

VMSRTP Mentors

Infection and Immunity

Adams, L. Garry (VTPB)

I have long been intrigued with the biological interface between hosts and etiological agents, and the resulting patterns of morphological lesions, especially lesions caused by infectious disease agents. The morphologic, cytokine/chemokine, transcriptomic, proteomic and metabolomic patterns of host and pathogen responses provoke a series of fundamental questions, e.g. what is the molecular pathogenesis of these lesions?; how does the host genome manipulate the pathogen or vice versa?; what host and pathogen cellular pathways are perturbed and dysfunctional in the disease processes?; what is the cause of death?; can we apply genomic pathology (the convergence of 'omics' and morphology) and systems biology to more fully understand infection biology as the basis for improved prediction of host and pathogen mechanistic genes and pathways critical to health and clinical illness? In response to these questions, my research is focused on the: 1) investigation of the comparative molecular pathogenesis of zoonotic intracellular bacterial pathogens in natural target host animal models, particularly salmonellosis, brucellosis and mycobacterial diseases, 2) development of vaccines and host gene expression-based diagnostics for zoonotic and select agent caused diseases, and especially 3) development of in silico host: pathogen interactome predictive models based upon bi-directional in vivo host (bovine/murine) and *Salmonella enterica* Typhimurium interactions at the target organ interface, enteric Peyer's patches.

Andrews-Polymenis, Helene (MPIM/VTPB)

Salmonella is a leading cause of food borne illness in humans and livestock. In humans, these organisms cause an estimated 1.4 million cases of *Salmonella* enteritis annually in the United States. We identify *Salmonella* genes needed during infection of model and natural hosts using genetics and determine their molecular function using a range of methodologies including cell culture, biochemistry, and larger scale systems biology approaches. Our work is funded by the National Institutes of Health, the USDA (NIFA), and other extramural sources.

Arenas, Angela (VTPB)

Considering the negative impacts in public health and agricultural productivity associated with endemic diseases transmitted from animals to humans, our research group is committed to the development of new and improved tools to diagnose, prevent and control infectious diseases. We are also dedicated to improve companion animal health. Training and capacity building in these aspects has been an integral part of our mission. The vast majority of our work has been focused on the control and prevention of brucellosis, a zoonotic bacterial disease that affects millions of people and animals all over the world

Cirillo, Jeffrey (MPIM)

My laboratory research is focused on developing interventions for respiratory diseases including tuberculosis, and pneumonias. Studies can include strategies to understand pathogenesis and develop novel vaccines, diagnostics or therapeutics. Technologies used will include genomics, tissue culture, molecular biology, animal models and bacteriology.

Cohen, Noah (VLCS)

Our research interests include improving equine bacterial disease immunity toward either *R. equi* or *Strep equi*.

deFigueiredo, Paul (MPIM/VTPB)

The de Figueiredo group exploits their expertise in cell biology, microbiology, molecular biology, genetics and genomics to tackle broad life science research questions.

Esteve-Gassent, Maria 'Loles' (VTPB)

My Research Team is interested in understanding how *Borrelia burgdorferi*, the causative agent of Lyme disease can spread from the site of the tick bite to other organs such as joints and heart.

Höök, Magnus (IBT)

The research in our laboratory is focused on determining the molecular pathogenesis of infections and inflammatory diseases. We are interested in two key areas in the pathogenic process; microbial adherence to host tissue and microbial evasion of host defense systems. We seek to identify the molecules involved in these processes, characterize the interactions in submolecular detail using detailed biochemical methods, and articulate molecular hypotheses describing the disease process. These hypotheses are then evaluated in model systems and compared to the clinical findings in human disease. Ultimately, we seek to translate our research findings into new or improved strategies to prevent and treat infectious diseases.

Lawhon, Sara (VTPB)

Dr. Lawhon research focuses on bacterial causes of disease in people and animals with the goal of improving animal and human health. Her laboratory group studies antimicrobial resistance and stewardship and *Salmonella* and *Staphylococcus* pathogenesis. We are particularly interested in how bacteria communicate with each other (quorum sensing) and how they respond to environmental signals found in the host.

McGregor, Alistair (MPIM)

Our lab studies various herpesviruses but the major focus of our research is on the study of cytomegalovirus. Human cytomegalovirus (HCMV or Human herpesvirus 5) is a large DNA virus (>235 kb) that belongs to the Betaherpesvirinae genus of the Herpesviridae family. Primary HCMV infection in immunocompetent individuals is usually benign but establishes a lifelong latent state. Immune suppressed transplant recipients or AIDS patients are particularly susceptible to life-threatening end-organ disease. The other vulnerable population is the developing fetus in utero. During pregnancy, the vertical transmission of the virus across the placenta to the fetus (congenital infection) can lead to serious symptomatic disease in newborns that include mental retardation and deafness. Congenital CMV is the leading cause of mental retardation/deafness in newborns with over 5,000 children each year in the US. HCMV is also considered to be a contributing factor to vascular disease and specific cancers (e.g., glioblastoma).

