OFFICE OF THE VICE PROVOST FOR RESEARCH

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Role of early developmental daylength of subsequent timing of reproduction and Migration

Ellen Ketterson, Department of Biology

Genetic and epigenetic mechanisms determine when animals migrate and breed and thus their ability to keep pace with our rapidly changing environment. This project will test the hypothesis that early developmental day length sets the day length at which an adult animal will migrate and breed by rearing dark-eyed juncos (*Junco hyemalis,* a songbird) from a high latitude population on shorter days and individuals from a low latitude population on longer days, and comparing the populations for physiological and epigenetic indices of migratory and reproductive timing. The researchers predict that animals that develop under longer day lengths will require longer days to exhibit gonadal growth and to activate genes associated with migration and reproduction. If instead timing differences between populations are fixed (genetic), population differences in timing will persist despite the altered developmental environment.

The interplay between queenliness, the honey bee microbiome, and colony health

Irene Newton, Department of Biology

The honey bee (*Apis mellifera*) is viewed by many as modern agriculture's most economically beneficial insect because of the pollination services of the thousands of foraging workers in each colony. Accordingly, there has been a focus in recent years on understanding how honey bee-associated microbial communities support worker function. With the use of meta-'omics techniques, the gut microflora of honey bee workers has been described as a consistent group of bacterial clades that are dominated by Gamma-proteobacteria, Firmicutes, and Actinobacteria. Basic characterization of these microbial groups has led to speculation about their role in honey bee health and whether they are responsible for provisioning nutrients to workers or assisting in the breakdown of plant-derived carbohydrates, as is the case for other insect-associated microbes. Although we are just starting to understand the functions of bee-associated microbial species, we do know that they can interact with each other *in vivo* and *in vitro.* For example, within the ileum of the honey bee, three distinct bacterial genera, *Gilliamella, Snodgrassella,* and *Lactobacillus*, form a biofilm that adheres to the lining of the host's digestive tract. Furthermore, the lactic acid bacteria found in the honey bee gut promote each other's growth when they are co-cultured, suggesting the potential for mutualistic or syntrophic interactions within living workers. These examples are intriguing and suggest that the microbial world inside a bee's body is complex and intertwined with the host's systems.

However, astonishingly little is understood about how honey bee associated microbes interact with the honey bee queen and how these interactions impact colony phenotype and function.

In 2015, this proposal's senior personnel published the first comprehensive characterization of the honey bee queen microbiota. Before that publication, only the microbiome of workers has been described while little to nothing was known about the bacterial communities that are associated with queens, even though queen health and proper function is central to colony productivity. In the sequencing study, using 16S rRNA gene amplicons, the researchers characterized the bacterial community that is associated with the digestive tracts of developing honey bee queens and their attending workers. Importantly, honey bee queens were tracked as they moved through the many host colonies that queens experience during their commercial production in North America (i.e., queens are hosted first by colonies that rear them as larvae, then by colonies as they mate as newly emerged adults, and finally by the host colonies when they are mature egg-laying queens). It was discovered: 1) that queen microbiomes are consistently and significantly different from the worker populations who care for them, 2) that queen guts may be colonized by bacteria from worker glands, 3) that queen microbiomes are dominated by enteric bacteria early in life but are comprised primarily of alpha-proteobacteria at maturity, and 4) that queens vary significantly in their microbial communities. This research argues that, out of all of the recognized challenges faced by honey bee populations, queen failure is the least well understood of the stressors that have been pursued by the scientific community. However, these studies directly address the health and productivity of honey bee queens. Furthermore, the studies have strong potential to provide clarity about how queen microbiota can impact worker communities, and their ability to deal with colony-wide stressors, such as pathogens and poor nutrition. The researchers hypothesize that microbes play a critical role in the development of larvae into adult queens and the maintenance of their health as colony monarchs. This project will generate a metagenomics and transcriptomic dataset for honey bee queen guts and perform a preliminary study to identify if manipulation of queen diet is possible in the laboratory.

