Group A
2018 ISU CVM SSRP Mentor Abstract #1

Project Title: Prevalence of antibodies to Zika virus and other viruses in pigs in Mexico

Principle Investigator(s): Brad Blitvich

Collaborating Investigator(s): Carlos Machain-Williams
(Universidad Autónoma de Yucatan, Mexico)

Veterinary Scholar Focused Abstract: (300 words or less):

The recent introduction of Zika virus (ZIKV) into the Americas has been officially declared a public health emergency by the World Health Organization. In humans, ZIKV infection has been associated with microcephaly and other devastating birth defects. However, the impact of ZIKV on veterinary animal health is not well understood. To address this gap in our knowledge, a veterinary summer scholar is required to assay sera collected from domestic pigs in the Yucatan Peninsula of Mexico for antibodies to ZIKV. Sera will be provided by Carlos Machain-Williams, a long-term collaborator at the Universidad Autónoma de Yucatan in Merida, Mexico. Sera will be assayed using a technique known as the plaque reduction neutralization test (PRNT). The PRNTs have been designed to detect antibodies to ZIKV in addition to several other closely-related, mosquito-transmitted viruses that occur in Mexico: West Nile virus, St. Louis encephalitis virus, Dengue virus and Ilheus virus. This project was prompted in part by a recent publication by researchers from the University of Saskatchewan who revealed that neonatal pigs are susceptible to experimental ZIKV infection.

Group A
2018 ISU CVM SSRP Mentor Abstract #2

Project Title: Assembly of large transport vesicles for collagen

Principle Investigator(s): Jinoh Kim

Collaborating Investigator(s):

Veterinary Scholar Focused Abstract: Collagen is a secreted protein and a major component of bones, ligaments and tendons. Collagen forms an unusually long (about 300 nm) and rigid triple helix. The unusual length and rigidity of collagen presents a challenge to the secretory system of a mammalian cell because typically transport vesicles are too small to accommodate such molecules. My laboratory studies how collagen exits the endoplasmic reticulum (ER), the first station of the secretory pathway in the mammalian cell. COPII transport vesicles are responsible for ER export of the vast majority of secretory proteins. We recently identified human diseases caused by mutations in the genes of the COPII machinery. Patients with these mutations show severe defects in cranial and skeletal bones, a clear indication of defective collagen secretion. Similar mutations in fish faithfully recapitulates human disease phenotypes, reinforcing the idea that the COPII machinery is essential for ER export and eventual secretion of collagen. We will generate transport vesicles in a cell-free reaction using purified COPII components and ER membranes. This *in vitro* assay will allow us to test whether COPII mutations influence the assembly of large COPII vesicles and packaging of collagen into large COPII vesicles. Data obtained from this study will provide critical insight into the molecular mechanism for the assembly of large COPII vesicles.

Group A
2018 ISU CVM SSRP Mentor Abstract #3

Project Title: Oncolytic viruses in cancer immunotherapy

Principle Investigator(s): Cathy Miller

Collaborating Investigator(s): N/A

Veterinary Scholar Focused Abstract: (300 words or less):

Immunotherapy using oncolytic viruses is emerging as a leading prospect for the treatment of cancers in humans and animals. Our laboratory studies the interaction of mammalian orthoreovirus (MRV) with cancer cells at the molecular level to provide basic science data to support the use of this virus as an immunotherapeutic treatment against human and animal cancers. We are particularly interested in defining the cell proliferation and checkpoint pathways that are disturbed during virus infection that contribute to tumor cell killing, as well as developing and characterizing virus vaccines that target specific cancer antigens. This summer scholar project will examine the impact of virus infection on tumor proliferation pathways (HIF-1□, AKT, and HER2) and activation of the immune response in HER2+ breast cancer cells in the absence and presence of current first line therapeutic monoclonal antibody (Herceptin). HER2+ breast cancer occurs in part as a result of overexpression of the HER2 protein, which leads to proliferation, angiogenesis, invasion and survival of the tumor cells. HER2 is overexpressed in 20-40 percent of breast (and other) cancers, and HER2+ tumors are highly aggressive with a poor prognosis. We hypothesize that MRV infection will induce the downregulation of tumor proliferation pathways triggered by HER2 overexpression, as well as induce activation of the immune response against these tumor cells. The project is expected to involve tissue culture propagation, immunoblotting, and ELISA techniques, as well as other molecular biology and virology protocols including cloning and replication and growth assays. We expect summer scholar students to get a well-rounded, hands-on experience with the basic science laboratory, as well as learn a great deal about oncolytic immunotherapy in theory and practice during this summer experience.

Group A
2018 ISU CVM SSRP Mentor Abstract #4

Project Title: Use of a gnotobiotic mouse community for gut microbiome studies

Principle Investigator(s): Gregory Phillips, M.A., Ph.D.

Collaborating Investigator(s): Michael J. Wannemuehler, M.S., Ph.D.

