Medical Microbiology and Immunology

Mission Statement
Infectious pathogens still remain a major cause of human diseases, whereas defective or excessive immunity causes an array of many other disorders including cancer, autoimmune disease, and allergic disease. The Department of Medical Microbiology and Immunology at the University of Toledo is dedicated to the fight against these common disorders.

Microbiology explores the relationships between microbial pathogens and their human hosts, and immunology studies the nature of host defense system against environmental insults. The Department contributes to the research mission of the University by advancing basic and translational research with the ultimate goal of developing innovative vaccines and therapeutics for infectious diseases, cancer, and inflammatory disorders caused by immune dysregulation. Cutting-edge technologies in biomedical science are provided through the Flow Cytometry Core Lab; Bioinformatics, Genomics/Proteomics Core Lab, and BSL-3 Lab housed in the Department. The Department also contributes to the teaching mission of the University by educating medical and graduate students in basic principles of immunology, bacteriology, virology, and host-pathogen interaction. Moreover, the Department contributes to the service mission of the University by providing advanced expertise in microbiology and immunology and by promoting regional, state, national and international research programs concerning infectious diseases, inflammatory disorders, and graft rejection.

How You Can Help
The Department has successfully competed for peer reviewed grant funding. The Medical Microbiology and Immunology Research Ventures Fund has been created to ensure that we continue our record of achievement. The Fund will support innovative, high-risk research projects, and faculty will use these start-up grants to prove their hypotheses and position themselves to attract NIH and other peer-reviewed funding. This is an investment in the Department's future and in creative new approaches to discovering the causes of and treatments for immunologic disease. To make your contribution please contact Howard Newman, Associate Vice President for Development, Health Science Campus at 419.383.6840.

Additional Contact Information:
419.383.4323
or
http://hsc.utoledo.edu/depts/micro/index.html

Faculty Research Interests
Viviana Ferreira, DVM, Ph.D.
Role of Complement Regulatory Proteins in Disease

Our laboratory has two components. One, funded by the National Science Foundation, focuses on gene exchange between bacteria (a source of virulence factors and antibiotic resistance genes), and the role played by restriction-modification systems in modulating this exchange. The second, funded by the National Institutes of Health, focuses on new strategies for treating bacterial infection while minimizing selection for antibiotic resistance. This work has been published in journals such as the Journal of Bacteriology, Nucleic Acids Research, BMC Microbiology, and Proceedings of the National Academy of Sciences.

Our research program is directed at understanding the immune function of platelets in both protection from infection with bacteria and viruses and platelets as a causative or compounding factor in autoimmune disease. In addition to their essential role in clot formation, platelets express many properties similar to white blood cells. We have found that platelets can recognize antibodies coating bacteria and lead to killing of the bacteria. Interestingly, platelets from patients with the autoimmune disease Systemic Lupus Erythematosus (SLE) have antibodies bound to them which causes the platelets to become hypersensitive and may lead to these patients being at high risk of stroke and myocardial infarction. We study platelets from the blood of healthy volunteers and patients with autoimmune diseases to determine differences in platelet function and characteristic features of platelet responsiveness. We have also developed animal models in which platelet numbers can be modulated in order to study the role of platelets in many disease states. Our studies have revealed various therapeutic targets that may be helpful in treating patients with autoimmune diseases and clotting disorders. These studies have been published in the American Journal of Pathology, J. of Clinical and Visceral Immunology, and Cell and Cellular Immunology.
Pathogenic bacteria have developed complex and dynamic surface structures that promote environmental persistence, infection, immune evasion and disease. However, the host immune system typically recognizes bacterial membrane proteins as ideal immune targets, initiating responses that inactivate or eliminate bacteria from the body. These proteins that are crucial to bacterial survival are also prime targets for antiviral therapies. Understanding the molecular mechanism of host responses, as well as strategies employed by viruses to evade them, is crucial to future work in the lab aimed at developing new and effective flavivirus-specific therapies.

