OREGON NATIONAL PRIMATE RESEARCH CENTER

UNDERGRADUATE SUMMER FELLOWSHIPS

Position Descriptions

Summer, 2024

Research that takes place at ONPRC/OHSU is undertaken to improve understanding of human health and disease. Animal models are essential in this pursuit, and applicants need to be aware that in certain cases invasive animal procedures are necessary. Ethical issues associated with research in humans and other animals can evoke strong controversy, yet animal research is presently our only means of answering certain critical questions that we hope will lead to improved therapies and/or cures for disease. Federal law mandates adherence to regulations that ensure our research procedures are both humane and justified in terms of their contribution to knowledge and medical practice. Persons who apply for apprenticeship positions at ONPRC should support the ethical conduct of animal research that is carried out in compliance with federal laws and regulations.

Mentor: Kristine Coleman, PhD

Oregon National Primate Research Center/OHSU: Division of Animal Resources & Research Support and Neuroscience

Dr. Coleman oversees the Behavioral Services Unit (BSU) at the ONPRC. This unit is responsible for attending to the behavioral and psychological needs of the monkeys at our facility. Research in the BSU is focused on examining ways to reduce stress and improve psychological well-being for laboratory primates. Such studies have included how differences in behavioral inhibition (shyness vs. boldness) affect stress-sensitivity in macaques, how predictability affects behavioral management practices, mate selection behavior and dominance in group-housed animals, and the effects of density on group dynamics.

Students will learn behavioral methodology, including the design and use of ethograms, how to use software specifically designed for behavioral observation, and statistical methods. S/he will also learn about species specific monkey behavior and how to improve the psychological well-being of captive animals.

Learn more about Dr. Coleman's research at http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/kristine-coleman.cfm

Mentor: Vincent Costa, PhD
Oregon National Primate Research Center/OHSU: Division of Neuroscience

Do you want to make better decisions? The ultimate goal of the Costa lab is to understand the neuroscience of learning and decision making in enough detail to be able to intervene and keep us from making bad decisions. Current research in the laboratory is focused on understanding how brain structures that are conserved across mammals and that control the motivation to act and feel, interact with the parts of the prefrontal cortex that underwent an evolutionary expansion in primates and that control learning and decision-making. Our general approach is to record the activity of hundreds of neurons using neural probes while the monkeys play video games we have designed to test their decision-making abilities. While nearly all members of the Costa lab are terrible at playing video games, the monkeys we work with quickly become experts. The speed and accuracy with which they solve the problems we challenge them with is amazing. By recording the activity of neurons in different brain regions we can ascertain their contributions to the monkeys' performance during the video game. In addition, we are using genetic tools that allow us to target specific types of neurons and selectively turn up or down their activity. This allows us to determine how specific connections in the monkeys' brains help or hinder their ability to make good decisions. Poor decision-making is a symptom of many neurological and psychiatric diseases including depression, anxiety, addiction, and dementia.

The teacher/intern will curate and analyze existing neurophysiology datasets where the activity of individual neurons is assessed in relation to the monkeys' behavior. They will also be trained to work collaboratively with nonhuman primates, training and testing them on operant tasks and record neural activity in awake, behaving primates. There also will be opportunities to conduct and design histological experiments probing the transcriptomic identities of specific neural circuits. Candidates with neuroscience, psychology, and/or engineering background and excellent computer skills are preferred but not required. The most important skill is being curious and motivated to learn about the neural bases of learning and decision making.

Learn more about Dr. Costa's research at https://www.ohsu.edu/people/vincent-costa-phd

Mentor: Verginia Cuzon-Carlson, PhD
Oregon National Primate Research Center/OHSU: Division of Neuroscience

Research in the Cuzon Carlson laboratory focuses on how mature and developing neuronal circuits are modulated by drugs of abuse, particularly alcohol. Our long-term goal is to contribute to the understanding of addiction and fetal alcohol spectrum disorders in order to reveal novel routes of therapeutic interventions for individuals with FASD or struggling with alcoholism. We focus on brain areas such as the dorsal striatum that are involved in cognition, decision-making, and behavioral control that may contribute to addiction. The laboratory uses a multidisciplinary approach including molecular biology techniques, patch clamp electrophysiology, genetic approaches using optogenetics and transgenic mouse lines, and behavioral paradigms to address our two overarching questions.

Our first area of emphasis is to understand the neural mechanisms that underlie the transition from acute drug exposure to chronic exposures that lead to addiction, tolerance, and dependence. To this end we want to gain a better understanding of the cellular and molecular mechanisms of GABAergic and glutamatergic synaptic plasticity in the striatum, its role in action-outcome and stimulus-response learning that we hypothesize plays a role in the

development of addiction. The effects of chronic ethanol exposure have been examined in multiple animal models including "Drinking in the Dark" and chronic intermittent exposure to ethanol via vapor in mice, as well as ethanol drinking for over a year in a non-human primate model. From these studies, it has been revealed that the GABAergic system in the dorsal striatum is particularly susceptible to the effects of ethanol. Using to advantage transgenic mouse lines as well as optogenetic and chemogenetic technology we test the hypothesis that specific GABAergic synapses are more susceptible to the effects of ethanol exposure than others within the subregions of the dorsal striatum and that by manipulating these circuits we can alter the operant responding to ethanol.

