A role of lamin A/C in preventing neuromuscular junction decline in aged mice

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During aging, skeletal muscles become atrophic and lose contractile force. This affects a large population of elderly regardless of ethnicity, gender, and wealth and 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 (NMJ) 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 NMJ structures and functions are disrupted in aged animals, little is known about underlying mechanisms. In contrast to NMJ formation, which has been studied extensively, much less is understood about mechanisms of NMJ maintenance, in particular in aged animals. To this end, we screened for proteins that are reduced in aged muscles and identified lamin A/C, intermediate filament proteins that determine the interphase nuclear architecture. The lmna gene is mutated in Hutchinson-Gilford progeria syndrome (HGPS), a disease of accelerated aging and premature osteoporosis. We found muscle-specific lamin A/C mutant mice had no problem in forming NMJs, but displayed age-related NMJ deficits including reduced AChR cluster size, increased cluster fragments, diminished innervation, and impairmed neuromuscular transmission. These deficits were not observed in mice lacking lamin A/C in motor neurons. These results suggest a role of lamin A/C in maintaining proper NMJ structure and function. Experiments are under way to investigate underlying mechanisms.