

A1 - Cho

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

Principal Investigator(s): Dr. Michael Cho

Collaborating Investigator(s):

Abstract:

Since the start of the pandemic nearly four decades ago, AIDS has claimed 33 million lives. About 1.7 million people have been newly infected just in 2019, and nearly 38 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.

A2 - Thippeswamy

Project Title: Disease-modification in experimental models of epilepsy

Principal Investigator(s): Dr. Thimmasettappa (Swamy) Thippeswamy

Collaborating Investigator(s):

Abstract:

Organophosphate (OP) pesticides are seizurogenic neurotoxins to humans and animals. Acute OP intoxication, in the long-term, will cause irreversible brain damage due to hyper excitability 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.

A3 - Singh

Project Title: Mechanism of therapeutic molecules for the treatment of genetic disorders

Principal Investigator(s): Dr. Ravindra Singh

Collaborating Investigator(s): Dr. Natalia Singh

Abstract:

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. Antisense oligonucleotides (ASOs) and small molecules that modulate transcription and/or splicing are becoming powerful tools to treat genetic diseases. The appropriate application of ASOs and small molecules for therapeutic application requires the target identification and characterization. It is also important that the off-target effects of ASOs and small molecules are properly understood before their use in clinics. Summer scholar in Singh lab will learn how to identify therapeutic targets and off-target effects of ASOs and small molecules. This collaborative project will employ a variety of techniques, including high throughput sequencing, bioinformatics, RT-PCR, molecular and cellular biology techniques. Findings of the successfully completed project by the summer scholar will be published in a peer-reviewed journal and summer scholar will have opportunity to earn co-authorship in the publication.