The second question examines the development of dorsal striatal circuitry and how teratogens, such as alcohol, disrupt normal circuit development. For this project, we use a mouse model that mimics exposure to ethanol spanning the entire human gestational period. We examine the effect of fetal alcohol on the GABAergic and glutamatergic neurotransmission and synaptic plasticity of the dorsal striatum as well as their contribution to behavioral abnormalities observed in Fetal Alcohol Spectrum Disorder such as altered decision-making processes, are determined.

Fellowship candidates should anticipate working directly with mice, analyzing large data sets, be computer literate, and have budding interests in animal behavior, brain circuitry, and addiction research.

Learn more about the research being conducted by Dr. Cuzon Carlson
http://www.ohsu.edu/xd/education/schools/school-of-medicine/academic-programs/graduate-studies/faculty/grad-studies-faculty.cfm?facultyID=828

Mentor: Meaghan Hancock, PhD
Vaccine and Gene Therapy Institute/OHSU

Dr Hancock's lab is interested in understanding the molecular mechanisms mediating latent viral infections, focused specifically on cytomegaloviruses (CMVs), including understanding the host and virus mechanisms surrounding the establishment, maintenance and reactivation from latency. Human CMV is a common virus that infects greater than 50% of the world's population, and normally cause benign childhood illness. However, HCMV can cause serious congenital infections and is a significant cause of morbidity and mortality in immunosuppressed individuals, such as those undergoing solid organ or hematopoietic transplantation. Therefore, understanding the mechanisms of how the virus enters and exits latency is key to preventing and treating CMV infections. Current studies in the lab focus on defining the role of HCMV-encoded microRNAs (miRNAs) in mediating aspects of latency and reactivation. Projects employ molecular and biological techniques to examine the targets of viral miRNAs and how they affect latency and reactivation in novel in vitro culture systems. Techniques include cell culture, molecular cloning, transfections, qRT-PCR, western blotting and recombineering to create mutant viruses.

The student trainee will learn how to culture human cells and infect with viruses, techniques in molecular cloning, transfections, qRT-PCR, western blotting and recombineering to create mutant viruses.

Learn more about Dr. Hancock's research at https://www.ohsu.edu/vaccine-gene-therapy-institute/meaghan-hancock-phd

Mentor: Meredith Kelleher, PhD
Oregon National Primate Research Center/OHSU: Division of Reproductive & Developmental Biology

Dr. Kelleher's research focuses on problems that can occur during pregnancy that result in preterm birth and poor outcomes for babies. We utilize clinically relevant non-human primate pregnancy models that are translational to human health and disease with the aim of reducing the burden of disease and disability caused by complications that occur during early life development. Current studies center on the early stages and mechanisms of infection that can cause preterm birth and fetal brain inflammation. We are also exploring new therapies for the treatment of hypoxia-ischemic brain injury at the time of birth.

The intern will perform cellular and molecular studies to examine mechanisms of preterm labor and fetal injury. The teacher/intern will have the opportunity to participate in studies designed to quantify expression of genes of interest, concentrations proteins by Western blot, and cellular localization of protein expression using immunohistochemistry.

Learn more about Dr. Kelleher's research at https://www.ohsu.edu/people/meredith-kelleher-phd

Mentor: Chris Kroenke, PhD
Oregon National Primate Research Center/OHSU: Division of Neuroscience

A major focus for the Kroenke laboratory is to advance the utility of magnetic resonance imaging (MRI) in characterizing fetal brain growth. The project available for the summer of 2024 will involve analysis of fetal brain growth in rhesus macaques using previously acquired fetal MRI data. Growth trajectories of a set of brain regions will be compared to similar measurements performed on other species, with the objective of integrating the cross-species data into a comparative model for brain growth.

Students will gain familiarity with fetal brain development in the rhesus macaque, and compare findings to corresponding data available for human subjects. Participants will delineate boundaries of brain regions in previously-acquired MRI data, and perform quantitative analyses of brain growth to improve our understanding of cellular factors that underly brain growth in the fetal period.

