CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Jessica H. Hui

Project Number

35671

Project Title

Do Lifespan Extending Drugs Reduce Mitochondrial DNA Mutations and Slow Muscle Aging?

Abstract

Objectives/Goals

Aging is a concern of our society as is the loss of muscle function in late life. Mutations of mitochondrial DNA (mtDNA) have been implicated in age-related muscle weakness. We hypothesized that rapamycin, a drug which increases mouse lifespan, might do so by reducing mtDNA mutations in mouse skeletal muscle.

Methods/Materials

We are using two approaches to measure mtDNA mutations in 22-month-old mouse skeletal muscles: 1) histological analyses for a loss of cytochrome c oxidase (cytOX) activity and 2) digital PCR analyses of mtDNA. We stained ten 10-micron thick muscle sections from 32 individual mice for cytOX activity. The number, length and cross sectional area of the abnormal fibers was measured in each section. MtDNA mutation analyses by digital PCR of the muscle samples are ongoing.

Results

We found 66 cytOX negative (cytOX-) muscle fibers from a total of 96,000 fibers examined, with an average of 2.13 affected fibers/mouse. When normalized to the volume of tissue examined, we found 0.0925 ± 0.012 cytOX- fibers in the control female mice versus 0.013 ± 0.010 cytOX- fibers in the rapamycin treated females. In performing a two-sample t-test, we found that the treated female mice contained fewer cytOX- fibers/tissue than female control mice at a p-level < 0.0001. We also found that six out of the eight rapamycin-treated females contained zero cytOX- fibers, while all eight female controls contained some cytOX- fibers. Males, however, demonstrated no difference between treated and non-treated male mice and even perhaps indicated a trend of increasing cytOX- fibers in rapamycin-treated males. In addition, we found that neither males nor females showed a statistically significant difference in cytOX- fiber region length between the male control and rapamycin-treated mice. From these same tissue samples, we are isolating DNA to perform digital PCR mutation analysis to measure the mtDNA deletion mutation frequency.

Conclusions/Discussion

Rapamycin reduces cytOX- fibers, but only in female mice and may even increase cytOX- fibers in males. Despite reducing the number of cytOX- fibers in female mice, rapamycin did not slow the growth of cytOX- fibers, suggesting that mutant mitochondria may be able to escape recycling. Lastly, we concluded that drugs used to treat age-related diseases and extend lifespan likely have sex-specific effects. DNA isolation for the digital PCR analyses is underway.

Summary Statement

By examining the effects of a known lifespan-extending drug, we found that reducing mitochondrial DNA mutations may be a source of slowing down muscle aging in mice.

Help Received

I would like to thank Dr. Wanagat for his mentorship and supervision in working in his lab at UCLA.