# OREGON NATIONAL PRIMATE RESEARCH CENTER

# UNDERGRADUATE SUMMER FELLOWSHIPS

## *Position Descriptions*

## Summer, 2020

*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: Rita Cervera-Juanes, PhD**
*Oregon National Primate Research Center/OHSU: Genetics Division*

The Cervera-Juanes lab studies genetic and epigenetic contributions to disease, including the epigenetic risk to develop a certain disease as well as how the epigenome is modified by the disease, thus further contributing to its progress. Recent work in the Cervera-Juanes lab has identified pre-existent DNA methylation signals that predict future alcohol consumption, as well as those that are induced by chronic alcohol consumption. The lab is interested in further understanding the role these regulatory regions and associated genes plan in modulating neuroadaptations and ultimately driving addictive behaviors, such as dependence and relapse. Other work seeks to decipher the epigenetic mechanisms underlying the heritability of risk for substance use disorders (SUD), the goal being to use pharmacological or gene-mediated interventions to modulate the function of novel genes and regulatory mechanisms causative of SUD. Preliminary work in this direction is promising and shows that by modifying these novel targets, either pharmacologically or by using knock-down approaches, the alcohol intake in mice is modified. The long-term goal is to test these promising targets in non-human primates.

*The student will learn general molecular techniques including DNA and RNA isolation, bisulfite conversion, reverse transcription, PCR and real-time PCR, immunohistochemistry, next-generation sequencing library preparation and data analysis.*

*Learn more about Dr. Cervera-Juanes's research at http://www.ohsu.edu/people/ritacerverajuanes/afe04aabe76c1a47772e1820670791e2*

**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: Victor DeFilippis**
*Vaccine & Gene Therapy Institute/OHSU*

Research in the DeFilippis laboratory focuses on understanding the innate immune response and ways in which it can be pharmacologically harnessed to provide clinical benefits. Innate immunity is the most rapid cellular response to microbial infection and cellular dysfunction that leads to secretion of cytokines and chemokines that ultimately direct and coordinate adaptive immune responses. These are crucial for establishing tissue states that are refractory to infection, eliminating diseased tissues such as tumors, and enabling wound repair. To investigate this the laboratory employs a combination of sophisticated molecular, cellular, and small animal models to test hypotheses and develop new research tools. As such, opportunities are available for exploring diverse phenomena using a variety of methods.

*The teacher/intern will perform cellular and molecular studies focused on examining mammalian innate immune signaling processes and phenotypes. These primarily involve the type I interferon response as induced by microbial and chemical stimuli. For this there will be diverse opportunities to utilize cell engineering techniques including CRISPR-based gene knockout and lentivector-mediated gene knock-in, PCR-based mRNA expression analysis, immunoblotting, immunofluorescence, and ELISA.*

*Learn more about Dr. DeFilippi's research at* https://www.ohsu.edu/vaccine-gene-therapy-institute/victor-defilippis-phd

**Mentor: Matthew Ford, PhD**
*Oregon National Primate Research Center/OHSU: Division of Neuroscience*

A 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). 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.

Another research interest is 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 $GABA_A$ receptors.

Fellowship candidates should anticipate working directly with mice or observing 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/research/centers-institutes/onprc/scientific-discovery/scientists/Matthew-Ford.cfm

**Mentors: Antonio Frias, MD; Victoria Roberts, PhD**
*Oregon National Primate Research Center/OHSU: Division of Reproductive & Developmental Biology and OHSU/Dept. of Obstetrics & Gynecology/Division of Reproductive & Developmental Sciences*

The overall goal of the Frias laboratory is to understand normal pregnancy, and to develop tools that will identify pregnancies that are compromised by placental dysfunction. Specifically, the Frias 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 and structure. They will have the opportunity to participate in studies designed to 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. Frias' research at*
*http://www.ohsu.edu/people/antoniofrias/ae70176c957642679890a7dccb3f000d*

**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](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 Sciences*

Premature or preterm birth (births at less than 37 weeks gestation) remains the leading cause of neonatal morbidity and mortality. Despite improvements in neonatal intensive care over the past few decades, premature infants still have higher rates of childhood learning disabilities, cerebral palsy, sensory deficits and respiratory illnesses than infants born at term, with half of all childhood neurological disabilities associated with preterm birth. The negative health and developmental effects of preterm birth often extend to later life resulting in enormous medical, educational, psychological and social costs (estimated to exceed $26 billion annually). Intrauterine infection is a leading cause of early premature births and our laboratory is interested in understanding the effects of infection and premature birth on the developing brain and in identifying therapies that may delay premature birth and improve the health of affected infants. We also have projects investigating novel agents to prevent cerebral palsy and are involved in the multi-center collaboration studying the effects on the immature brain of Zika virus infection during pregnancy. We utilize important and clinically relevant non-human primate pregnancy models that are translational to human health and disease with the aim of reducing the burden of perinatally-acquired disease and disability, particularly neurological and developmental disorders.