Learn more about Dr. Kroenke's research at http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/christopher-kroenke.cfm

Mentor: Victoria Roberts, PhD
Oregon National Primate Research Center/OHSU: Division of Reproductive & Developmental Sciences

The overall goal of the Roberts laboratory is to understand normal pregnancy, and to develop tools that will identify pregnancies that are compromised by placental dysfunction. Specifically, the group focuses on developing non-invasive methods to study and understand the placenta during pregnancy, and to correlate *in vivo* function with *in vitro* analysis post-delivery. *In vivo* ultrasound and Magnetic Resonance Imaging (MRI) techniques implemented in nonhuman primate models of perturbation (e.g., maternal dietary manipulation), are used in combination with tissue collection for *in vitro* analysis of placental structure and function. This approach facilitates correlation of blood flow to the placenta, as the main determinant of maternal supply, with how the placenta functions in order to optimize development of the baby.

Students will participate in studies that ultimately contribute to the understanding of placental function. They will have the opportunity to participate in studies that utilize a 3-dimensional placenta organoid model to examine early structural development, quantitate the expression of proteins by Western blot, and cellular localization of protein expression using immunohistochemistry. In addition, the student will have the opportunity to learn microscope techniques and perform structural analysis.

Learn more about Dr. Roberts' research at https://www.ohsu.edu/people/victoria-hj-roberts-phd

Mentor: Larry Sherman, PhD
Oregon National Primate Research Center/OHSU: Division of Neuroscience

Dr. Sherman's lab is focused on understanding ways to promote the repair of the damaged nervous system in a number of conditions including multiple sclerosis, Alzheimer's Disease, and following chemical insults including cancer chemotherapy drugs and heavy drinking. The Sherman lab discovered that a sugar molecule, called hyaluronan (HA), regulates how neural stem cells and progenitor cells differentiate and proliferate, and that abnormal synthesis and degradation of HA prevents nervous system repair. A major goal of the lab is to develop novel strategies to promote nervous system repair by altering the catabolism of HA. They are currently looking at gene therapy, stem cell-based therapies, and drug discovery approaches to achieve this goal. The successful candidate will be expected to actively participate in designing, performing and interpreting data from these experiments. Candidates will be included on any publications arising from their time in the laboratory.

Learn more about Dr. Sherman's research at
http://www.ohsu.edu/people/larrysherman/02b1371a44e64745adee23343fdf439a

Mentor: Rebecca Skalsky, PhD
Vaccine & Gene Therapy Institute/OHSU

Dr. Skalsky's lab is focused on understanding how chronic virus infections, such as Epstein-Barr virus infection, lead to the development of lymphoproliferative disease and cancers including B cell lymphoma. Elucidating molecular mechanisms that participate in virus-host dynamics is essential in developing approaches to prevent and treat viral disease. Current studies are centered on defining the role of RNA interference and non-coding RNAs in anti-viral responses, virus persistence, and oncogenic processes. Ongoing projects employ genome-wide molecular, biochemical, and bioinformatics-based strategies to examine how non-coding RNAs critically impact cell-state transitions and govern aspects of the viral life cycle that contribute to pathogenesis.

The intern will learn a variety of RNAi-centric molecular, biochemical, and/or bioinformatics methods to experimentally investigate targets of non-coding RNAs, specifically those produced by EBV and the non-human primate homolog, rhesus LCV. Wet-lab techniques include cell culture, qRT-PCR, molecular cloning, immunoblotting, and luciferase assays. Dry-lab techniques include sequencing data processing, generating/implementing work-flows for RNA-seq analysis, and visualization of transcriptomics datasets.

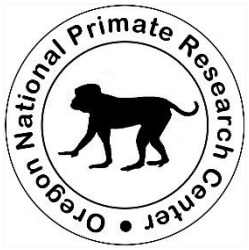
Learn more about Dr. Skalsky's research at https://www.ohsu.edu/vaccine-gene-therapy-institute/skalsky-laboratory

Mentor: Brandon Wilder, PhD
Vaccine & Gene Therapy Institute/OHSU

The Wilder Lab uses a broad range of laboratory techniques to address one of the world's oldest and deadliest diseases: Malaria. We work closely with multiple labs across campus to design novel vaccine candidates using immunology as a guide. To do this, we have an insectary that allows us to grow mosquitos and infect them with the malaria parasite to recapitulate the entire life cycle. Our work ranges from completely in vitro (in petri dishes) to multiple "in vivo" models including mice, humanized liver mice and non-human primates (NHPs). Current projects include: using NHP models to understand the immunology behind malaria infection and protection from infection; the interaction between malaria infection and subsequent vaccination; discovering antibodies that act in unconventional ways; and testing vaccine candidates and monoclonal antibodies in NHPs and humanized mice.

Students will have the opportunity to learn the basics of propagating the malaria parasite through mice and mosquitos, mosquito handling and dissecting, immunological techniques such as ELISA, and general laboratory techniques including PCR, Western Blots, and molecular cloning. Interested students may have the opportunity to work with rodents and/or NHPs as part of ongoing vaccine efforts.

Learn more about Dr. Wilder's research at: https://www.ohsu.edu/vaccine-gene-therapy-institute/brandon-wilder-phd


Oregon National Primate Research Center