edlind (Professor) has published three papers first-authored by members of his laboratory in the well regarded journals, *Molecular Microbiology*, *Current Genetics*, and *Antimicrobial Agents and Chemotherapy*. He and his laboratory members served as collaborators on an additional publication in *Journal of Antimicrobial Chemotherapy*. The Edlind laboratory presented 3 posters at the ICAAC meeting, and 3 posters at the ASM Conference on *Candida* and *Candidiasis*. Dr. Edlind was an invited presenter at two prestigious meetings: *Trends in Medical Mycology* and the *Gordon Research Conference on Cellular and Molecular Fungal Biology*. He and Dr. Fred Krebs collaborated on a provisional patent application relating to combination therapy of vulvovaginitis. Three new and two revised NIH grant applications were submitted; one is awaiting review and the others were outside the funding range.



Dr. Thomas Edlind

He has continued his contribution to Medical Microbiology in both the traditional and PIL tracks (9 lecture hours). For first year graduate students, he continued his contributions to *Molecular Biology* (4 hours) and *Microbial Pathogenesis* (7 hours). His mentorship duties were rewarding but time-consuming, including 2 graduate students (JP Vermitsky who recently defended and new student Shriya Raj), a Drexel coop student (Kathryn Crump, Recipient of Best Poster Award at

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**Drexel University
College of Medicine**

In the tradition of Woman's Medical College of Pennsylvania and Hahnemann Medical College

In This Issue...

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Judy Rieger

BS - Biotechnology
East Stroudsburg University
Advisor: Dr. Richard Rest

Bacillus anthracis is a gram positive bacterial pathogen that can cause three different forms of infection in humans; inhalation, cutaneous and gastrointestinal. The major virulence factors of this bacteria are the presence of a Poly-D-glutamyl capsule and a 3 component anthrax toxin. Dr. Rest and

collaborators have recently discovered a previously unidentified cholesterol-dependent-cytolysin named ALO. We are now focused on the characterization of this molecule, its regulation and also how it interacts with cells of the human immune system.



Hangjun Ke

MS - Immunology
Tongji Medical College of
Huazhong University of
Science and Technology
Advisor: Dr. Akhil Vaidya

Malaria remains a severe infectious disease in many tropical and sub-tropical regions. It kills one to three million people annually, of whom children under the age of five in Sub-Saharan Africa are the major

victims. Among all malaria parasites, *Plasmodium falciparum* is the most dangerous, as it has the highest rates of complications and mortality. The parasite mitochondrion is an organelle that holds promise as anti-malarial drug target. The discovery in the late 1980s of *Plasmodium*'s mitochondrial DNA revealed an unusually small 6 kb DNA molecule. In mammalian and yeast cells, mitochondrial ATP synthesis is carried out by a multisubunit rotary enzyme, F₀F₁ ATP synthase, located within the inner membrane, utilizing the proton motive force produced by the electron transport chain. The recently completed genome sequence of *P. falciparum* has revealed the presence of genes encoding all the basic components of the F₁ sector and subunit c of the F₀ sector; still, little is known about the localization and function of these subunits. Without subunits a and b of the F₀ sector, the classical function of ATP synthesis is in question. I have initiated a project to determine the intracellular localization of these subunits, find out if they do form a complex similar to F₀F₁ ATP synthase in other eukaryotes, and further analyze their function in vivo. Initially, I am studying the β subunit of the F₁ sector, I have amplified the F₁ β gene by PCR from the genome of *P. falciparum* and cloned it into the malaria expression plasmids pHHGFP and pHHMYC for expression with C-terminal GFP and myc tags, respectively, allowing localization studies after stable transfection into cultured parasites. Additional studies may include investigations to determine which other proteins are complexed to or interact with the β subunit and attempts to knockout the β subunit gene to ascertain its essentiality in vivo, which may vary with different stages of the parasite's life cycle.

