NATHAN SHOCK CENTERS OF EXCELLENCE IN THE BASIC BIOLOGY OF AGING

PILOT AWARDEE SPOTLIGHT

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2021 San Antonio NSC Pilot Award
Biology of skeletal muscle aging: Therapeutic potential of FGFBP-1 in preventing sarcopenia

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How did you become interested in aging?
Given their druthers, most people would opt for long and healthy life. However, aging itself is a driver of common chronic conditions and diseases. As I grew up, I saw my grandparents suffering from age-associated metabolic diseases that made me worried about my parents too. During my graduate studies in India, I first had the opportunity to consider a career in research. The most impactful courses included cell biology and metabolism. The realization that alteration in a metabolic pathway can affect health span is fascinating. This interest positively influenced my decision to study skeletal muscle aging during my postdoctoral training.

Briefly describe your project in non-scientific terms. What questions are you trying to answer?
As we age, there is a constant decline in skeletal muscle function and their force generation capacity. This is the most common cause of age-related loss of independence, frailty, and mortality. As the elderly proportion in the population continues to increase, the potential social and economic burden of muscle aging is becoming enormous. The neuromuscular junction is a synapse between motor neuron terminals and skeletal muscle fibers that transmit signals from motor neurons to muscle fibers. The neuromuscular transmission is critical for the control of muscle contraction and is thus essential for our physical mobility and daily life. Extensive research has revealed insight into the pathophysiological mechanisms of muscle aging. However, although neuromuscular junction structures and functions are disrupted in aged animals, little is known about the underlying mechanisms. In addition, much less is understood about the mechanisms of neuromuscular junction maintenance in aged animals. This proposal will test an innovative hypothesis that neuromuscular junction function and its maintenance in aged animals depend on insulin signaling, a pathway that is required for muscle growth and function.

What previous research or experience informed the development of this proposal?
Very recently our lab published the role of skeletal muscle AKT signaling in muscle mass and performance and identified that AKT regulates both mTORC1 and FOXO1 pathways to control muscle mass and performance. Importantly, we observed that loss of insulin signaling via AKT accelerates skeletal muscle aging. While working on these mechanisms we found that insulin signaling is critical for the maintenance of neuromuscular junction through the release of a myokine that is associated with neuromuscular junction disintegration during aging.

What's exciting about your project's potential impact?
The project utilizes an AAV-mediated gene therapy approach to prevent/reverse skeletal muscle aging. It will lead to the identification of new therapeutic avenues that may be targeted to prevent skeletal muscle aging and improve the quality of life of the elderly.

If your project is successful, what is the next step?
If the project is successful, the next steps would be to identify strategies to modify the biological drivers of aging to slow their progression and prevent or delay their onset.

How has support from and collaboration with the NSCs helped further this project and/or your research overall?
Being new to the aging field, the support from Nathan Shock Centers in providing necessary resources and generating preliminary data related to this pilot grant is tremendously helpful. The project supported by this pilot grant will be useful to apply for extramural funding that would help me to establish myself in the aging field.