2016 Biomedical Sciences Summer Research Projects

Luiz Bermudez

2. Intestinal microbiome and lung immunity. Different types of diet may impact the innate immunity in the lung. Learn how to work with cells, prepare DNA and work with mice.
3. Mycobacterium avium disease: M. avium is an animal and human pathogen. We plan to study the relationship of the bacterium with neutrophils and endothelial cells.
4. Monitoring the environment and patients in the ICU. Involves microbiological techniques, PCR and gel/enzymes digestion.

Patrick Chappell

• Secretory dynamics of Kisspeptin (Kiss-1) neurons in vitro: The neuropeptide Kisspeptin is a potent stimulator of GnRH secretion in mammals and is crucial for pubertal progression and normal reproductive function in both males and females. In females, kiss1 is expressed in two distinct hypothalamic populations, which allows for ovarian estrogen (E2) to exert both positive and negative feedback on GnRH secretion. We have generated two novel immortalized neuronal cell lines representative of these Kiss-1 populations, and have determined that they secrete Kiss-1. One summer project available is to perform serial cell perifusions using these cells in conjunction with model GnRH neurons (GT1-7 cells) to explore effects of E2 exposure on the real-time secretion patterns of Kiss-1 and how these alter temporal patterns of GnRH secretion in vivo, as determined by radioimmunoassay.

• A second project involving the above Kiss-1 lines will be to evaluate the contribution of activation of different E2 receptors (ERα/ERβ/non-classical) on kiss1 expression, using specific ligands. Changes in kiss1 expression following exposure will be evaluated via real-time qRT-PCR.

• Our lab is also exploring the effects of inappropriate light at night (LAN) exposure and subsequent circadian clock disruption in the etiology of mammary cancer, using mouse models in vivo and tumor lines in vitro. Our preliminary studies have shown profound effects of LAN exposure on clock rhythms within mouse mammary chain, as measured by mPer2::luciferase bioluminescence rhythms using a lumicycle, as well as significant changes in ERα and ERβ expression. Since these data were generated in ovary-intact females, a summer study would need to explore the role of the steroid milieu in this phenomenon by using ovariectomized (OVX) and E2-replacement models in female mice.

• In our exploration of the role of intracellular circadian oscillators throughout the reproductive axis, we have generated mice in which the clock has been genetically ablated specifically in either Kiss-1 or GnRH neurons, and have noted effects on fertility and estrous cyclicity. A summer project would determine if the LH surge in these animals is temporally “unlocked” from its normal window on the afternoon of proestrus in cycling
animals or in OVX, E2-primed females. This project would require performing survival surgery on mice, cardiac puncture at sacrifice, and radioimmunoassay for LH.

**Drs. Morrie Craig and Jennifer Duringer**

*Detection of gliotoxin, a mycotoxin produced by the common hospital fungal pathogen* *Aspergillus fumigatus*

Aspergillus fumigatus is a common fungal contaminant in hospital ventilation systems, and poses a pathogenic risk in immunocompromised patients and those with underlying pulmonary conditions. Disease resulting from infection by this organism is termed aspergillosis. In addition, A. fumigatus can produce the mycotoxin gliotoxin which has immunosuppressive effects, further complicating the treatment and return to health for patients. No dependable, robust technique exists at this time for detection of gliotoxin. The goal of this project will be to develop and validate a mass spectrometry assay for detection of gliotoxin in urine, the biomatrix most commonly used in mycotoxin surveys.

**Brian Dolan**

*Differential Innate Immune Components in Exotic Ungulate Species:*

Innate immune responses are important to all animals and the innate immune system comprises many different components. Despite its importance, innate immune responses have been studied in wild animals using very rudimentary analyses whose data are not easily interpretable. We are developing new methods for measuring innate immune responses using samples obtained from Wildlife Safari Park and ODFW to determine how innate responses vary in different ungulate species.

*Cytokine Responses in Zebrafish Upon Exposure to Pathogens:*

Zebrafish are an important model organism for biological research, but quantifying immune responses Danio has remained challenging. We are measuring different cytokine gene expression in fish exposed to a variety of pathogens which are found in many Zebrafish facilities to determine how chronic, sub-lethal exposure to pathogens alters cytokine signaling. We are also testing newly developed monoclonal antibodies which allow for more accurate quantification of the cytokines.

**Ling Jin**

1) *Developing new test and control strategies against KHV latent infection*

Cyprinid herpesvirus 3, or koi herpesvirus (KHV), is a deadly virus that affects koi and carp worldwide. It causes severe gill necrosis and nephritis, dermal ulceration, hemorrhage, and mass mortality of up to 100% of affected fish. Fish that survive KHV infection are latently infected lifelong carriers, which can shed infectious KHV under stress conditions. Our previous work has demonstrated that in KHV-infected koi, the virus becomes latent in leukocytes or white blood cells. Similar to many mammalian herpesviruses, a latency-associated viral gene, ORF6,
was also recently identified in KHV-infected white blood cells. The protein of this viral gene (ORF6) is made during latent infection. In this research application, we plan to detect this latent protein by making monoclonal antibody and use it to detect latent infection. In addition, we hypothesize that ORF6 protein is required for maintaining the latent infection, and blocking ORF6 protein expression will result termination of KHV latency. To test our hypothesis, we plan to test drugs that can block the latent protein expression and investigate treatments that can eliminate KHV infection.