Timing and Duration of Androgen-mediated Protection After Spinal Cord Injury
Dale Sengelaub, Psychological and Brain Sciences

The pathophysiology of spinal cord injury (SCI) is complex, and after the initial injury a protracted period of progressive damage occurs, causing spreading of the lesion and further segmental destruction. We have previously demonstrated that after SCI, remaining spinal motoneurons undergo dramatic dendritic atrophy with concomitant behavioral deficits. Given that we currently cannot replace dead motoneurons, developing the ability to protect surviving motoneurons from secondary atrophy is an important goal. We have also previously demonstrated that treatment with testosterone is protective and/or therapeutic after SCI, protecting surviving motoneurons from dendritic atrophy as well as preventing atrophy in their target muscles. We will assess the feasibility of testosterone treatment as a potential therapeutic strategy in a spinal cord injury model in rats. We will determine if treatment with testosterone after SCI results in long-term restoration of motoneuron morphology and function, or if it is limited to the duration of treatment. We will also determine if treatment with testosterone after SCI must be administered immediately after injury or can be applied

effectively at later time points. We will assess behavioral function, motoneuron electrophysiological response, motoneuron number, motoneuron dendritic and somal morphology, muscle weight, muscle fiber cross-sectional area, as well as lesion volume and tissue sparing. We anticipate that testosterone treatment will prove to be a feasible, clinically relevant new therapeutic approach for SCI, protecting motoneurons from secondary effects of SCI, and resulting in a long lasting post-treatment restoration of central spinal circuitry. We will generate preliminary data to demonstrate feasibility/proof of concept for the use of estradiol as a neurotherapeutic agent after SCI in females. Following SCI, female mice show better recovery than males, improved motor function, reduced lesion size, increased white matter sparing, and earlier cytokine release and astroglial response. However, the potential effects of estradiol treatment on motoneurons after SCI are completely unknown. We will also generate preliminary data to demonstrate feasibility/proof of concept for the effects of gonadal steroids on propriospinal pathways that could potentially impact lower motoneuron morphology and function. The propriospinal neurons provide local and segmental input to spinal motoneurons, and are critically involved in motor reflexes, voluntary movement, and sensory processing. Furthermore, spontaneous functional recoveries after SCI have been mainly attributed to the plasticity of propriospinal neurons. However, the potential effects of treatment with gonadal steroids on propriospinal neurons after SCI are completely unknown.

What Public? Examining the Use of Social Media Metrics for Measuring Broader Impact in Science

Cassidy Sugimoto, School of Informatics and Computing

The objective of this project is to characterize the nature of the producers and audience of scientific discourse on social media. This work will develop large-scale algorithmic approaches for classifying and describing stakeholders participating in scientific discourse online, and analyze their demographics and communication patterns. The work is motivated by an increased availability of social media metrics and the use of these metrics in the evaluation of scholarship and allocation of scientific resources. Knowledge about who is generating traces of attention is a necessary factor in establishing the credibility of social media metrics and validating (or dismissing) the use of these indicators by science policy makers and administrators.

Assessment of genetic background and ecology on the efficacy of CRISPR-Cas9 gene drive and drive reversal safeguards

Michael Wade, Department of Biology

The goals of this project are to (1) assess the biological risks of the proposed use of molecular gene drives based on CRISPR-Cas9 genome editing technology to suppress populations of crop pests; and (2) evaluate the efficacy of drive reversal safeguards for halting the spread of a gene drive and preventing future propagation of unwanted drives. (Note that, if successful, these methods would also suppress populations of disease vectoring insects.) The researchers propose to construct gene drives and introduce them into populations of the flour beetle, Tribolium castaneum, a storage grain pest. This project proposes to develop gene drives for genes with a range of different effects on fitness ranging from small (eye color mutations) to large (male fertility genes). The project proposes to identify key factors governing the spread of

gene drives in randomly mating populations as well as in genetically subdivided populations comparable to regional agricultural fields. Genetic variation in target populations can affect drive efficacy, which depends on sequence homology between drive and target. In particular, natural sequences immune to drive (ITDs) mitigate population suppression by changing the relative fitness of driven genes. Because of genetic variation in the natural population, a drive and its safeguards engineered on a laboratory background will differ in its spread dynamics in a wild population. We proposed to develop gene drives on six genetically diverse backgrounds from South American, Africa and Asia. Some of these populations exhibit partial barriers to free reproduction with one another (e.g., Demuth and Wade 2007 a and b; Drury and Wade 2011; Drury et al. 2009; Drury et al. 2011.). We also proposed to investigate gene drives and their safeguards in varying nutritional and competitive environments and for their capacity to jump to other, closely related species in the genus Tribolium. Our results and methods will inform the development of guidelines for regulatory agencies charged with evaluating the likelihood of success of proposed drive releases.