

# RESEARCH INTERESTS OF BIOLOGY FACULTY AND THEIR SENIOR PROJECT STUDENTS

Eleven faculty members in the Biology Department will be advising senior project students during 2020-21. They are: Drs. Casey Bradshaw-Wilson, Lauren French, Brad Hersh, Tricia Humphreys, Mahita Kadmiel, Ron Mumme, Margaret Nelson, Lauren Rudolph, Yee Mon Thu, Matthew Venesky, and Lisa Whitenack. The research opportunities available in their laboratories, and the types of research activities that their senior project students typically pursue, are described below. (Drs. Catharina Coenen and Becky Dawson will not be advising senior research students during 2020-21.)

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## **CASEY BRADSHAW-WILSON**

My research interests are mainly in freshwater ecology and herpetology, but I have worked on more general ecology projects with students as well (outside of aquatics). I also have interests investigating impacts of habitat loss, fragmentation and alteration in salamanders movement patterns and abundance. My personal research investigates the impacts of an invasive fish species (Round Goby) on native fauna (aquatic macroinvertebrates, fishes, amphibians and mussels). Comp projects often involve field studies in the fall and follow-up lab experiments and data analysis during winter. Given my background in wildlife and fisheries, comp students could have a wide range of topics in the realm of ecological research.

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## **LAUREN FRENCH**

My research interests fall under the general heading of Cellular and Molecular Neuroscience. I am interested in exploring what makes individual neurons unique from one another, how they “talk” to each other to transmit information in the nervous system, and how drugs and toxins affect their function. The projects in my lab involve both neurophysiology and molecular biology techniques.

Pharmacology is critical to the study of the nervous system; to learn how proteins such as ion channels contribute to normal function, and to discover the mechanism underlying pathological conditions. One project involves a genus of hunting snails whose venom is very complex and potent, acting solely on the prey’s nervous system. Many of the snail venom compounds have applications in medicine as well as in basic bench research. My goal is to find pharmacological agents that target some specific calcium and potassium ion channels in order to further understand the role these proteins play in the nervous system.

Another project involves a type of ion channel called the BK channel and its possible role in the pathology of Alzheimer’s disease. The activity of this channel has been shown to be inhibited by a protein called Amyloid Beta. I’m interested in characterizing this interaction and discovering how the peptide affects the channel behavior.

Another line of research involves the crayfish as a model organism to study adult neurogenesis. We used to believe that the nervous system was only capable of producing new nerve cells during development, but we now know that neurogenesis is ongoing throughout animals’ lifetime in certain areas of the brain. I am interested in studying the mechanisms underlying this process, and how it can be promoted or inhibited.

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## **BRAD HERSH**

Though virtually all cells in an animal contain the same DNA sequences, different cell types (for example, muscle cells and nerve cells) have distinct physical properties. These differences are achieved during growth and development of the organism by switching on and off specific sets of genes within the common DNA sequence. Research in my lab encompasses two main areas:

1) Identifying and characterizing the DNA sequences that control when, where, and at what level gene expression is switched on and off in the developing animal body. The long term goal of this research is to understand the mechanisms by which Hox proteins, involved in shaping the head-to-tail patterning of all animals, regulate their target genes. We use the fruit fly, *Drosophila melanogaster*, to examine the DNA sequences that respond to the Hox protein Ultrabithorax and either activate or repress gene expression in the fly hindwing. We are also interested in identifying the genes, possibly targets of Hox proteins, that are important for differences between insect species to understand how evolutionary changes occur in the developmental processes that produce animal shape.

2) Characterizing the role of gap junction proteins in the immune response of the fly to various pathogens. The long-term goal of this research is to understand how cell-cell communication influences the innate immune response. The fly has genes for eight gap junction subunits, and we use molecular techniques to increase or decrease their activity and determine the effect on survival of flies exposed to bacterial pathogens or parasitoid wasps.

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## **TRICIA HUMPHREYS**

My research focuses on the obligate human pathogen *Haemophilus ducreyi*, which is most well known for causing chancroid, a sexually transmitted disease that is prevalent in resource-poor areas of the world. Previously, chancroid was of interest because it is associated with an increased risk of transmission and acquisition of the human immunodeficiency virus (HIV). More recently, *H. ducreyi* has been linked to limb ulcers in children in the Pacific Island Countries and Territories (Papua New Guinea, Solomon Islands, Vanuatu, Samoa, etc.). Students in my lab have studied the evolutionary relationships among isolates of *H. ducreyi*, differences in antibiotic susceptibility among isolates, and the potential to use essential oils as treatment for chancroid. My students are also interested in why more men than women have chancroid and they are trying to find out the biological basis for this sex bias. Furthermore, we are interested in figuring out why this organism that was previously thought to be only sexually transmitted is apparently being transmitted by some other, unknown, route. We address these questions with a variety of lab techniques, including DNA sequencing, classic bacteriology assays, bioinformatics, biochemical approaches, and work with biological vectors of disease.