Our research focuses on defining viral and host factors essential for alphasaturs to replicate and cause inflammation of the brain. These enveloped RNA viruses are transmitted by mosquitoes to birds and mammalian hosts, and are related to rubella viruses that spread person-to-person and not by insect bite. The long-range goal is to investigate the mechanisms by which rubella and alphaviruses replicate and control host responses determining infection outcome, i.e., persistence, cell death or curing of the infection. Other studies focus on the replication requirements of coronaviruses (common cold, SARS). Our work has been published in the Journal of Virology, and PLoS Pathogens, and has been funded through the National Institutes of Health.

Our research is focused on inducing of long-term allograft survival (transplantation tolerance) and development of new immunosuppressive therapies using our HTP screening platforms, and c) development and validation of in vitro assays to identify skin sensitizing and skin irritating chemicals. Very recently, we have identified a new leukocyte population that exhibits the surface phenotypes and functional properties of both neutrophils and DCs. This population, termed “neutrophil-DC hybrid,” plays dual protective roles against bacterial infection by processing and presentation of bacterial products, and our results indicate that the bacterial products regulate the production of TNFα levels in vivo. We have found that production of TNFα occurs when leucocytes are exposed to multiple bacterial products, and our results indicate that the bacterial products regulate the production of TNFα in a synergistic manner. The control of infection is likely to be best understood on this level. This represents an important pathogenic phenomenon occurring during bacterial infection. Our experiments provide information that is both unique and potentially important, and will significantly expand and enhance our understanding of how inflammation is induced at sites when multiple bacterial products are present simultaneously.

Tumor necrosis factor alpha (TNFα) is considered one of the key inflammatory mediators during bacterial infection. This powerful protein, secreted mostly by human leukocytes such as monocytes/macrophages, acts as a host defense against bacterial infections. However, when TNFα levels rise too much, it can lead to inflammatory disorders. A wide variety of stimuli have been shown to induce the production of TNFα, but bacteria products are considered major inducers during bacterial infections. To date, most research on the production of TNFα has been focused on understanding how TNFα is induced by a bacterial product. We have found that production of TNFα occurs when leucocytes are exposed to multiple bacterial products, and our results indicate that the bacterial products regulate the production of TNFα in a synergistic manner. The control of infection is likely to be best understood on this level. This represents an important pathogenic phenomenon occurring during bacterial infection. Our experiments provide information that is both unique and potentially important, and will significantly expand and enhance our understanding of how inflammation is induced at sites when multiple bacterial products are present simultaneously.

We research the mechanisms by which bacteria sense and respond to their extracellular environment. *Vibrio cholerae* is the bacterium that causes epidemic cholera, a disease that continues to spread in areas of the world where people lack access to clean drinking water. Due to increasing antibiotic resistance among *V. cholerae* strains, there is a need to develop additional therapeutic agents for cholera treatment. Current projects in the Matson lab include identification and characterization of small molecule inhibitors of a *V. cholerae* stress response pathway that may be developed into cholera therapeutics. Additional studies aim to characterize transcriptional responses of *V. cholerae* to various stresses to determine pathways associated with bacterial fitness and pathogenesis.

Our research is focused on the vector-borne members of Flaviviridae family, including West Nile virus, dengue virus and tick-borne encephalitis virus. Flaviviruses are significant human pathogens and we currently have limited treatment options. By evaluating interactions of virus and cellular proteins, Dr. Taylor has identified strategies that may promote antiviral responses. Understanding the molecular mechanism of host responses, as well as strategies employed by viruses to evade them, is crucial to future work in this lab aimed at developing new and effective flavivirus-specific therapies.

"My research is focused on the pathogenesis of autoimmune inflammatory disease, allergic disorders, and cancer, and in vivo impact of the above cytokines and small compounds on the development of neutrophil-DC hybrids."