Veterinary Scholar Focused Abstract: (300 words or less):

Recent experimental evidence reveals that the bacterial communities (microbiota) that comprise the mammalian gastrointestinal (GI) tract can have a profound influence on the health of the host. Diseases ranging from colorectal malignancies to inflammatory bowel diseases have been linked to an abnormal microbiota (dysbiosis) in humans and animal models. Despite the importance of bacteria to the wellbeing of both humans and animals, how the microbiota influences health and disease is still not well understood. To better understand how specific microorganisms interact with the host, we are using a using a unique gnotobiotic mouse community, the altered Schaedler flora (ASF), were the rodents are colonized with only 8 known bacterial species. Despite the low complexity of the microbiota, ASF mouse exhibit normal immune system development and growth. Use of this resource includes monitoring the changes in relative number, spatial distribution and gene expression in response to alterations in immunological function, diet and following infection with bacterial pathogens. Independent student projects include, but are not limited to, using qPCR to measure changes in the abundance of individual ASF community members in response to infection with *Escherichia coli*, as well as identifying genetic changes in the ASF that occur in response to changes to the gastrointestinal (GI) tract through DNA sequencing. Also, localization of the ASF members within specific regions of the GI tract using hybridization technologies on fixed tissues is relevant to the studies. Opportunities for experience in gnotobiotic lab animals management and sample collection are also part of this project. The overall impact of these studies will lead to a better understanding of how the GI microbiota influences human and animal health and disease.

Group A
2018 ISU CVM SSRP Mentor Abstract #5

Project Title: Investigating the glial source of nitric oxide as a target for mitigating the long-term effects of organophosphate-induced neurotoxicity

Principle Investigator(s): Thimmasettappa (Swamy) Thippeswamy

Collaborating Investigator(s): None

Veterinary Scholar Focused Abstract: (300 words or less):

Organophosphate (OP) pesticides are seizurogenic neurotoxins to humans and animals. Acute OP intoxication, in the long-term, will cause irreversible brain damage due to hyperexcitability of neurons, reactive gliosis, and neurodegeneration. If these are not adequately controlled at a very early stage, they will lead to the development of epilepsy, cognitive dysfunction, and other neurological deficits. Currently there is no treatment for the long-term neurotoxic effects of OP. The symptomatic drugs atropine, oxime, and diazepam (DZP) are inadequate to prevent OP-induced long-term brain injury. DZP controls seizures, but not neuropathology. We have found that OP-induced seizures cause reactive gliosis and increase the levels of reactive oxygen/nitrogen species (ROS/RNS) in the hippocampus. We have also discovered inducible nitric oxide synthase (iNOS) as a major source of RNS production in glial cells in the rats that were exposed to neurotoxins. Incidentally, our studies in the rat suggested that 1400W, a potent and highly selective iNOS inhibitor, is blood-brain barrier permeable and ameliorates long term neuropathology in the rat kainate model of epilepsy (PMID: 27208748). Therefore, our overarching hypothesis is that 1400W, if given soon after the symptomatic drugs, will prevent OP-induced long-term brain pathology. To test the hypothesis, we will use our established diisopropylfluorophosphate (OP agent) rat model to replicate a real life scenario of OP poisoning. In the proposed study, Veterinary Scholar will perform cognitive (the Morris water maze) and motor function tests, video-EEG analyses for seizures, and utilize various histological and biochemical assays from serum and brain samples to investigate the pathogenesis of OP-induced brain toxicity, and the long-term neuroprotective effects of 1400W in OP poisoning.

Group A
2018 ISU CVM SSRP Mentor Abstract #6

Project Title: Identifying genes specific to major immune cell types in the domestic pig, an important biomedical model

Principal Investigator(s): Chris Tuggle, Crystal Loving

Collaborating Investigator(s):

Veterinary Scholar Focused Abstract: (300 words or less):

The pig is increasingly recognized as an important biomedical model, yet its immune system is poorly understood. As human immunity has become deeply characterized at the molecular and epigenetic level, animal models must follow suit. A first step in better understanding of porcine immunity in comparison to human is determining the unique transcriptome in circulating immune cells with known specific functions. We have developed flow cytometric methods to separate the major nucleated cell types in porcine blood, such as B cell, monocytes, and several types of T cells. We wish to determine the transcriptome of these specific cell populations. Because cell populations have already been separated and stored, the Summer student would be able to start right away with designing sets of assays to use q-RT-PCR to validate these populations, as well as participate in more comprehensive transcriptomic profiling of selected cell types. The project will provide hands-on experience in flow cytometry, assay design and validation, and bioinformatic analyses of gene expression. This project can also connect to a larger project to characterize the immune phenotype of Severe Combined Immune Deficient (SCID) pigs, as an additional question the Summer student can address with their cell-type-specific RNA assays is the cells present at different ages in the blood of SCID pigs. Such molecular characterization will benefit this NIH-supported project as well.