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## **MAHITA KADMIEL**

Improved understanding of the molecular mechanisms of human diseases could lead to better diagnostics and treatment options. My research focuses on understanding how hormones work at molecular and cellular levels to coordinate various activities throughout the body. The hormones I am most interested in are glucocorticoids and their interactions with sex hormones (estrogen, progesterone and androgen).

Glucocorticoids (GCs) are primary stress hormones routinely used in clinical care for inhibiting inflammation (calming down the immune system) and for stopping the growth of new blood vessels. For example, GCs are used to treat diseases such as leukemia, asthma, eye infections, and diabetic retinopathy. Although synthetic GCs

are life-saving drugs, there is a down side to them. Long-term use or high doses of glucocorticoids can cause adverse effects such as osteoporosis (brittle bones), cataract (cloudy lens), and glaucoma (optic nerve damage). The specific signaling pathways triggered or altered by GCs responsible for the beneficial as well as adverse events in different tissues of the body are not completely discovered. I am interested in elucidating the molecular actions of GCs in the eye using human cell lines from ocular tissues such as the retina and the cornea, and genetic mouse models of human diseases. Previous work has demonstrated that GC signaling through its receptor, the glucocorticoid receptor, is essential in mice for maintaining normal immune environment and vasculature in the eye and for the normal development of the eye. My current research plan is to investigate the molecular mechanism of GCs in the eye under systemic diseases or conditions such as diabetes and hormonal imbalances caused by menopause or endocrine disrupting chemicals in the environment.

A variety of techniques are employed in my lab including mammalian cell culture, cell death and cell viability assays, migration assays, dissections, RNA extraction, reverse transcription, quantitative polymerase chain reaction (PCR), signaling pathway analyses using bioinformatic programs, protein purification, western blots, tissue histology, immunofluorescence, microscopy, and imaging.

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## **RON MUMME**

My primary research interests are animal behavior, behavioral ecology, and evolutionary biology. Although most of my own research involves field work with birds, my senior project students have pursued laboratory and field projects on a wide variety of organisms, including insects, fish, amphibians, reptiles, birds, and mammals. For examples of senior projects conducted by my students, see <https://sites.google.com/a/allegheeny.edu/ron-mumme/student-research>

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## **MARGARET NELSON**

I am interested in the way in which signal transduction pathways allow cells to interpret and respond to external cues during development. My research largely focuses on the role that the FbxA protein plays in the development of the eukaryotic social amoeba *Dictyostelium discoideum*. FbxA is a member of an evolutionarily conserved protein family that regulates cell behavior by targeting specific components of signal transduction pathways for degradation. Malfunctions in this degradation system have been implicated as a potential causative agent in several human diseases, including Alzheimer's disease, Parkinson's disease, and cancer.

One current area of interest is a possible role for FbxA in response to the signal molecule DIF, a chlorinated hexaphenone that acts to steer cells towards a specific subset of cell fates, in part by altering the subcellular localization of several transcription factors. We have also recently begun to explore a potential role for FbxA in regulation of the cell cycle, an effect that seems to depend on FbxA-mediated ubiquitination and degradation of the cAMP phosphodiesterase RegA, and consequent alteration in the activity of PKA (cAMP-dependent protein kinase). The RegA-PKA circuit appears to be part of an evolutionarily ancient stress response mechanism that originally led to encystation of amoebae and has, more recently, been adapted to serve roles in differentiation and chemotaxis.

Data from former comp projects suggest that the FbiA protein may be another target of FbxA-mediated ubiquitination and degradation. Proteins homologous to FbiA are found in a wide array of eukaryotes, including fungi, plants, *C. elegans*, *Drosophila*, mice, and humans. The function of these FbiA homologues is, however, unknown. Hence, further characterization of FbiA's role in *Dictyostelium* development (as well as that of its close homologue FbiB) may shed light on the function of another conserved protein family.

Depending upon the project you choose, you might employ any of the following techniques: restriction digests, agarose gel electrophoresis, plasmid & genomic DNA preps, PCR, introduction of recombinant DNA molecules into cells (bacteria, *Dictyostelium*), cell propagation & sterile technique (bacteria, *Dictyostelium*), protein purification, protein gels, Western blots, histochemical staining, spectrophotometric monitoring of  $\beta$ -galactosidase reporter activity, phase contrast microscopy, immunofluorescent microscopy, bright-field microscopy (stereozoom scope), or digital photography.

