Project Title: Testing mosquitoes and ticks from the United States and Mexico for novel viruses by next-generation sequencing

Principle Investigator(s): Brad Blitvich (2116 VMPM; blitvich@iastate.edu)

Collaborating Investigator(s): none

Abstract: (300 words or less):

The advent of next-generation sequencing technologies has revolutionized microbiology by facilitating the identification of both known and previously unrecognized viral pathogens in biological and environmental samples. In this project, next-generation sequencing will be used to identify viral sequences in mosquitoes and ticks collected from various study sites throughout Iowa and the Yucatan Peninsula of Mexico. Mosquitoes from 10 species and three genera (Aedes, Anopheles and Culex) and ticks from five species and three genera (Amblyomma, Dermacentor and Ixodes) will be tested. Viruses of greatest interest will be further characterized. In particular, the abilities of select viruses to replicate within various vertebrate and insect cell lines will be assessed in order to identify viruses that have the potential to infect humans and vertebrate animals.
A2 - Dr. Brewer

Project Title: Model for studying the immune response to parasitic nematodes

Principle Investigator(s): Matt Brewer

Collaborating Investigator(s): Doug Jones

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

Larval stages of parasitic nematodes invade the tissues of vertebrate hosts, where they can either cause disease or remain quiescent (hypobiotic) for long periods of time. Hypobiotic larval stages are of interest for veterinary studies, however, they often have a diffuse distribution throughout the body and are nearly impossible to locate. Our group has developed a small device that can be implanted subcutaneously and then retrieved at a later time. In this study, our hypothesis is that larval nematodes can be placed in the device, implanted subcutaneously, and then retrieved to study cell types and cytokines associated with the anti-parasite immune response. The parasites used will vary depending on availability and may include Haemonchus, Toxocara, or Dirofilaria. The student will be responsible for developing a technique to trap larval nematodes within the device, and then successfully recover live nematodes from the device. If this milestone is achieved, the student will participate in a study where the device containing nematodes is placed subcutaneously in animals, recovered, and analyzed for host cell types and cytokines.
A3 - Dr. Cho (1)

Project Title: Development of a vaccine against human immunodeficiency virus (HIV-1).

Principal Investigator(s): Michael Cho

Collaborating Investigator(s):

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

Since the start of the pandemic nearly four decades ago, AIDS has claimed 35 million lives. About 1.8 million people have been newly infected just in 2017, and nearly 37 million are currently living with AIDS. To date, there is neither a vaccine nor a cure. A vaccine is urgently needed against HIV-1, the virus that causes AIDS. Although neutralizing antibodies (nAbs) can provide effective prophylaxis against the virus, eliciting those that are broadly reactive against many antigenically diverse HIV-1 isolates has been a major scientific challenge and it remains a critical roadblock for the AIDS vaccine development. In my laboratory, we use multidisciplinary approaches to generate immunogens, characterize their biochemical, antigenic and immunogenic properties, and evaluate their ability to induce broadly neutralizing antibodies (bnAbs). We are currently evaluating a number of novel immunogens based on HIV-1 glycoproteins gp120 and gp41 and testing a few vaccine strategies in rabbits and mice. Through participating in these research projects, students will gain better understanding of virology, molecular biology, protein biochemistry, vaccinology and immunology. Although HIV-1 is not a veterinary pathogen, students can apply the learned knowledge to develop vaccines against many veterinary pathogens.
Project Title: Development of a universal vaccine against swine influenza virus.

