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Effect of mitochondrial catalase expression on age-related mitochondrial abnormalities in mouse skeletal muscle.

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The loss of muscle may be one of the most devastating age-related changes, not only due to its impact on physical function, but also in its universality. Studies in humans show a steady decline that begins in the mid 20s and continues unabated reaching nearly a 40% decrease by age 80. This loss of muscle touches on every aspect of life in the elderly including activities of daily living, mobility, and loss of independence.

In skeletal muscle, we hypothesize that mitochondrial genetic and enzymatic abnormalities, possibly secondary to life-long oxidative damage, disrupt cellular processes or trigger cell death. The ensuing skeletal muscle fiber dysfunction or loss contributes to sarcopenia, the age-related loss of skeletal muscle mass and function.

We are addressing, by the *in situ* analyses of skeletal muscle from aged rodents, the questions of the etiology and biological impact of mitochondrial abnormalities. Earlier studies suggest a specific sequence of events linking mitochondrial oxidative damage to sarcopenia. We propose to directly test this hypothesis by assessing the efficacy of transgenic over-expression of a mitochondrially-targeted antioxidant, catalase (mCAT), in preventing or delaying the progression of age-associated mitochondrial abnormalities and their associated cellular impact. The mitochondrial targeting of catalase decreases life-long oxidative damage and increases mouse life span.

We are examining changes in muscle mass, fiber number and fiber type in both transgenic mCAT and wild-type littermates including the thigh and calf muscle groups. Immunohistochemical staining for the transgenic catalase demonstrates a mosaic distribution of mCAT across individual fibers that is not related to fiber type. Changes in mosaic mCAT expression with age are being examined as is the effect of mCAT expression on mitochondrial enzymatic and genetic abnormalities.

These studies may shed light on the basic mechanisms of aging and may stimulate the development of therapeutic interventions directed at preventing the functional declines of aging and enhancing the independence of older adults.