PADUA DAYS ON MUSCLE AND MOBILITY MEDICINE 2026

International Conference

March 3rd to 6th Euganean Thermae and Padua, Italy

BASICS IN AGING

ATTENUATING THE LYSOSOMAL PHENOTYPE IN AGED MUSCLE WITH TRAINING AND SULFORAPHANE

Anastasiya Kuznyetsova, Thulasi Mahendran, David A. Hood

School of Kinesiology and Health Science, Muscle Health Research Centre, York University, Toronto, Canada.

Skeletal muscle plays an extensive role in supporting the healthspan of aged individuals. The aging population undergoes a progressive loss of muscle mass, strength and function, termed sarcopenia, thereby impeding the quality of life. Within skeletal muscle cells, lysosomes are organelles responsible for the breakdown and turnover of cellular debris. The acidic environment of lysosomes houses hydrolytic enzymes and proteases responsible for the degradation of various cargos such as mitochondria. The importance of mitochondria in aged skeletal muscle lies in their ability to adapt to various physiological conditions that contribute to the aging phenotype (1). The turnover of mitochondria via lysosomes is termed mitophagy and is crucial for preserving the quality of the mitochondrial reticulum within muscle. Current literature suggests that a defective mitophagy pathway mediated by an accumulation of dysfunctional lysosomes may be driving impaired signaling pathways and perturbations within aged muscle (2, 3). In contrast to the effects of age, exercise training is well known to attenuate the aging phenotype including producing significant improvements in mitochondrial content and function (1). Sulforaphane (SFN), a nutraceutical, has also been implicated in inducing improvements in the mitochondrial reticulum, alongside the upregulation in lysosomal-related proteins (4). In this project we have studied the response of lysosomal adaptations in skeletal muscle from young and old mice following a 6-week voluntary wheel running exercise training protocol, with or without a SFN-enriched diet compared to sedentary and control-diet groups. Interestingly, both training and SFN attenuated the aging-induced loss of muscle mass and muscle strength and elicited an additive effect. Lysosomal content was greater in the aged sedentary control cohort, however lysosome proteolytic function, assessed in purified lysosomal fractions, was reduced (5, Figure: dark green lysosomes). Both training and SFN improved lysosomal function (light green lysosomes) independently in both young and aged muscle, and the combination of training and SFN appeared to have an additive effect. Thus, our results showed that aged muscle has a dysfunctional lysosomal pool which can be attenuated by exercise training and altered with a SFN diet. These adaptations can improve skeletal muscle health and quality of life within the aged population.

Keywords: *aging muscle, lysosomes, exercise training, sulforaphane, nutraceuticals.*

BASICS IN AGING