

Graduate Program-INTO

Luiz Bermudez

Mycobacterial pathogenesis and new therapies to mycobacterial infection. *Mycobacterium tuberculosis*, *Mycobacterium avium*, *Mycobacterium abscessus* and *Mycobacterium avium* subsp *paratuberculosis*.

Infection of the human and animal host, survival mechanism in the host, biofilm and its role in disease.

Macrophages, Natural Killer cells and T lymphocyte participation in host defense against mycobacterial infection.

Rob Bildfell

The majority of my research efforts are in the form of pathology-related support services for my colleagues, ranging from projects involving the pathogenesis of neoplasia to virulence mechanisms of *Mycobacterium spp.* I am also currently participating in studies related to diseases of wildlife, such as cervid adenoviral hemorrhagic disease and deerpox viral disease, as well as diseases of public health significance such as cryptosporidiosis.

Linda Blythe

My current research is in collaboration with Dr. Morrie Craig's lab. We are working to determine the threshold of toxicity of perennial ryegrass infected with endophyte in UAE camels. We have 24 camels on 4 different levels of lolitrem B produced by endophytes in perennial ryegrass, consuming this grass straw over 60 days. Camels are videotaped in UAE twice a week as individuals and I observe them for onset and presence of neurological signs. This is a major importance to the AgFibre and the export industry in order to only ship "safe feed" to the Middle East, a newly opening market.

Patrick Chappell

Work in my lab broadly focuses on basic mechanisms underlying endocrine control of reproduction, exploring the role of the molecular circadian clock in the brain's timing of reproduction in female mammals, investigating how circadian disruption may initiate breast and prostate cancers, and how the hormonal control of reproduction evolved from more ancient species such as corals.

E. Morrie Craig

The focus areas of my research are: 1) the detoxification of plant alkaloids, including a long, established history of experience in mycotoxin research, and 2) the bioremediation of organic compounds, including those found on Super Fund sites. Within these two programs, the emphasis has been on defining the metabolic pathway of plant and environmental toxins in the animal and identifying the key microbes and/or genes that contribute to metabolism in the host animal.

Lia Danelishvili

Dr. Lia Danelishvili's research is mainly focused on study the mechanisms of *Mycobacterium tuberculosis* pathogenesis. Dr. Danelishvili's research identifies and characterizes virulence genes and proteins that are required for the early events of macrophage infection, survival and cell-to-cell spread. She studies the molecular mechanisms of the pathogen-host interaction and the associated cellular processes, such as apoptosis, autophagy and necrosis. The multidisciplinary approaches employing bacterial genetics, high throughput screening libraries, gene knockout systems, cell biology, high-

resolution microscopy, bioinformatics and mass-spectrometric sequencing are used in the laboratory.

Brian Dolan

Research in my lab is focused on two main areas. The first is the biology of antigen presentation, the process by which the cells of the body alert the adaptive immune system to the presence of intracellular pathogens, such as viruses, or oncogenic transformation. We are trying to determine which cellular pathways are necessary to successfully present the foreign peptide on major histocompatibility complex class I (MHC I) proteins at the cell surface, which serve to flag down disease specific cytotoxic T cells.

Jean Hall

My research is concerned with how nutrition affects immunity. I am interested in nutrigenomic technology, or the study of how nutraceuticals affect the expression of genes involved in the immune response. My projects involve sheep and cows supplemented with selenium and its effects on the immune response.

Claudia Hase

The genus *Vibrio* consists of a group of Gram-negative bacteria that naturally inhabit aquatic environments worldwide. Among this diverse group of microorganisms are a few human pathogens, namely *Vibrio cholerae* and *Vibrio parahaemolyticus*. In addition, our lab studies some *Vibrio* species that cause disease in aquaculture (*Vibrio tubiashii*) and corals (*Vibrio coralliilyticus*). We are applying various modern molecular techniques to better understand the virulence properties and environmental survival strategies of these pathogens. In addition, we are developing detection assays that can be used in aquaculture facilities to reduce the economic impact of vibriosis.

Jerry Heidel

My research activities are focused on health issues related to aquatic animals. Currently, we are examining the causes of mortality in ornamental fish, from the time of collection in the field, through holding and shipping, to their arrival and holding at import facilities. By identifying and characterizing health problems associated with infection, environmental change, and handling, we are working towards establishing best practice procedures for the husbandry of these fish during this crucial period, and in so doing, reduce shipping related losses in this industry.