Praveen Balabaskaran Nina

MVS - Avian Diseases, Indian
Veterinary Research Institute
Advisor: Dr. Akhil Vaidya

Investigators working in Dr Vaidya's laboratory focus on understanding the basic molecular function of malaria parasites in order to develop new antimalarial drugs. The project I am working on seeks to investigate the involvement of metabolic enzymes in the energy metabolism of the malaria parasite *Plasmodium falciparum*, using recently developed genetic knock-out methods. Initially, I am focussed on succinate dehydrogenase, an important component of both the TCA cycle and the mitochondrial electron transport chain. These pathways contribute to oxidative phosphorylation, which is the major source of energy in most eukaryotic organisms. However, evidence to date indicates that oxidative phosphorylation is not important in malaria parasites, at least in the erythrocytic stages. Furthermore, we have shown that, in the erythrocytic stages, electron transport is required primarily to recycle the pyrimidine biosynthesis enzyme dihydroorotate dehydrogenase, and not for the overall energy metabolism.



**2nd Year Graduate Trainees
Choose Advisors and Research
Projects in the Department of
Microbiology & Immunology**

Viraj Sanghvi

BS - Rochester Institute of
Technology
Advisor: Dr. Laura Steel

My research in the laboratory of Dr. Steel focuses on the role of RNAi pathway in HIV pathogenesis. RNA interference (RNAi) is a mechanism of sequence-specific gene regulation that is conserved across a broad range of eukaryotic organisms. RNAi plays an important role in normal cell processes including differentiation, proliferation, stress, and apoptosis. It is mediated by genomically encoded RNAs called microRNAs (miRNAs). In plants, the RNAi pathway is a significant component of the cellular anti-viral defense system, and it is increasingly evident that it can have a similar function in mammalian cells. We are exploring the interplay between HIV-1 and the endogenous RNAi pathway in infected cells. Second, we are examining the potential of different HIV-1 strains to counter an RNAi-based cellular defense. The HIV-1 Tat protein has been identified as a suppressor of RNAi. We are also interested in determining whether alterations in the Tat protein sequence can affect its ability to suppress RNAi, and whether this, in turn, can be correlated with the pathology of the parental HIV-1 strain.



Amy Cernetich

MS - Molecular Microbiology
and Immunology

Johns Hopkins University

Advisor: Dr. James Burns

Malaria is a serious public health concern that is caused by a protozoan parasite of the genus *Plasmodium*. Despite many advances there is no vaccine currently available. Investigators working in the laboratory of Dr. Burns are focused on the development of protective immunity against blood-stage malaria and primarily studies merozoite surface proteins (MSPs) such as MSP-8. We have also developed a chimeric antigen (MSP-1/8) and are testing its ability to elicit protective immune responses in a variety of mouse models including lethal *P. yoelii* 17XL and non-lethal *P. yoelii* 17X. We have discovered that immunization with MSP-8 causes *P. yoelii* 17XL, which normally invades both mature and immature red blood cells (i.e., reticulocytes), to preferentially invade reticulocytes. DNA microarray analysis of breakthrough parasites from immunized animals reveals differential expression of several members of the *pyst-a* and *yir* gene families, which are predicted to encode parasite proteins expressed on the RBC surface. Specifically my project will focus on characterization of these proteins and will examine their potential role in parasite adherence to reticulocyte-rich regions such as spleen and bone marrow. In vitro adherence assays using reticulocyte-restricted *P. yoelii* 17X and DNA microarray analysis will be utilized to aid in this characterization.