Principal Investigator(s): Michael Cho

Collaborating Investigator(s): Phil Gauger, Kyoung-Jin Yoon

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

Influenza virus is a major public health concern as it causes significant morbidity and mortality. The CDC estimates that the virus infected 9.2-35.6 million people, of which 12,000-56,000 died annually since 2010. The total economic burden related to influenza infections in humans is estimated at more than $86 billion/year. Influenza virus can also cause acute, severe respiratory diseases in many animal species, such as swine, horses, cattle, dogs, cats and poultry. Currently, influenza vaccines are produced annually, based on circulating virus strains predicted to be most prevalent during the following flu season. The overall protection of current vaccines is conferred by antibodies against the globular “head” domain (HA1) of hemagglutinin (HA), which is highly variable. Consequently, the efficacy of flu vaccines is quite low (10-60% in humans). Besides the low efficacy, there are significant drawbacks and limitations with the current vaccine approach, including having to produce and immunize every year, slow production process, and inability to provide protection against new pandemic strains. Thus, a universal vaccine that can provide broad protection against all or most influenza strains is highly desirable. We recently generated a novel immunogen based on the “stem” domain (HA2) of HA, which is more conserved than HA1. The vaccine, which was derived from an H3 strain, provided 100% and 70% protection against lethal homologous (H3) and heterologous (H1) virus challenges in mice, respectively. We just finished generating much-improved second-generation immunogens based on consensus sequences of H1 and H3 swine influenza viruses. We plan to evaluate their immunogenicity and protective efficacy in pigs with funding from the National Pork Board and Iowa Pork Producers Association. Through participating in this research project, students will gain better understanding of virology, molecular biology, vaccinology and immunology. Students can apply learned knowledge to develop vaccines against any veterinary pathogens.
A5 - Dr. Kanthasamy (Anumantha)

Project Title: Diagnostic evaluation of Misfolded proteins in Animal and Human Brain Neurodegenerative Diseases

Principle Investigator(s): Dr. Anumantha Kanthasamy

Collaborating Investigator(s):

Veterinary Scholar Focused Abstract: (300 words or less):
Protein misfolding is a key pathophysiological process of many neurodegenerative diseases including prion disease, Alzheimer’s disease, and Parkinson’s disease but the diagnosis of these disorders remains to be developed. We have developed a new sensitive method to specifically detect misfolded toxic using a recombinant protein based amplification technique that can be readily applied to various neurodegenerative diseases affecting both human and animals. We intend to further expand the new assay platform by determining whether extracellular vesicles present in biofluids can be used as diagnostic markers of neurodegenerative diseases including prion diseases. Thus the specific objective of this project is to characterize and evaluate the diagnostic efficiency of these extracellular vesicles in the diagnosis of prion diseases as well as human protein misfolded diseases. Biofluid samples from a wide host species form captive and wildlife as well as humans will be used in this project. Some of the skills a student will learn to pursue this project include, cell culture, recombinant protein extraction and purification, protein analysis, advanced plate reader assays, qRT-PCR and Western blot. The students will be trained in data analysis and manuscript preparation.
A6 - Dr. Kanhasamy (Arthi)

Project Title: Elucidation of the neuroinflammatory role of a redox sensitive kinase, Src family kinase, Fyn in Parkinson’s Disease (PD) pathogenesis

Principle Investigator(s):
Arthi Kanhasamy Ph.D

Collaborating Investigator(s):
Anumantha Kanhasamy Ph.D

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

Neuroinflammation has been implicated as a major pathophysiological process of Parkinson’s disease (PD) in recent years. Among various neuroinflammatory triggers, protein aggregates have been shown to be a predominant pathological trigger for microglial activation and subsequent proinflammatory cytokine and chemokine release in the brain, which in turn contributes to the accelerated progression of neurodegenerative processes. Also, emerging evidence indicates that aggregated pathogenic proteins, including α-synuclein (αSyn), are packaged into exosomes, which propagate protein aggregates from affected neurons to other brain cells, via a prion-like mechanism, thereby leading to a heightened neuroinflammatory response and resultant dopaminergic neuronal degeneration. Despite these advances, the cellular mechanisms underlying microglia-mediated neuroinflammatory events following stimulation with αSyn aggregates and αSyn-containing exosomes remain poorly defined. Our lab is primarily focused on characterizing the mechanism of Fyn kinase, a redox sensitive kinase in NLRP3 inflammasome activation mechanism subsequent to the activation of astrocytes and microglia (support cells of the brain) by αSyn aggregates and exosomes containing αSyn aggregates and its impact on dopaminergic neuronal cell death. To fulfill our research goals we utilize cell culture models, animal models of PD as well as in postmortem PD brain tissues. More importantly, our lab is interested in developing targeted immunotherapeutic drugs for PD. Also, state of the art biochemical, cellular and neurochemical approaches will be used to achieve our study goals. Taken together, delineating the role of Fyn kinase in αSyn-induced microglial activation and PD like neuropathology will not only provide novel mechanistic insights into the progression of neurodegenerative processes in PD, but may also pave the way for developing novel disease modifying therapies for PD.
Breast cancer (BC) consists of a number of different subtypes, depending on the history and genetic background of the cells from which the tumor develops. One subtype of BC is termed HER2+ as a result of overexpression of the human epidermal growth factor receptor 2 (HER2). HER2 positive tumors are highly aggressive and associated with poor prognosis. Passive immunotherapy in the form of monoclonal antibodies Trastuzumab (Herceptin) and pertuzumab (Perjeta) has improved prognosis for patients with both early and advanced disease. However, while many patients respond to passive immunotherapy, others do not respond at all, or alternatively, progress to therapy resistance during treatment.