2) Investigating ORF6 protein sumoylation following heat stress in vivo.

It has been shown that SUMO-2/3 conjugation to proteins occurs in response to cellular stress (4). Our previous study demonstrated that KHV becomes latent in B cells of koi, the ORF6 protein can be detected in the latently infected B cells. We hypothesize that SUMO-2/3 conjugation to ORF6 occurs in KHV+ B cells following heat stress. To test this hypothesis, SUMO-2/3 conjugation to the ORF6 protein will be investigated in KHV+ B cells from koi that are stressed.

3) Investigation of host proteins associated with latency reactivation.

It has been shown that histone modification is involved in HSV-1 reactivation from latency (5). We hypothesize that ORF6 protein interacts with chromatin modification proteins following stress and turn on KHV reactivation from latency. To test our hypothesis, proteins targeted by the ORF6 protein will be immunoprecipitated by ORF6 antibody and investigated by mass spectrometry.

Deidre Johns

Medicinal chemistry/synthetic organic chemistry. We are interested in discovering small molecule therapeutics for infectious diseases and cancer. Specifically, we synthesize small molecules to advance the discovery of new medicines. The small molecules are prepared using modern multi-step organic synthetic methods. We contribute to the development of new synthetic methods as needed to prepare medicinally relevant compounds. Two projects are currently available: (1) synthesis of compounds to inhibit a virulence factor that is important for biofilm formation. This project is in collaboration with Dr. Sikora’s lab, Pharmaceutical Sciences, who studies the disease and pathogenesis. (2) Development of a synthetic method to prepare functionalized cyclopentane rings in order to efficiently prepare a natural product that is known to sensitize MRSA to methicillin.

Anna Jolles

1. Risk sensitive foraging in African buffalo.

This project examines how wild African buffalo balance parasite exposure risk versus nutrient intake in their foraging decisions. The study is based at Kruger National Park, South Africa, and uses observational and experimental approaches to evaluate to what extent avoiding parasites (ticks and GI helminths) drives habitat utilization patterns by buffalo. This work extends the concept of the “landscape of fear”, which posits that wild herbivores must balance predation risk versus nutrient intake, to include parasites as natural enemies that might be just as relevant to
foraging behavior as predators. The project is led by a PhD student under Dr. Jolles’ supervision. There is scope for a veterinary student to contribute to the project by defining a portion of the project that s/he can be responsible for, according to her interests, and conducting the field and lab work needed to complete it. This will involve long days in the field and lab, and will require working well as part of a close-knit research team, as well as independently.

2. **Linking animal personality with immunity and pathogen exposure patterns.**

The term “animal personality” refers to the finding in behavioral studies that there is strong variation among individual animals in their behavioral responses, and that this variation is consistent across a range of situations. I.e., individuals can be classified as bold vs shy, or inquisitive vs not, or leader vs follower, etc, and respond to new situations in predictable ways according to their personality. The question investigated here is to what extent personality traits in buffalo are associated with variation in immunity and infections. For example, inquisitive animals may tend to encounter more pathogen / parasite exposures than less curious animals, due to increased exploratory behaviors, -- and this may underlie some of the variation in immunity that we observe among buffalo. This project is led by a PhD student under Dr. Jolles’ supervision, and is based in Kruger National Park, South Africa. In summer 2015 we will use a series of behavioral field experiments to classify buffalo personalities, which we can then correlate to immunological and infection data that we are collecting on the same animals. A veterinary student could contribute to this project by focusing on particular personality, immune or infection traits (according to her / his interests), carving out a research project of manageable scope. This will involve long days in the field and lab, and will require working well as part of a close-knit research team, as well as independently.

**Dr. Christiane Löhr**

My work focuses on research driven by diagnostics especially pathology. My primary areas of interest are all aspects of Cancer including Pathogenesis, Diagnosis, Prevention, Intervention, and Treatment, diseases of New World Camelids, Goats, and Aquatic Animals, and disease of the Skin and Eye. Cellular and molecular mechanisms leading to disease have intrigued me throughout my career particularly when examined in the context of tissues and whole organisms. I have two specific projects, but would be happy to entertain other research ideas within the areas of diagnostic pathology and cancer biology. A few specific neoplastic entities I am currently examining are feline injection site sarcoma, canine acanthomatous ameloblastoma, oral squamous cell carcinoma, and ovarian carcinoma.

