NATHAN SHOCK CENTERS OF EXCELLENCE IN THE BASIC BIOLOGY OF AGING

PILOT AWARDEE SPOTLIGHT

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2022 UAB NSC Pilot Award
Establishing mitochondrial dysfunction as a hallmark of ovarian aging

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How did you become interested in aging?
We developed a conditional knockdown of mitochondrial function in whole animal and discovered the overall aging phenotype in the mouse. This led to interest and a significant shift in our research focus on aging.

Briefly describe your project in non-scientific terms. What questions are you trying to answer?
The ovary is the first organ to age in the women's body, affecting fertility and driving overall health and disease in women. Increasing evidence supports that mitochondrial dysfunction plays a critical role in ovarian aging. In addition to natural ovarian aging in all women, premature ovarian insufficiency (POI) is reported in up to 2% of women. Notably, mutations in at least eight nuclear genes, including POLG1 (encoding mtDNA polymerase γ), known to function within mitochondria, are also reported in women with POI. However, it is unknown whether mitochondrial dysfunction is the cause or the consequence of aging in the ovary. The proposal will establish a mouse model for ovarian aging induced by mitochondrial dysfunction that will provide a valuable tool for translational research in human reproductive aging and longevity.

What previous research or experience informed the development of this proposal?
Previous research on understanding the role of mitochondria in health and disease, particularly our recent research in utilizing a ubiquitous knockdown of mitochondria in whole animal, led to the development of this proposal.

What's exciting about your project's potential impact?
Currently, there is no genetic model to study ovarian aging and longevity. The proposed studies will provide much needed experimental model for the study of aging in ovaries that can provide molecular, genetic, and preclinical data to target mitochondria for the prevention and/or intervention of ovarian aging and infertility in people.

If your project is successful, what is the next step?
Develop drugs to reverse or delay ovarian aging by restoring mitochondrial function in ovaries.

How has support from and collaboration with the NSCs helped further this project and/or your research overall?
The planned collaboration will help determine whole genome epigenomic and genomic changes to identify how mitochondrial dysfunction impacts ovarian aging. In addition, the collaboration will identify novel pathways involved in ovarian aging.