Stuart Helfand

Our laboratory investigates targeted small molecule inhibitors of tyrosine kinases, signaling molecules that regulate cancer cell growth and migration. Tyrosine kinase inhibitors (TKIs) are a recent advance in cancer therapeutics that offer promise for treatment of a variety of human and animal cancer. Cancers of interest in our laboratory include canine hemangiosarcoma, osteosarcoma, and feline oral squamous cell carcinomas for which we have identified several TKIs with anti-cancer activity against these tumors. Additional research interests include approaches to harness the immune system to control cancer through the use of immunostimulatory proteins, cancer vaccines, and reduction of immunosuppressive regulatory lymphocytes. Bone marrow transplantation for canine lymphoma is another focus area.

Michael Huber

Research projects included surgical manipulation of endometrial cups in mares to manage infertility associated with pregnancy loss, and the impact of bone fragments on joint health. Focusing on some innovative ideas for limiting reproduction in BLM and Tribal horse and burro populations and development of an instrument to facilitate a surgical procedure.

Arup Indra

Skin development, diseases and cancer. Our laboratory is investigating into the mechanisms of skin development in space and time from *stem cells* using mouse genetics, biochemical, cellular and molecular approaches. In collaboration with Mark Leid and Gitali Ganguli-Indra, we discovered that transcriptional regulatory protein CTIP2 regulates key processes during skin formation. The mechanisms of activation of CTIP2 with response to external cues, its dynamic role in integrating with multiple other signaling cascades thus allowing formation of an intact and healthy skin are some areas of active research. We have identified key factors that are essential to maintain a balance in skin tissue, lack of which can lead to childhood mortality (e.g. lamellar ichthyosis) or can trigger onset of inflammatory skin diseases such as Atopic dermatitis (AD). The mechanisms of protective skin barrier formation and contribution of skin cells in triggering such immune responses due to a leaky barrier are being investigated. A lipidomic approach to profile skin lipids and predict disease outcome in AD patients are currently underway in collaboration with faculties at OHSU and OSU.

The mechanisms by which many of these developmental processes are deregulated in cancer is another research focus. We are studying the cell-cell signaling that are functional within a tumor-microenvironment and contributing to cancer metastasis. We have discovered that nuclear receptor (NR) signaling between skin keratinocytes & melanocytes can contribute to formation of malignant melanomas. The crosstalk of NR signaling with other signaling pathways and their role in melanoma promotion and in mediating metastasis and de-differentiation are being investigated. We have developed multiple novel pre-clinical models of human diseases such as those exhibiting skin barrier defects (ichthyosis), AD, skin pigmentation disorder, and for invasive melanomas. In collaboration with medicinal chemists (Taifo Mahmud, Fred Stevens), we are utilizing these animal models to screen for natural compounds as new drug leads for effective therapeutic intervention.

Ling Jin

My lab is interested in understanding of the mechanism of viral diseases and virus evolution. Latency of herpesviruses is the main focus of research in my laboratory. My lab uses several different herpesviruses to study the mechanism of herpes virus latency-reactivation cycles, the pathogenesis of herpes viruses, such as Herpes Simplex Virus 1 (HSV-1), Herpes Simplex Virus 2 (HSV-2), Leporid herpesvirus 4 (LHV-4), Koi herpesvirus (KHV) and other animal herpesviruses, and host-virus interaction in central nervous system. In addition, my lab is interested in anti-viral drug development, new emerging viral disease diagnosis, such as deer pox virus, deer adenovirus, goldfish tumor virus. Currently, we have research projects on HSV, LHV-4, KHV, Bovine Herpes Virus 1 (BHV-1), goldfish tumor virus, and deer adenovirus.

Anna Jolles

Dr. Anna Jolles is a disease ecologist and epidemiologist at Oregon State University, where she has appointments in the College of Veterinary Medicine and the Department of Zoology. The Jolles lab studies the ecology and eco-immunology of infectious diseases in wild mammals.

Current study systems include infectious diseases of African buffalo (bovine tuberculosis, brucellosis, Rift Valley Fever, Foot and Mouth Disease, gastro-intestinal parasites, blood-borne parasites), feline

immunodeficiency virus in African lions, Hanta virus in small mammals in Oregon, and a broad range of mammal species in which we study comparative immunology.