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## **LAUREN RUDOLPH**

My research interests are in the field of neuroendocrinology-the relationship between hormones and the nervous system. I am interested in how steroid hormones (e.g., testosterone, estradiol) control the development and maintenance of the structure and function of neural systems systems that regulate behaviors in rodents. One nucleus I study is the spinal nucleus of the bulbocavernosus (SNB), a sexually dimorphic motor nucleus found in male rodents and involved in reproduction. Features of the SNB such as cell number, size, and dendritic lengths develop and are maintained by androgens (e.g., testosterone, dihydrotestosterone). Steroid hormones can act through a variety of mechanisms, as transcription factors through intracellular receptors, and at the cell membrane through rapid pathways. Work in my lab is involved in understanding how steroid hormones act at the membrane to modulate various aspects of the SNB neuromuscular system including cell morphology, steroid receptors, and behaviors mediated by this system.

In addition to these specific research interests, I am interested broadly in sex differences, the role of hormones in a wide range of behaviors across species, and interactions between the nervous, endocrine, and immune systems.

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## **YEE MON THU**

All cells have a capability to propagate themselves. Before they can divide, cells must first duplicate the genetic information with great accuracy. This process is made possible by a highly coordinated structure, known as the replication fork. The replication fork has to copy the genome in a timely and accurate manner. Failure to do so can have deleterious outcomes, such as mutations, DNA damage and/or chromosomal rearrangements. Any condition, which compromises the function of the replication fork is generally referred to as replication stress. For example, ultra violet irradiation or genotoxic chemicals can damage the template DNA strands and introduce replication stress when cells are copying their DNA. Similarly, uncontrolled proliferation in cancer cells also exerts stress on the replication machinery. Replication stress is often a prelude to genome instability and cancer. It is also a “chronic” condition symptomatic for many cancer cells. This suggests that cells especially those that are cancerous can manage replication stress to a certain degree. Previous research suggests that cells can keep on proliferating in the presence of replication stress, if the damage is within the limit of cells’ ability to repair. However, if the damage is beyond repair, cells must undergo death to prevent propagation of a faulty genome. Much less is understood how the fine line between tolerance and cell death decision is determined.

My research interest lies in the regulation of specific post-translational modifications (PTM), namely ubiquitin and SUMO (small ubiquitin like modifier), when replication stress ensues. Previous work has shown that these PTMs influence the balance between replication stress tolerance and cell death. Using biochemistry, bioinformatics, genetics and molecular biology, I aim to further under the mechanisms which defy replication stress and the role of ubiquitin/SUMO axis in this context. I use *Saccharomyces cerevisiae* (budding yeast), an

organism highly amenable for genetic manipulation, and also use mammalian cell culture system to address my research questions. Techniques used in my research lab include, but not limited to, PCR, gene editing techniques, molecular cloning, immunofluorescent microscopy, cell culture techniques, Western blot and flow cytometry. Elucidating these processes will bring us one step closer to understanding how cancer cells live with constant replication stress and genome instability, thus revealing the “Achilles’ heel” of cancer.

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### **MATTHEW VENESKY**

The emergence of infectious diseases is one of the largest threats to human and wildlife health. The overall aim of my research is to better understand the consequences of parasite infection on wildlife and the cascading effects that parasites have on species interactions. I take a multidisciplinary approach to studying host-parasite interactions and I integrate molecular, physiological, and ecological approaches in my research. Currently, most of the research in my lab falls under three general themes within disease ecology: (1) understanding the relationship between host physiology and disease risk, (2) identifying host traits that reduce, or amplify, pathogen transmission, and (3) surveying natural populations of aquatic vertebrates for parasites. My laboratory is equipped to study various aquatic pathogens; however, most of my students work with amphibians and the fungal pathogen *Batrachochytrium dendrobatidis* (“Bd”). Bd is one of the deadliest organisms on the planet and it is linked to amphibian declines and extinctions on every continent except Antarctica.

In addition to studying wildlife diseases, I have expertise in ecology and herpetology (the study of amphibians and reptiles) and I can oversee comp projects that fall under numerous categories in these fields.

Please visit my website for more info about past and current research projects as well as my own research interests: <https://sites.google.com/site/veneskylab/>

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### **LISA WHITENACK**

My general research interest is on the evolution of shape. My main focus is on functional morphology, the relationship between form and function, in extinct and extant organisms. My primary tool for this is biomechanics, the application of engineering techniques to determine how organisms perform mechanical functions, the design of morphological systems, and the relationship of these to the organism's environment. I also use shape as a diagnostic tool for species delimitation in the fossil record via geometric morphometrics, as well as determining paleoecological relationships. My research has historically concerned teeth and jaws of sharks and other fishes, the biomechanics of marine gastropods and their predators, and jumping mechanics of salamanders. Potential comp projects in my lab could concern invertebrate or vertebrates; extinct or extant; biomechanics, morphometrics, or paleoecology. Previous comp topics in my lab include sexual dimorphism in macaque monkeys and great horned owls, northern pike bite force, bluegill feeding kinematics, and biomechanics of various aspects of locomotion in fishes, lizards, frogs, salamanders, and humans. A complete list of comps from my lab can be found at: <https://sites.google.com/a/allegHENY.edu/whitenack/student-research>

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