RESEARCH STATEMENT – Joel Sharbrough

Cellular energy – a billion years of separate inheritance

The enzymes that carry out cellular respiration are distributed across two entirely distinct and separately inherited genomes, yet eukaryotic health and fitness is critically dependent upon their successful interaction. Moreover, maternally inherited cytoplasmic genomes rarely undergo sexual recombination and exist in dozens to thousands of copies per cell, while corresponding nuclear genomes are bi-parentally inherited, one or more copies from each parent, via sexual reproduction. My research investigates how, in the face of these fundamentally different genetic systems, mitochondria are able to successfully maintain the molecular machinery responsible for nearly the entire supply of cellular energy.

While the genes encoded by the mitochondrial genome play a critical role in mitochondrial function, the overwhelming majority of proteins (>1000) that function in the mitochondria are encoded by the nuclear genome and are directly affected by sexual reproduction. Using *Potamopyrgus antipodarum*, a New Zealand freshwater snail characterized by multiple separate transitions from obligate sexual reproduction to obligate asexual reproduction, I am comparing deleterious mutation accumulation in nuclear-encoded mitochondrial genes relative to genome-wide patterns in sexual vs. asexual lineages in collaboration with Dr. Kristi Montooth at University of Nebraska-Lincoln. Because the extent of mitonuclear coevolution in sexual *vs*. asexual lineages must ultimately be evaluated in terms of mitochondrial function, my Ph. D. advisor, Dr. Maurine Neiman, Dr. Montooth, and I have received a $189,998 award from the National Science Foundation to compare mitonuclear coevolution and oxygen consumption in extracted, living mitochondria from sexual vs. asexual lineages (role: co-author, Senior Personnel).

Our dedicated investigation over the past five years into genotype-phenotype connections in *P. antipodarum* has already uncovered astounding biology. For example, in 2016 we discovered that *P. antipodarum* underwent a relatively recent whole genome duplication, which has tremendous potential to affect cellular biology, including mitochondrial function (Sharbrough et al., 2017 *Am J Bot*). Even more recently, I discovered that *P. antipodarum* and its close relative *Potamopyrgus estuarinus* exhibit signs of intra- and inter-molecular mitochondrial recombination, a process thought to be rare or absent from bilaterian mitochondrial genomes. Mitochondrial recombination in *Potamopyrgus* appears to be associated with a genome architecture that is remarkably reminiscent to that of chloroplast genomes, and my experience with plant organelle genomes as a postdoctoral researcher in the Sloan lab opened my eyes to this astounding possibility. Though often neglected in animal mitochondrial research, mitochondrial recombination has tremendous potential to influence the evolution of mitochondrial genomes and mitochondrial function. In particular, we suspect this recombination activity is playing a role in DNA damage repair, but over evolutionary time, it may also aid in the maintenance of separate inheritance of cytoplasmic genomes by facilitating the removal of deleterious mutations.

At St. Edward's University, I will continue to investigate cytonuclear co-adaptation in species, like *P. antipodarum*, whose unique reproductive systems and life histories can tease apart the co-dependency and separate inheritance of nuclear and cytoplasmic genomes. Taking particular advantage of the Wild Basin Creative Research Center, I will engage undergraduates in research projects relating to the evolution of eukaryotic energy production and homeostasis, training them in techniques and methods including computational genomics, transcriptomics, population genetics, molecular and cellular assays of mitochondrial function, and even organismal function and fitness assays.