Michael Kent

Dr. Kent's research focuses on diseases of fishes and parasitology. Currently he is leading projects investigating diseases of importance to zebrafish in research facilities as this fish is now a very important model in biomedical research. Two groups of pathogens that he is studying are mycobacteria and microsporidia that infect zebrafish. He also is investigating diseases of importance in wild salmonid fishes, and presently is studying multiple pathogens associated with prespawning mortality in Chinook salmon.

Chrissa Kioussi **Organ Development and Tissue Regeneration**

The goal of regenerative medicine is to build body parts to correct birth defects in newborns or replace body parts in the aging. Mammalian cells that are reset to the proper developmental state appear to have the ability to integrate into aged or improperly formed tissues and organs. Such reprogrammed cells may potentially form replacement body parts. Thus, it will be necessary to understand the underlying mechanisms that mammalian genomes use to create the many cell, tissue, and organ types. Cell types are defined at the molecular level during embryogenesis by a process called pattern formation. The Kioussi lab is interested to study the developmental programs that define the sets of genes available to each particular cell type in the body, and the biochemical signaling interactions used at any given time and place.

Mark Leid

The Leid laboratory is primarily focused on the in vivo role of the transcriptional regulatory protein known as Ctip2/Bcl11b. The laboratory discovered the protein and cloned the corresponding cDNA in 2000. The Leid group subsequently defined the molecular and cellular basis for the activity of this transcription factor, and demonstrated that the protein plays key roles in the development of several organ systems. The latter studies were conducted using a mouse that was conditionally null for Ctip2/Bcl11b expression, which was created in collaboration with the group of Daniel Metzger (IGBMC, Illkirch, France). We are particularly interested in the role of this protein in development of the craniofacial complex and are using both biochemical and genetic approaches to address this point.

Christiane Löhr

My research focuses on the molecular pathology as it applies to a wide range of diseases especially carcinogenesis, cancer prevention and treatment and infectious diseases. As a board certified anatomic veterinary pathologist with an appointment in the Veterinary Diagnostic Laboratory I encounter new or poorly understood disease conditions with regularity. Such cases provide excellent opportunities to identify specific, potentially novel, causes and mechanisms of disease processes. Much of my research is conducted in collaboration with colleagues in the College, on campus and outside the University. I find it very rewarding to provide critical input and data to large projects and to contribute to the training of researchers at all levels.

Kathy Magnusson

Our laboratory has found a selective vulnerability of the NMDA receptor to aging. This decline in NMDA receptors correlates with declines in memory function. We will be exploring the effects of drug

or micronutrient intervention on these receptors during aging with the use of stereotaxic surgery, chronic drug administration, and/or behavioral testing using mice as our model system. We may also be examining the effects of interventions on receptor binding density, and subunit mRNA and protein expression with the use of receptor autoradiography, in situ hybridization and Western blots, respectively.

Hadi Mansouri

Project Title:

Detailed macroscopic, microscopic and ultrastructural study of the alpaca pancreas

The camelid pancreas is an organ of great interest. Reported pathological conditions involving the camelid pancreas include pancreatic necrosis and pancreatic atrophy with diabetes mellitus. Compared with other domestic animals, camelids have low plasma concentrations of circulating insulin, partial insulin resistance and a weak insulin response to hyperglycemic challenge. *The effect of IKVAV-Peptide on spinal cord regeneration following spinal cord injury.* This research has been done to measure efficacy of local treatment with IKVAV-peptide on spinal cord regeneration following compression injury at T12 in Balb-c mice. Spinal cord injury (SCI) often causes lifelong and devastating neuromuscular consequences with few treatment options. In the short term, using the spinal cord clip clamp mouse model, functional recovery following spinal cord injury is improved using an IKVAV-peptide placed at the site of injury. We showed that nanofibers promoted reactivation of neurons in the gray matter of the spinal cord. Furthermore, increased reactive astrocytes may be a factor in which function of motor neurons may be restored in the short term of 28 days. These findings indicate the possibility that IKVAV-peptide may facilitate the reactivation of neurons which may result in functional improvement following SCI. Further research is

Erica McKenzie

Dr Erica McKenzie is a specialist in large animal medicine and sports medicine and rehabilitation. Her research interests are largely related to exercise physiology and muscle function. Some of her projects have therefore included studying effective drugs for preventing muscle damage in horses, and the study of specific aspects of exercise physiology and disease in racing Alaskan sled dogs. As a large animal clinician, Dr McKenzie occasionally performs research projects relevant to internal medicine in alpacas.