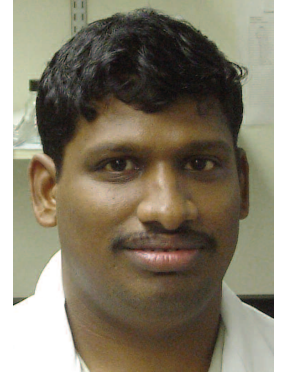


Suresh Maddur Ganesan

MVS - Veterinary Parasitology,
Indian Veterinary Research
Institute

Advisor: Dr. Akhil Vaidya

Malaria is reemerging as perhaps the biggest infectious killer. Three to five hundred million people are infected annually, and approximately 2–3 million people die of malaria every year, which includes one child every 30 sec. With resistance to anti-malarial drugs on the rise, new treatments are badly needed. Parasite mitochondrial functions are potential targets for anti-malarial drugs, either in use or in development. The main focus within the laboratory is the elucidation of the mitochondrial physiology and mechanisms of action and resistance to drugs that target the parasite's mitochondrion. Earlier studies provided insights into the mode of action for atovaquone, which inhibits ubiquinol-cytochrome c oxidoreductase, an enzyme complex of the electron transport chain (ETC) in the parasite's mitochondrial inner membrane, and into the synergistic effect of proguanil with atovaquone. We recently found that in culture *Plasmodium falciparum*, the most lethal human malaria parasite species, can survive 48 hours of exposure to atovaquone and are continuing to investigate how the parasites develop resistance to this drug. Our recent findings suggest that the ETC, which is blocked by atovaquone, is not necessary for energy production in the parasites. The importance of the ETC rather lies in pyrimidine biosynthesis, at least in the erythrocytic stages. Currently, I am involved in a project that includes expression of the pyrimidine biosynthesis enzyme dihydroorotate dehydrogenase in the rodent malaria parasite *P. berghei*. Additionally, I plan to study the dynamics of parasite clearance and death in atovaquone-treated mice.



Saifur Rahman

MS - Biotechnology
Indian Institute of Technology
Advisor: Dr. Brian Wigdahl

Human T cell leukemia virus type 1 (HTLV-1), the first human retrovirus identified, is the causative agent of adult T cell leukemia (ATL) and HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP), causing both immune and nervous system diseases. Thus, HTLV-1

serves as a useful model pathogen to study the immuno- and neuropathogenesis of retroviruses. Approximately 20 million people are infected with HTLV-1 worldwide, predominantly in tropical areas.

One of the major research areas of investigations in the laboratory involve delineating the role of viral factors and host immune response in the progression of HAM/TSP, a debilitating neurodegenerative autoimmune disease with some similarities to multiple sclerosis. A number of in vitro studies have indicated a potential role for the HTLV-1 transcriptional transactivator protein Tax in the demyelination and neuroinflammation caused by HTLV-1. But to date there is no systematic in vivo study confirming the direct role of Tax protein (cell-free and/or cell-associated) in this process because of the absence of a well characterized animal model for HAM/TSP. Therefore, a major thrust of my research will be to establish an animal model for studying Tax-mediated neurodegeneration during HTLV-1 infection. This model will also be utilized to study the host immune response with particular emphasis on characterizing the role of dendritic cells in HTLV-1-induced disease progression.



Meghan Wynosky

BS - Biology
Kutztown University
Advisor: Dr. Richard Rest

Bacillus anthracis (BA) is a Gram positive, rod shaped, aerobic spore-forming bacterium that causes an acute infection found mainly in wild and domesticated animals. Humans may become infected when in close contact with infected animals or through inhalation of spores. BA has three

well studied virulence factors: lethal toxin, edema toxin, and a capsule composed of polyglutamic acid. We are focused on a newly discovered toxin, anthrolysin O (ALO). This toxin is a cholesterol-dependent cytolysin, which has been shown to have cytotoxic properties in human polymorphonuclear cells (PMNs). We are working to further characterize this toxin. One point of focus is determining the effects of ALO on PMNs at sublethal concentrations, determining chemotactic and degranulation effects. In trying to define ALO expression, we have added a plasmid containing ALO to BA and observed a 1000-fold increase in ALO expression. It was observed that there is a gene upstream of ALO that may be a regulator of ALO expression. When this gene was deleted, ALO expression decreased by 100-fold. The gene was named Arp for its function in modulation ALO expression (ALO regulatory peptide). We are continuing to characterize ALO and the mechanism of Arp action in regulating the expression of ALO.

