Institute of Successful Longevity
Research Interests - Michelle Parvatiyar

My research interests have long been centered on disease development – many of which are associated with advancing age. My past training has been to examine the role of SSPN in Duchenne Muscular Dystrophy muscle function and troponin mutations in development of hereditary cardiomyopathies. I have been involved in researching a small protein, sarcospan (SSPN), which is situated within the muscle membrane. It has an important role in stabilizing the muscle cell membrane, particularly of the heart and skeletal muscle. SSPN exists within the greater dystrophin-glycoprotein complex (DGC), which is linked with a variety of skeletal and cardiac muscle disorders. Associated disorders are hereditary in nature and cause several distinct characteristic outcomes including muscle degeneration, atrophy, and weakness of heart and skeletal muscles. Outside of the context of neuromuscular disorders, many of which arise in childhood, little is understood about the role of DGC proteins in the setting of aging and how they may contribute to disease development.

My laboratory has been studying the protein SSPN using genetic mouse models including a global SSPN knockout (KO) mouse. This mouse exhibits normal life expectancy, however, it appears more susceptible to a variety of acute stressors. Currently, we have been investigating the role that SSPN plays in muscle mechanotransduction. Cells can convert external mechanical signals to biochemical signals that affect muscle function and their force generating capacity. Examination of muscle tissue from SSPN knockout mice has revealed several key findings – aged SSPN KO muscles are more prone to fibrotic deposition than equivalent aged non-genetically modified wild type (WT) mice. In addition, using immunofluorescence techniques to illuminate specific proteins at the muscle membrane it was found that young SSPN KO have a diminished amount of DGC proteins at the membrane than WT mice that further decline with age.

A novel discovery regarding SSPN function came from our study in young mice that showed that muscle fibers obtained from SSPN KO mouse hearts exhibited much higher force generating capacities than WT mouse hearts. This indicates that SSPN plays a role in regulating force production of striated muscle. SSPN KO mice have higher force production while mice overexpressing SSPN (OE) exhibit lower force. In a recent paper by Ubaida-Mohien et al. eLife 2019 it was shown that SSPN is an age-associated protein that increases in abundance with age. A loss of muscle strength and decline in muscle mass is one of the most striking phenotypes associated with age. Subsequently a reduction in muscle strength/mass/quality has a direct impact on the quality of life in aged individuals. We are interested in understanding the mechanisms underlying that ability of SSPN to regulate muscle strength and force production. We first plan to examine aged skeletal muscles in WT mice to determine how SSPN levels correlate with strength. Recently, we obtained adenovirus-associated virus-SSPN that we can use to manipulate the levels of SSPN in WT and SSPN KO muscle. We are working on developing a specific mouse model that has inducible conditional expression of SSPN that allows us to control its expression temporally and spatially in skeletal muscle. Other goals include testing of known compounds that decrease/increase SSPN expression so that we can examine how these improve/exacerbate aged muscle force generating capabilities. We believe our studies will provide insight on the role SSPN plays in muscle aging and may provide us a viable target aimed at improving muscle strength thereby enhancing the chances of individuals to maintain ambulation and increase their longevity.