Mulenga, Albert (VTPB)

For generations ticks and tick borne diseases have had significant impact of animal health and livestock productivity around the world. In public health the effect of ticks and tick borne diseases is also tremendous. Since the 1980s when the causative agent of Lyme disease was described, numerous human tick borne diseases have been reported. In absence of effective vaccines against major tick borne diseases, prevention of animal and human tick borne disease infections relies on the use chemicals (acaricides) to kill ticks. Although acaricide based tick control methods are effective in the short-term, they do not offer a permanent solution because of serious limitations such as ticks developing resistance and contamination of the environment and the food chain. Immunization of animals against is a validated alternative tick control method. The attraction is that tick vaccines will be effective against both acaricide resistant and susceptible tick populations. The major limiting factor is the availability of effective tick vaccine targets. The tick cannot cause damage to host or transmit disease agents without successful feeding. Thus, our plan is to understand molecular mechanisms of how ticks accomplish feeding. In this way we will find targets that will be used for development of effective tick vaccines. We are currently studying the feeding physiology of the blacklegged tick (*Ixodes scapularis*) and the Lone Star tick (*Amblyomma americanum*). According to the US Centers for Disease Control, these two medically important tick species transmit a combined nine of the 14 human tick borne disease agents in the United States. Major work is on discovery and characterization of proteins that the Lone Star and the Blacklegged tick into animals every 24h through out feeding. The area of particular emphasis is to understanding roles of serine protease inhibitors (serpins) the blacklegged tick and the Lone Star tick inject into animals during feeding. We have identified serpins that the two tick species inject into animals during tick feeding.

Samuel, James (MPIM)

Our laboratory works with the obligate intracellular bacterial pathogen, *Coxiella burnetii*, the etiologic agent of Q fever and a category B biothreat agent. Because of their obligate intracellular growth restriction, they have become exquisitely adapted to their specific niche, which is similar to a typical terminal phagolysosome that evolves into a large, replicative vacuole. *C. burnetii* depends on various strategies to down-regulate the normal innate host response to bacterial infection. The organism is extremely sensitive to oxidative stress, lacking several repair genes essential to mitigate oxidative DNA damage, has a reduced requirement for and uptake systems for acquisition of iron, and actively inhibits activation of an oxidative burst by phagocytic cells through the secretion of an acid phosphatase. Isolates that originate from acute Q fever patients are able to induce acute, atypical pneumonia in rodent challenge models while isolates from chronic Q fevers patients (most commonly endocarditis and hepatitis) do not cause acute disease in animal models, confirming distinct pathotype virulence potentials between isolate groups.

Scott, H. Morgan (VTPB)

Our laboratory has several currently funded projects focusing on understanding the microbial ecology and molecular epidemiology of antimicrobial resistant foodborne pathogens and other enteric bacteria, especially in response to antimicrobial use in food animals and management practices developed to mitigate their rise. We employed advanced molecular culture-based and non-culture-based approaches to these problems and have equipment and other technologies that are second to none in the world. The projects we assign to students can be completed within the timeframe of the summer and will involve whole genome sequencing of bacterial isolates of *E. coli* and *Salmonella*, along with metagenomic analysis of the samples from which they arose; typically, from dairy and beef cattle in Texas, including clinical specimens.

Skare, Jonathan (MPIM)

My laboratory studies *Borrelia burgdorferi*, the spirochetal bacterium that causes Lyme disease. *B. burgdorferi* is the most common arthropod-borne infectious agent in the United States, with approximately 300,000 cases diagnosed annually. Given these numbers, it is clear that Lyme disease is a significant public health concern.

The goals of my research are to understand how *B. burgdorferi* causes disease and adapts to different niches it occupies by: (1) addressing the role of attachment, colonization and subsequent dissemination using molecular genetic methodologies to inactivate genes involved in adherence of *B. burgdorferi* to host tissues; and (2) understanding how *B. burgdorferi* responds to the hosts they infect to modulate gene expression accordingly.

Xu, Yi (IBT)

Our lab is interested in the connection between microbes and colorectal cancer. We focus a bacterial pathogen called *Streptococcus gallolyticus* subsp. *gallolyticus* (Sgg), previously known as *S. bovis* biotype I. Sgg is known to have a strong clinical correlation with colorectal cancer, however its role in development of cancer was not known. Work from our lab demonstrated that this pathogen actively promotes tumor growth. Currently we are studying how Sgg promotes tumor growth, what are the bacterial factors involved in this activity and what host factors and processes are targeted by the bacteria. We use a combination of in vitro cell cultures, animal models and patient samples in our studies.

Zhu, Guan (VTPB)

Our laboratory conducts translational research with an ultimate goal to discover new anti-parasitic therapeutics by targeting metabolic enzymes and other molecules critical or essential to the parasite infection, survival and development, such as those involved in the lipid and energy metabolisms and interacting with host cells in *Cryptosporidium* and other protozoan parasites. Other research areas include functional genomics and molecular evolution of apicomplexan parasites, and parasitic diseases important to the conservation of wild animals.