Mammalian orthoreovirus (MRV) is a member of the Reoviridae family of segmented dsRNA viruses. MRV is a clinically benign virus that has emerged as a therapeutically relevant oncolytic virus that preferentially infects and kills tumor over non-tumor cells. In animal models and clinical trials, MRV also activates the adaptive immune system against tumor cells that it infects. Existing pre-clinical and clinical studies on MRV killing of different BC subtypes strongly support the virus as a feasible therapy option for this cancer. However, very little is known about the impact of MRV specifically on HER2+ BC, either alone, or in combination with approved therapies such as Herceptin and Perjeta.

This project involves investigation of the impact of MRV infection on HER2+ BC cells. Experiments will be performed examining how MRV alters HER2+ BC cell survival when co-administered with Herceptin and Perjeta. Additional studies will attempt to create a recombinant MRV that expresses HER2 peptides for testing as a vaccine against HER2+ BC. Altogether work performed during this summer scholar project has the potential to improve the therapeutic options for treating HER2+ BC, and aid in the development of a novel field of MRV-based vaccine delivery.
Project Title: Circular RNA-based biomarkers of animal and human diseases

Principle Investigator(s): Dr. Ravindra Singh
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Veterinary Scholar Focused Abstract: (300 words or less):

Gene function is intimately linked to the production of coding and/or non-coding RNAs. In most instances, a single gene produces multiple RNAs due to alternative splicing, alternative transcription start and/or stop sites. Recent studies confirm production of circular RNAs (circRNAs) by most genes. In general, circRNAs are more stable than their linear counterparts. Several functions, including transcription and translation regulations have been attributed to circRNAs. Evidence that circRNAs could also serve as markers of disease prognosis and therapy are rapidly emerging. Summer scholar(s) in Singh lab will learn how to identify circRNAs from cells, tissues and biological fluids.
A9 - Dr. Zhang

Project Title: Adjunctive therapy for Antibiotic-resistant Campylobacter

Principle Investigator(s): Qijing Zhang, Veterinary Microbiology and Preventive Medicine

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

Campylobacter jejuni is a major foodborne pathogen and causes gastroenteritis in humans. Currently, fluoroquinolone and macrolide antibiotics are used for clinical treatment of Campylobacter infection in humans. However, Campylobacter has developed resistance to both classes of antibiotics, and antibiotic-resistant Campylobacter has become a serious concern for public health. Thus alternative strategies are urgently needed to combat antibiotic-resistant Campylobacter. In this project, we will test the feasibility of using antisense peptide nucleic acid (PNA) as an adjunct therapy for clinical treatment of Campylobacter infection. PNA will be designed to target the antibiotic efflux transporter in Campylobacter and will be evaluated in the chicken model. The hypothesis is that the PNA will inhibit the antibiotic efflux mechanism in Campylobacter, making it susceptible to antibiotic treatment. Several groups of chickens will be purchased from a commercial supply and will be inoculated with antibiotic-resistant Campylobacter. After the birds are colonized, they will receive treatment with fluoroquinolone or macrolide antibiotics in the presence or absence of PNA. Cloacal swabs and cecal contents will be periodically collected for culturing Campylobacter. In addition to enumeration of the bacterial cells in fecal contents, antimicrobial susceptibility tests will be performed with selected Campylobacter isolates. The efficacy of the PNA will be evaluated by statistical analysis of the Campylobacter numbers in different group. The project will test a new concept for adjunctive therapy and may potentially identify an effective way to extend the utility of existing antibiotics against drug-resistant Campylobacter.