OREGON NATIONAL PRIMATE RESEARCH CENTER

UNDERGRADUATE SUMMER FELLOWSHIPS

Position Descriptions

Summer, 2022

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: Divisions of Comparative Medicine 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: 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: Robert Friedman, PhD
Oregon National Primate Research Center/OHSU: Division of Neuroscience

How does the brain produce perception, thought, and behavior? The Friedman laboratory studies how the functional modules of the cerebral cortex (roughly 200 um in size) underlie visual and tactile perception and mediate goal directed behavior. The lab's experimental approaches include the use of implanted 'windows on the brain', intrinsic optical imaging, single and multielectrode recording arrays, anatomical tracing techniques, intracortical brain stimulation with electrical, optogenetic and near infrared laser methods, fMRI, and visual and tactile illusions. The lab is very interested in technology development and brain-machine interfaces. One goal of this combined behavioral, functional, anatomical, and neuroengineering approach is in the development of future mind-machine interfaces that can restore or enhance function after injury.

Fellowship candidates should anticipate working on analyzing large data sets (imaging, electrophysiological, and/or anatomical), be computer literate, and have budding interests in animal behavior, brain circuitry, and perception. Candidates with neuroscience, psychology, and/or engineering background and excellent computer skills are preferred.

Learn more about the research being conducted by Dr. Friedman at https://www.ohsu.edu/people/robert-m-friedman-phd

Mentor: Kathleen Grant, PhD
Oregon National Primate Research Center/OHSU: Division of Neuroscience

Cognitive functions such as memory, cognitive flexibility, self-control, learning and attention enable an individual to achieve favorable outcomes throughout the lifespan. Alcohol use and abuse has negative consequences on the cognitive functions such as decision making. In the Grant laboratory, we use non-human primates to study alcohol-drinking behavior, effects of chronic alcohol intake on behavioral flexibility and whether assessment of the predisposition to acquire habitual behaviors in individuals might help to predict heavy alcohol use.

Summer undergraduate research assistants participate in experimental work that was designed to explore and compare cognitive flexibility in male and female non-human primates. They will learn about cognitive testing and experiment design in animal models and how the experimental results are translated to human alcohol use disorders. Specific experiences include data acquisition and post-experimental data analysis.

Learn more at https://www.ohsu.edu/people/kathleen-a-grant-phd

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

The Hennebold laboratory focuses on defining the processes occurring in the ovary that are necessary for female fertility. Based on data obtained from recent genomic studies conducted in our laboratory, our group's research interests include defining the molecular and cellular pathways responsible for rupture of the ovarian follicle, the release of an egg that is competent to undergo fertilization and subsequently develop into a preimplantation embryo, as well as the

formation of the corpus luteum. The teacher will participate in studies that ultimately contribute to the development of novel approaches to control fertility, including the identification of processes that promote fertility in women seeking to have children or for the development of non-hormonal female contraceptives. The Hennebold laboratory is also interested in Assisted Reproductive Technologies (ARTs) and the use of recently developed gene editing tools, such as CRISPR or TALENs, for creating relevant models of human disease.

The intern will perform cellular and molecular studies of the primate follicle and/or corpus luteum. The teacher/intern will have the opportunity to participate in studies designed to quantitate the level of specific mRNAs using state of the art real-time or microfluidic PCR, the expression of proteins by Western blot, and cellular localization of protein expression using immunohistochemistry. Research opportunities are also available that involve generating and testing CRISPR/TALEN gene editing reagents.

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

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 2022 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 learn 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: 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

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: Elinor Sullivan, PhD
Oregon National Primate Research Center/OHSU: Division of Neuroscience

The Sullivan lab studies the influence of the environmental factors (maternal nutrition, maternal obesity, maternal mental health, maternal stress) during gestation on offspring brain development and behavior. The primary focus is examining the influence of these environmental risk factors on behavioral regulation with an emphasis on behaviors related to mental health and behavioral disorders, including anxiety, depression, attention deficit hyperactivity disorder (ADHD), and autism spectrum disorders (ASDs). One specific focus is the influence of maternal nutrition during the perinatal period on the behavior, and physiology of the developing offspring.

Students will learn about the fields of behavioral neuroscience and developmental origins. Specifically, students will learn about infant and child behaviors related to mental health disorders, methodologies for quantifying behavior, software for behavioral coding and statistical analysis. Opportunities will also be available to learn cellular and molecular techniques such as immunohistochemistry.

Learn more!
https://www.ohsu.edu/people/elinorsullivan/afe032779b02189f056c5fcf1bc79985

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 recently joined the Vaccine and Gene Therapy Institute at OHSU to expand the vaccine efforts on the West Campus to include malaria research. We work closely with multiple labs across campus to design novel vaccine candidates using immunology as a guide. To do this, we have implemented 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 using mouse models, humanized mouse models and non-human primate (NHP) models (in vivo). Current projects include: using NHP models to understand the immunology behind malaria infection and protection from infection; discovering antibodies that act in unconventional ways and kill the liver stages of the malaria parasite; and testing a vaccine candidate in NHPs.

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 at: https://www.ohsu.edu/vaccine-gene-therapy-institute/brandon-wilder-phd

Mentor: Mary Zelinski, PhD

Oregon National Primate Research Center/OHSU: Division of Reproductive & Developmental Sciences

Dr. Zelinski and her team are studying the development, growth and maturation of the ovarian follicle and its enclosed oocyte (egg) in nonhuman primates. Current studies center on cryopreservation of ovarian tissue prior to cancer therapy for subsequent transplantation in vivo and/or oocyte maturation in vitro to eventually obtain an offspring. Additional research is focused on understanding follicle loss that occurs with ovarian aging and impacts fertility as well as investigating interventions to delay menopause. Studies on the basic processes whereby follicular growth is stimulated and disrupted are aimed at producing novel agents to alleviate infertility or control fertility.

The student will learn cellular approaches to studying ovarian function in the rhesus monkey, including how to use general laboratory equipment and microscopes, as well as the techniques of cryopreservation, cellular localization of proteins using immunohistochemistry, image analysis, and statistical analyses of experimental data.

Learn more about Dr. Zelinski's research at
http://www.ohsu.edupeople/maryzelinski/afe02d9aaec70d0dbc02086215002c97