**Kathy Magnusson**

Declines in brain functions during aging, including memory and cognitive flexibility, affect almost half of the human population over 65 years of age, interfering with quality of life and independent living. The Magnusson lab has the overall goal of determining how aging affects cognitive function and how we can prevent that decline. We have projects planned that could involve cognitive testing of older humans taking multivitamins/minerals, reestablishing hippocampal slice electrophysiology in the lab in order to test effects of micronutrients or
microbiome secretions, and drug delivery to the brains of mice in order to enhance brain function during aging.

**Aquatic Animal Health Program: Aquatic Animal Health Management and Research Summer Internship (Hatfield Marine Science Center). Mentor: Dr. Tim Miller-Morgan, Lead Aquatic Animal Health Program**

This is a unique opportunity to gain hands-on aquatic animal health management experience at the aquatic facilities in Newport and other sites in Western Oregon and complete a research project related to emerging or ongoing issues related to aquatic animals in captivity. We currently have three potential project areas for interested students:

1. Characterization of potential bacterial pathogens among imported ornamental fish in Oregon
2. Characterization of mycobacterial species among captive reared seahorses
3. Development of a case definition for sea star wasting disease and a standard hematology and clinical chemistry panel for the ochre sea star, *Pisaster ochraceous*

**Kathy O’Reilly and Peggy Dearing, Veterinary Diagnostic Laboratory**

*Molecular diagnosis of Campylobacter abortion.*

Campylobacter (particularly *C. fetus ssp fetus*, and *C. jejuni ssp. Jejuni*), are associated with late term abortions and stillbirths in ruminants. Diagnosis relies in finding the organism by darkfield microscopy and isolation from fetal stomach/abomasal contents, liver, lung or placenta. Campylobacter are fastidious organisms requiring specialized techniques, media, and atmosphere for their isolation; and isolation and identification can take as long as two weeks. The purpose of this study is to identify and validate a real-time PCR assay useful in the rapid identification of Campylobacter species in clinical specimens submitted for abortion screens using archival material from 2015-2016.

**Kathy O’Reilly and Janell-Bishop-Stewart, Veterinary Diagnostic Laboratory**

*The prevalence of lungworm in dogs and cats in Oregon.*

Lungworms are parasitic worms that cause respiratory problems in a number of species including cats and dogs. Clinical signs include coughing and shortness of breath, and untreated can lead to more serious signs including pneumonia. Cats are generally affected by *Capillaria sp.* and *Aelurostrongylus sp.* , while the most common lungworm in dogs is *Oslerus sp.* Traditionally, lungworm has not been considered a major pathogen in Oregon; however, recent studies have shown that it is present in higher than expected levels in dogs (DeBess, OSPHL, Personal communication). The purpose of this study is to determine the prevalence of lungworms in Oregon cats and dogs, both healthy and those showing respiratory disease.

**Kathy O’Reilly and Janell-Bishop Stewart, Veterinary Diagnostic Laboratory**

*Molecular diagnosis of Giardia lamblia.*

Giardia lamblia is a flagellated protozon parasite that reproduces in the small intestines of a number of host species and can cause mild to severe diarrhea in susceptible individuals. There
are multiple assays to detect Giardia lamblia, and the OSU Veterinary Diagnostic Laboratory uses iodine staining or fluorescent antibody staining to identify trophozoites and cysts, respectively. The purpose of this study is to identify and validate a real-time PCR assay useful in the rapid identification of Giardia lamblia in clinical specimens that can be included in multiplex assays that will test for multiple agents (e.g., Salmonella and Cryptococcus), in multiple host species (dogs, horses, camelids, cattle, goats, sheep).

**Dan Rockey and Stephen Ramsey**

*Project to model chlamydia mutagenesis screen*

What genes are critical for the growth of an intracellular bacterium? Genomics and computational biology provide one way to address that question. In this project, the student will work on a computational simulation of a mutagenesis screen for chlamydia genes that are essential for growth under conditions of cell stress, but not under unstressed conditions. The simulation will be used to optimize the mutagenesis screen and to determine the relationship between the numbers of clones screened and the study's power to detect essential genes. Familiarity with the R or python programming language is required.

**Dan Rockey and Mike Kent**

*Parasitic copepods as vectors for Aeromonas salmonicida, the cause of furunculosis in salmon.*

Drs. Dan Rockey and Michael Kent will team up to co-mentor an interested student to pursue the study of a blood-feeding parasitic copepod, *Salmincola californiensis*, as a potential vector of furunculosis in a salmon. Furunculosis is a common disease of salmon and trout in hatcheries, caused by *Aeromonas salmonicida*, where it is transmitted among fish in this crowded environment. Our preliminary evidence suggests that this common copepod parasite may be an important vector for transmission of the bacterium in wild salmon. The student will conduct preliminary experiments designed to visualize and quantify the bacterial pathogen within the copepod, and help us develop an understanding of this potentially important host-microbe interaction.