Kirk Miller

Dr Kirk Miller is Certified in Canine and Feline Practice through the American Board of Veterinary Practitioners. He was in private small animal general practice for more than 12 years before joining the faculty at OSU. Dr Miller is a Clinical Instructor and teaches the Small Animal Primary Care rotation which takes place at the Oregon Humane Society in Portland. His current research projects include looking at the natural incidence of dirofilaria immitis in dogs in the northern willamette valley and another project evaluating a novel spay technique in cats.

Tim Miller-Morgan

Dr. Tim Miller-Morgan is an extension veterinarian focusing on aquatic species and the ornamental fish industry. He leads the Oregon Sea Grant Aquatic Animal Health Program which provides the ornamental fish industry, aquatic research laboratories, and public aquaria with cutting-edge, scientifically based, conservation minded disease management techniques, consultation and training. Our research focus is on applied research aimed at current and emerging animal health issues

generally associated with the management of wild-caught ornamental fish species and the management of disease throughout the chain of custody from the collector/farmer to the end consumer the ornamental fish hobbyists.

Milan Milovancev

My research topics can be broadly categorized as (1) cancer related or (2) clinical challenges in soft tissue surgery. My cancer related research centers around improving our understanding of the biologic behavior of canine sarcomas (e.g. soft tissue sarcomas, oral fibrosarcomas, and osteosarcomas) as it relates to development of novel diagnostic, prognostic, and therapeutic methods. The research I perform related to clinical challenges in soft tissue surgery is generated from specific problems encountered during my clinical treatment of patients. These include development of novel minimally invasive surgical techniques, evidence-based evaluations of different surgical methods, and case-based reports.

Hong Moulton

Morpholino oligomers are a class of antisense macromolecule that have been widely used to knock down gene expression, modify pre-mRNA splicing or inhibit miRNA maturation and activity. Injection of Morpholinos into single-celled embryos of many creatures results in specific knockdown of targeted genes with little toxicity. Morpholino oligomers have revolutionary potential for treatment of a broad range of human diseases, including viral, bacterial, age-related and genetic diseases, but they suffer from poor intracellular delivery into cells. My long term research interest has been in inventing methods for enhancing *in vivo* delivery of Morpholinos in a tissue-specific manner for a given disease by chemically modifying and/or formulating Morpholinos. My current interest is to develop and validate a high throughput *in vivo* model to assess the efficacy and toxicity of an intracellular delivery method.

Debbie Mustacich

My research interests include determining the role of oxidative stress/antioxidant status during mechanical injury and toxicant exposure and to determine the ability of antioxidants/bioactive food components to: 1) prevent secondary damage following spinal cord injury, 2) modulate pathways involved in metabolism and elimination of drugs and environmental toxicants and 3) prevent side effects of chemotherapeutic agents, for improved outcomes and quality of life for veterinary and human patients.

Kathy O'Reilly

- 1) Development of assays for diagnosis and epidemiology of important veterinary and zoonotic diseases. (Prefer MS students only).
- 2) Examination of various aspects of *Bartonella henselae* pathogenesis including reactivation of quiescent infection in cats.

Manoj Pastey

Dr. Manoj Pastey's laboratory is conducting research work on the pathogenesis of influenza, HIV, and respiratory syncytial virus (RSV).

Dan Rockey

Interactions between chlamydiae and the mammalian host.

All species of chlamydiae are obligate intracellular bacteria that cause disease in a wide variety of animal species. In humans, *Chlamydia trachomatis* and *C. pneumoniae* cause a variety of diseases of the eye, genital tract and lung. These conditions affect millions of people worldwide and lead to billions of dollars in medical expenses yearly in the U.S. alone. Additionally, chlamydial infection is associated with certain types of arthritis and, most surprisingly, arterial sclerosis. Very little is known about how chlamydiae interact with the host to cause a particular chlamydial condition, and why some infected people have serious disease and others are asymptomatic.

Craig Ruaux

Intestinal infections. Inflammatory diseases of intestines.

