ONPRC Undergraduate Summer Fellowships
Position Descriptions
Summer, 2016

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

The Hennebold laboratory focuses on defining the processes in the ovary that are necessary for female fertility. We are conducting molecular and cellular studies that will provide insight into the mechanisms responsible for follicle rupture and the release of the oocyte as well as the development and regression of the corpus luteum. Through recent genomic studies conducted in our laboratory we are beginning to understand how various cellular activities lead to the rupture of the ovulatory follicle and the release of a fertilizable oocyte. Areas of focus include defining the significant cellular reorganization and extracellular matrix remodeling that occur prior to and following ovulation, as well as the role bioactive lipid metabolites such as prostaglandins play in coordinating events necessary for follicle rupture.
Students 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.

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

Mentor: Martha Neuringer, PhD
Oregon National Primate Research Center/OHSU: Division of Neuroscience

The macula is the critical region of the retina responsible for high acuity central vision, and is present only in higher primates. This region is particularly vulnerable to damage, and age-related macular degeneration is the leading cause of blindness in the elderly. By using the exceptional resource of the Primate Center’s large monkey colony, we have shown that macaque monkeys spontaneously develop this disease, and thus they are uniquely valuable for defining environmental and genetic risk factors and for testing potential therapies. Together with collaborators from the Casey Eye Institute, we are testing promising new therapies, including gene therapy and stem cell therapy. We also are examining the roles of nutritional factors, including omega-3 fatty acids and carotenoids, in retinal health. In addition, we are examining the effects of these nutritional factors on brain development, function and aging. Methods employed include noninvasive retinal imaging, new brain MRI techniques, electrophysiological recording and behavioral tests of cognitive function. Candidates must be enthusiastic about working with animals. Biology, neuroscience and/or psychology background and excellent computer skills are preferred.

Learn more about Dr. Neuringer’s research at http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/martha-d-neuringer.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/xd/research/centers-institutes/onprc/scientific-discovery/scientists/larry-sherman.cfm
Alcoholism is a chronic, progressive disorder often characterized by patterns of binge drinking that leads to poor health, interpersonal problems and a great economic burden on society. Alcohol is known to produce subjective effects (i.e. feelings of intoxication) that are associated with the perpetuation of binge drinking, suggesting that these subjective effects contribute to alcohol’s abuse potential. Laboratory animals cannot verbally tell us how they feel, but they can be trained to engage in a specific behavior if they perceive the effects of intoxication and in a different behavior if they do not feel the effects of intoxication. This differential responding is known in behavioral research as a discrimination task (that is, discriminating between the intoxicated and the non-intoxicated state). Training a discrimination task based on if the animal was given alcohol or water is a reliable behavioral assay that can be used to explore the neural basis of intoxication. While a great deal of research has been dedicated to alcohol’s action on neural activity, very little is known about the circuitry that underlies ethanol’s subjective effects. Importantly, there are no published studies to date that have directly examined brain circuitry that mediates ethanol subjective effects in monkeys. Mapping circuitry that mediates the subjective effects of ethanol in the primate brain will help bridge our understanding of brain mechanisms mediating alcohol intoxication from rodents to primates and improve targeting strategies for potential pharmacotherapies.

This research opportunity will provide an understanding of how to conduct and evaluate the drug discrimination assay, as well as provide an introduction to the pharmacology of ethanol (drinking alcohol).

Learn more about the research being conducted by Dr. Grant at [http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/kathleen-a-grant.cfm](http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/kathleen-a-grant.cfm)

Mentor: Trevor McGill, PhD

Dr. McGill’s lab is focused on determining the causes and mechanisms of photoreceptor degeneration, their effect on visual function, and testing promising new therapies for retinal degenerative diseases. These therapies include gene therapy and stem cell transplantation strategies to replace lost sensory neurons or prevent their degeneration. The work is performed using both rodent and monkey models. These studies use a series of state-of-the-art imaging and functional measurement methods to examine the detailed structure and function of the living retina noninvasively in both normal and degerminating conditions. Our imaging methods are combined/compared with standard histological and immunohistochemical techniques. Candidates must be willing to work closely with animals. Biology, neuroscience and/or psychology background and excellent computer skills are preferred. Histology experience would be a valuable asset.

Learn more about Dr. McGill’s research at [http://www.ohsu.edu/xd/research/research-expertise/researchers/index.cfm?personid=2834](http://www.ohsu.edu/xd/research/research-expertise/researchers/index.cfm?personid=2834)
Mentor: Jonah Sacha, PhD  
Oregon National Primate Research Center/OHSU: Division of Pathobiology & Immunology

With more than 20 million dead and greater than 30 million currently infected with HIV, the development of a prophylactic HIV vaccine is a top global health priority. However, despite 30 years of intense research there is no vaccine and new approaches are urgently needed. Viral sequence diversity is the Achilles' heel of traditional vaccine approaches to HIV and poses one of the greatest hurdles to vaccine development. The Sacha laboratory aims to determine which antigens should be targeted to overcome the formidable obstacle of HIV viral sequence diversity. In addition to HIV vaccine studies, the Sacha laboratory is embarking on a new line of research investigating the role of macrophages as latent reservoirs of HIV during highly active antiretroviral (HAART) treatment. The successful candidate will be expected to actively participate both experimentally and conceptually in these experiments and will be included on any publications arising from their time in the laboratory.