*Students will participate in studies that contribute to our understanding of how intrauterine infection and hypoxia contributes to neuroinflammation or abnormal development in the immature brain and other organ systems, and to evaluate the efficacy of potential new treatments to prevent this injury. Methods used will involve tissue histology, immunohistochemistry and microscope technique; western blot and ELISA to determine expression of proteins of interest; and assays to measure the concentrations of therapeutic agents.*

*Dr. Kelleher's webpage is under construction.*

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

A major focus for the Kroenke laboratory is to understand the cellular and biophysical underpinnings of image contrast that can be observed by magnetic resonance imaging (MRI). One particular MRI procedure, termed "diffusion weighted MRI" can potentially be used to characterize changes in the shapes of neurons as they form new circuits in the developing brain, or as they respond to environmental stressors such as exposure to alcohol. A firm understanding of the cellular-level determinants of MRI signal intensity could make it possible to monitor cellular changes with development and pathology in living individuals rather than requiring analysis using a microscope on post mortem tissue. The project available for the summer of 2020 will involve performing histological measurements on tissue that has previously been characterized by MRI. The histological measurements will be quantitatively compared to the MRI data to assess the accuracy of the proposed mathematical relationship, which will be of value in guiding the interpretation of future diffusion weighted brain MRI measurements.

*Students will learn immunohistochemical staining procedures, and quantitative image analysis methods. Depending on interest, students may be exposed to MRI theory and practical applications, and may learn image analysis computer programming skills.*

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

**Mentor: Anna Roe, PhD**
*Oregon National Primate Research Center/OHSU: Division of Neuroscience*

How does the brain produce perception, thought, and behavior? The laboratory of Anna Roe 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. Roe at*
http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/Anna-Wang-Roe.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 and Gene Therapy Institute; Oregon National Primate Research Center (Division of Pathobiology); OHSU*

An estimated 15% of human cancers are associated with viral infection. Members of the gamma-herpesvirus family, such as EBV and KSHV, are linked to AIDS-associated non-Hodgkin's lymphomas and other B cell malignancies. The molecular mechanisms driving lymphomagenesis are not well defined, presenting a major challenge in treating these diseases. A major focus of the Skalsky laboratory is to understand how g-herpesviruses interact with post-transcriptional regulatory processes and how these processes shape the viral life cycle, modulate host-virus interactions- specifically, cytokine signaling and the development of antiviral responses, and contribute to viral pathogenesis. Current research projects include characterizing immune signaling pathways manipulated by small, non-coding, regulatory microRNAs during herpesvirus infection, and elucidating ncRNA functions in g-herpesvirus latency and reactivation using in vitro and in vivo models.

*Available summer projects will involve characterization of miRNA targets using reporter assays, gene expression analysis (real-time PCR), and/or bioinformatic methods. Students will be involved in all steps of experimental set-up, data collection, and analysis. An interest in biology, virology, chemistry, and/or computer science is preferred.*

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

**Mentor: Jeff Stanton, DVM, MA, DACLAM**

*Oregon National Primate Research Center/OHSU: Division of Comparative Medicine, Education & Training Unit*

Dr. Stanton, Head of the Education & Training Unit, is a laboratory animal veterinarian within the Division of Comparative Medicine (DCM) at the Oregon National Primate Research Center (ONPRC). DCM is responsible for the veterinary care and management of all animals on the ONPRC campus. There are currently 8 clinical veterinarians and 2 surgical veterinarians who provide veterinary care for the nonhuman primate (NHP) population. Veterinary care includes the provision of routine preventive medicine, management of animals with clinical illness, surgery, and the provision of research support to Principal Investigators utilizing NHP animal models. DCM veterinarians also lead research projects in a number of areas aimed at improving animal health and welfare. Projects include, but are not limited to, refining animal models, effects of sedatives and anesthetics, assessing and improving clinical and/or surgical treatment efficacy, the impact of gut microbiome on NHP animal models, and assessing the impact of social housing status on the NHP animal model.

*Students will learn a variety of research skills depending on the research project in which they participate. These may include data analysis, animal observation using video recordings, design and use of scoring systems, oral communication and presentation skills.*

*Learn more about animal care at ONPRC at https://www.ohsu.edu/xd/research/centers-institutes/onprc/caring/index.cfm*

**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 stress) during gestation on offspring brain development and behavior. The primary focus is examining the influence of the metabolic and dietary environment 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 impact of exposure to maternal obesity and high-fat diet consumption during the perinatal period on the behavior, and physiology of the developing offspring using a non-human primate model.

*Students will learn about the fields of behavioral neuroscience and developmental origins. Specifically, students will learn about non-human primate behavior, 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 the Frueh lab to design novel vaccine candidates using the cytomegalovirus (CMV) vaccine platform in search of an effective malaria vaccine, and have implemented an insectary to allow for the generation of mosquito stages of the malaria parasite and other mosquito-based research. Our work ranges from completely in vitro (in a test tube) to using mouse and non-human primate (NHP) models (in vivo) and working with mosquitoes. Current projects include: developing a NHP model for the relapsing human malaria, Plasmodium vivax; discovering antibodies that act within liver cells to target parasites; testing a vaccine candidate in NHPs; addressing limitations in our understanding of hypnozoite (dormant parasites in the liver) formation; and learning how gametocytes (sexual stage transmitted to mosquitoes) are infectious after relapse malaria.

*Students will have the opportunity to learn the basics of malaria culture, mosquito rearing and experimental techniques, 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

**OPERM** (Oregon Permanent Contraception Research Center)
The goal of the Oregon Permanent Contraception Research Center (OPERM) is to identify and develop methods of non-surgical permanent contraception for women. In support of OPERM, this internship will focus on performing cell culture analysis with candidate reagents and immunohistochemistry (IHC) to detect changes in treated tissues.

*The intern will work collaboratively in a team science setting and develop skills in aseptic cell culture, culture medium preparation, bright filed imaging on a microscope, tissue sections preparation for basic cell structure labeling and immuno-detection techniques. This position does not involve animal work.*

*Learn more about OPERM at https://www.ohsu.edu/oregon-permanent-contraception-research-center*