Mahfuzur Sarker

The long-term goal of my research program is to develop strategies to inactivate *Clostridium* spores and to control *Clostridium*-mediated diseases. We mainly focus our work on spores of *C. perfringens* (*Cp*) causing *Cp* food poisoning, which currently ranks as the third most commonly reported food-borne disease in the USA. *Cp* also causes non-food-borne gastrointestinal (GI) diseases in humans and GI diseases in domestic animals. Specifically, we investigate the molecular mechanisms of *Cp*: i) spore heat resistance; ii) spore germination; iii) spore-host interactions; and iv) spore inactivation.

Stacy Semevelos

Her research on molecular expression changes in osteochondrosis has explored the quantitative and spatial alterations of matrix molecules, growth factors, and cell-to-cell signaling in this important disease. In addition, she has discovered age-related changes in gene and protein expression patterns of matrix molecules, growth factors and paracrine factors in articular cartilage of normal growing horses throughout postnatal development. She has also investigated musculoskeletal disorders of llamas and alpacas, using molecular, biochemical, and histological techniques to evaluate suspensory apparatus breakdown in these species.

Natalia Shulzhenko

My laboratory studies interactions between the immune system, metabolism and gut commensal microorganisms (microbiota) in mouse models and human diseases. Microbial cells exceed ten times the number of our own body cells and contribute to several physiological processes. With the advent of new genomic technologies, the role of microbiota in health and disease is a rapidly evolving field of research. We apply novel systems biology approaches such as network reconstruction to analyze host and microbiota simultaneously. Our recent work on chronic enteropathy in immunodeficient hosts revealed a crosstalk between the immune system, the microbiota, and the epithelial cells affecting both intestinal and systemic lipid metabolism. Using metagenomic sequencing, we plan to reveal the microbial players contributing to this disorder and to test them in a mouse model of this disease. In another project, we are studying adverse effects of antibiotics on the intestinal immune system and on microbiota and how this disruption contributes to metabolic syndrome and type 2 diabetes.

Aleksandra Sikora

The emergence and increasing occurrence of bacterial strains that are resistant to all classes of available antibiotics is a global problem. Treatment of infections caused by antibiotic resistant bacteria

requires new approaches and agents with novel modes of action. The bacterial extracellular proteome (cell envelope, membrane vesicles and secreted proteins) plays a fundamental role in establishing infection by enabling the microbes to adhere to and invade host cells, facilitating nutrient acquisition, host tissue destruction, and suppression of host immune responses. Hence the components of the extracellular proteome are promising targets for drugs/vaccines aimed at preventing bacterial infections. The long-term goal of our research is to enhance our understanding of the phenotypic plasticity of the bacterial extracellular proteome and utilize this information to identify attractive targets for development of new therapeutic interventions. Currently, our research focuses on the role of bacterial extracellular proteomes in colonization and circumvention or exploitation of host immune response using two model organisms *Neisseria gonorrhoeae* and *Vibrio cholerae*. We examine these issues using comprehensive proteomic approaches, chemical genomics, and state of the art genetic, molecular and biochemical methods.

Drs. Susanne Stieger-Vanegas and Sarah Nemanic

The research interests of the veterinary imaging group at Oregon State University focuses on using imaging to diagnose and monitor disease in companion animals. We have a large interest in developing better methods using advanced cross-sectional imaging techniques to diagnose musculoskeletal disease and monitoring the response to new treatments. We are also developing a system to perform MRI guided stereotaxic biopsies of brain lesions in dogs. We are also continuously interested in developing improved computed tomography protocols to better diagnose gastrointestinal and cardiac disease in veterinary patients.

Trainees in the veterinary diagnostic imaging group will be exposed to the different imaging modalities available at the College of Veterinary Medicine and Oregon State University

Sue Tornquist

My areas of research include hematology, metabolic disease and infectious diseases of camelids and use of immunocytochemistry in diagnosis and prognosis of neoplasia.

Katja Zellmer

My general research area is the pathophysiology and treatment of osteoarthritis – especially in horses. More specifically, we are currently investigating different routes of administration of the drug tiludronate, which is a bisphosphonate that decreases bone breakdown. This drug is exciting, as it is the 1st time that veterinarians are trying to affect the subchondral bone pathology in the development of osteoarthritis! Further, I am collaborating in the investigation into signaling changes that may be responsible for the development of osteochondrosis (a developmental joint disease) in foals, as well as in the use of synovial-derived cells for bioengineering of meniscal replacements in dogs. In the future, I am hoping that we will determine whether synovial-derived mesenchymal stem cells are of benefit in the treatment of osteoarthritis in horses.