Learn more about the Sacha lab: http://www.ohsu.edu/vgti/Sacha_Lab/Welcome.html

Mentors: Sergio R. Ojeda, DVM/Hollis Wright, PhD  
Oregon National Primate Research Center/OHSU: Division of Neuroscience

Sergio Ojeda and his collaborators seek to understand the process by which the brain controls the initiation of mammalian puberty. An important goal in their laboratory is to gain insights into the molecular and genetic mechanisms underlying deranged sexual development, particularly sexual precocity and delayed puberty of cerebral origin. Ojeda's team focuses on identifying molecules responsible for the interactions that occur between neurons and glial cells in the hypothalamus, a region in the base of the brain that controls several bodily functions, including hormone secretion, reproduction, response to stress, feeding and sex behavior. One group of hypothalamic neurons produces gonadotropin-releasing hormone (GnRH), a substance that controls the secretion of reproductive hormones from the pituitary gland.

The Ojeda lab uses cellular, molecular, genetics and systems biology strategies, in addition to high-throughput approaches and computational biology methods to develop three interrelated concepts: 1) That mammalian puberty is controlled by genetic networks that, operating within different cell contexts in the neuroendocrine brain, coordinate the activity of GnRH neurons at puberty, 2) That these networks are controlled at the transcriptional level by a repressive mechanism exerted by discrete subsets of gene “silencers”, and 3) That this transcriptional regulation is under epigenetic control, i.e., a mechanism by which environmental factors (such as nutrition, man-made chemicals, changes in light/dark cycle, etc.) regulate gene activity without modifying the actual sequence of the encoding DNA. Dr Hollis Wright, a postdoctoral fellow in Ojeda’s lab, has a PhD degree in bioinformatics and this allows him to implement and develop a variety of computational biology methods that he uses to gain novel insights into the biology of the pubertal process and study the behavior of the genetic networks involved in the epigenetic and transcriptional control of puberty. The lab seeks interns interested in exploring and implementing bioinformatics and systems biology methods that can be used to analyze the large and diverse data sets derived from the study of this important biological process.

Learn more about research in the Ojeda lab at http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/sergio-ojeda.cfm
Mentor: Matthew Ford, PhD  
Oregon National Primate Research Center/OHSU: Division of Neuroscience  

The primary interest of the Ford laboratory is polydrug abuse; alcohol and nicotine specifically. We are studying this co-abuse issue with a combination of self-administration and drug discrimination procedures. From the drug discrimination angle we have been studying how alcohol and nicotine may be interacting at the level of their subjective drug effects, and have identified dual mechanisms of overshadowing and potentiation that occur (see [http://www.ncbi.nlm.nih.gov/pubmed/22763667](http://www.ncbi.nlm.nih.gov/pubmed/22763667)). We are now undertaking additional studies to explore the receptor mechanisms and brain loci involved in nicotine’s ability to potentiate the ethanol cue. As far as self-administration, we are developing a model of concurrent oral intake of both drugs, and have uncovered some interesting findings that are consistent with the discriminative stimulus findings (mainly, that nicotine enhances ethanol intake as would be expected based on epidemiological evidence from human co-abusers). So far our studies have been in mice, but we are in the process of developing an e-cigarette procedure for nicotine delivery in cynomolgus macaques to facilitate the study of nicotine addiction as well as alcohol-nicotine co-abuse.

Additional laboratory projects include:

1) Interactions between stress and excessive ethanol intake. We have developed a schedule-induced drinking model in mice and are looking at the stress axis mediators that are associated with excessive intake and elevated blood ethanol concentrations (see [http://www.ncbi.nlm.nih.gov/pubmed/23827168](http://www.ncbi.nlm.nih.gov/pubmed/23827168)). We will be looking at pharmacological interventions to alleviate stress-induced drinking in the future.

2) Self-administration and discrimination of methamphetamine. Our laboratory has been working with collaborators in developing an oral intake model of methamphetamine (see [http://www.ncbi.nlm.nih.gov/pubmed/22280875](http://www.ncbi.nlm.nih.gov/pubmed/22280875)). We are now using a combination of self-administration and drug discrimination procedures to identify receptor mechanisms with promise for therapeutic intervention. Some preliminary findings from discrimination work are pointing to the involvement of nicotinic and muscarinic receptor compounds.

3) Therapeutic intervention for excessive alcohol self-administration in macaques. We are investigating the role of gene therapy following delivery of adeno-associated virus directly into reward-related brain areas as well as pharmacotherapy via oral dosing with a novel compound with activity at GABA<sub>A</sub> receptors.

Fellowship candidates should anticipate working directly with mice or macaques, analyzing large data sets of behavioral data, be computer literate, and have budding interests in animal behavior, pharmacology, and addiction research.

Learn more about the research being conducted by Dr. Ford  
[http://www.ohsu.edu/xd/education/schools/school-of-medicine/academic-programs/graduate-studies/faculty/grad-studies-faculty.cfm?facultyid=815](http://www.ohsu.edu/xd/education/schools/school-of-medicine/academic-programs/graduate-studies/faculty/grad-studies-faculty.cfm?facultyid=815)
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: Cynthia Bethea, PhD
Oregon National Primate Research Center/OHSU: Division of Neuroscience

The Bethea lab studies the effects of steroid hormones in various neural systems in male and female macaques, as well as the neurobiology of stress resilience in macaques.

Serotonin and norepinephrine neurons in the midbrain regulate aspects of mood with pathologies such as depression and anxiety. In addition, they play a role in vigilance and aggression. The serotonin neurons are located in a midbrain region called the raphe nucleus and the norepinephrine neurons are located in a midbrain region called the locus ceruleus. Currently we are working with NHP models of female depression, stress-induced infertility, and male aggression. The selected intern will use immunocytochemistry to examine functional aspects of either serotonin or norepinephrine neurons in one of our projects. He or she will also learn image analysis to quantify the immunocytochemical signal of the neurons. Data will be organized in Excel and entered into a statistics program for analysis and graphing.


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.