Application number/Title: 32339 - Investigation of the epistatic effects between the mitochondria, the Y-chromosome, and the nuclear genome in relation to health-related traits

Applicant PI: Professor Kenneth Fedorka

Application Institution: University of Central Florida, Orlando, USA

Keywords provided by the Applicant PI to describe the research project:
epistasis, longevity, mitochondria, y-chromosome

Application Lay Summary:

Because the mitochondria is solely maternally inherited, it does not experience selection in males. This allows for the accumulation of male-specific deleterious mutations on the mitochondria. Research on this phenomenon, termed "Mother's Curse", in Drosophila has shown evidence of mitochondria affecting longevity, fertility, and other traits in males. We aim to investigate these effects of the mitochondria in humans on traits such as longevity, fertility, as well as mitochondria-related diseases that disproportionately affect males, such as LHON. Furthermore, the Y-chromosome, being present only in males, is an ideal candidate for the location of compensatory mechanisms. Epistasis is the non-additive interaction between genetic elements. It is a largely neglected but very important part of understanding complex health-related traits such as longevity. Through our research we will be able to uncover new relationships between genes and health-related traits. We will also be able to investigate previously ignored sex-specific aspects of these traits, potentially allowing for more personalized treatment of future individuals. Finally, with mitochondrial replacement therapy having been approved in the United Kingdom, it is critical now more than ever to understand how mitochondria interact with other genetic elements in human complex traits. We will be using a statistical / bioinformatic approach to investigate the relationship between genetic elements and health-related traits. Specifically, we will examine how different types of mitochondria (haplotypes) affect traits differently in men than in women. This will include disease prevalence, specifically of sex-biased diseases such as LHON (Leber?s Hereditary Optic Neuropathy). Finally, we will examine whether other genetic elements, such as the Y-chromosome, might ameliorate the effects of the mitochondria on health-related traits. We would require the full cohort to maximize the power of the study, which would provide the most information.