Recent Faculty Highlights FY05/06 (continued from page 1)

the 2005 Philadelphia Alliance for Minority Participation Research Symposium), 3 undergraduate, and 4 high school research interns. Locally, Dr. Edlind continued to serve on the University Biosafety Committee and Appointments and Promotions Committee, and began service on the Library and Information Technologies Committee. Nationally, he served on two NIH study sections: Microbiology and Infectious Diseases Research Committee and an ad hoc panel ZRG1 AARR-A(04). He continued his service on the Editorial Board of Antimicrobial Agents and Chemotherapy, but most recently was promoted to Editor of this journal, and reviewed manuscripts for several additional journals. Finally, he served on the Noxafil Regional Advisory Board organized by Schering Plough to review development of their new antifungal posaconazole.



Dr. Stephen Jennings

Dr. Stephen Jennings (Professor) arrived in the department this past July from the University of Louisiana along with several members of his laboratory. During his first year in the department, Dr. Jennings has re-established his research program in the College of Medicine and has published his first paper at Drexel and submitted or prepared for submission of five more manuscripts that will lay the foundation for the competitive renewal of his ongoing NIH-funded R01 grant next year. Dr. Jennings and members of his laboratory have made considerable progress towards understanding the interaction between innate and acquired immune responses to HSV-1. A second grant has been submitted to the NIH, and a third grant is in preparation for submission early next year. Dr. Jennings is also Co-Investigator on three additional grant proposals: two from Drexel University; and one from Louisiana State University. He has presented lectures to the graduate students of the Department of Microbiology and Immunology of the College of Medicine, and the Department of Biosciences and Biotechnology at Drexel University. Dr. Jennings is now a member of five graduate student committees both in the College of Medicine and Drexel main campus. He has participated in small group/laboratory education of medical students in the areas of microbiology and immunology. Dr. Jennings is a member of the Faculty Steering Committee for the Drexel University College of Medicine.

Dr. Peter Katsikis (Professor) received a 5-year 1.8 million dollar renewal for the NIAID R01 grant entitled "In vitro stimulation of HIV-specific CD8+ T cells". This R01 grant renewal brings Dr. Katsikis' total NIH funding to four NIH R01 grants, a sign of Dr. Katsikis' high productivity and recognition as a national and international leader in research focused in the area of autoimmunity and the cell-mediated immune response to viral infection. Dr. Katsikis serves as the Director of the Center for Immunology and Vaccine Science within the Institute for Molecular Medicine and Infectious Disease. Dr. Katsikis also serves as the Director of the Flow Cytometry Laboratory within the Center for Protein and Cell Science within the Institute for Molecular Medicine and Infectious Disease in the Drexel University College of Medicine. Dr. Katsikis has served on a number of grant review committees as an Ad Hoc



Dr. Peter Katsikis

reviewer. He was Ad Hoc reviewer for the Center for Scientific Review of the National Institutes of Health (NIH) on the AIDS Immunology and Pathogenesis Study Section (AIP) and the Immunity and Host Defense Study Section (IHD). He was also Ad Hoc reviewer for the National Cancer Institute's (NCI), NIH, P01 Immunotherapy Cluster Review, the PENED grant review of the General Secretariat of Research and Technology (GSRT), Ministry of Development, Greece, and an Ad Hoc Member for the Veterans Administration (VA) Merit Awards Grant review. Dr. Katsikis also organized a scientific conference on "Crossroads between Innate and Adaptive Immunity" under the auspices of Aegean Conferences in Rhodes, Greece. The Conference had more than 100 attendees and was widely praised for its success. Dr. Katsikis has published 4 peer-reviewed manuscripts and one book chapter during the last year, and was editor of a book for the Advances in Experimental Medicine and Biology Book Series. He reviewed 17 manuscripts for five journals.



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