Seeking Perfect Health

1809 Lakehurst Rd., Spicewood, Texas
mikeclark@seekingperfecthealth.com
www.seekingperfecthealth.com
cell: 512.736.5033

Autophagy & Muscle Loss (and more)

Recent research has discovered that autophagy is a critical modulator of a wide range of diseases and disorders

Autophagy: The term is derived from the Greek "auto," meaning self, and "phagein," meaning to eat. During autophagy, the cell consumes parts of itself in a regulated manner.

Think House Cleaning and taking out the trash.

Muscle Loss and Autophagy

Even if they eat plenty of protein, older people often cannot maintain muscle mass, probably because their bodies cannot turn proteins into muscle fast enough to keep up with the natural rate of the tissue's breakdown.

Moreover, the muscles of older people undergo lower levels of autophagy, a process that under healthy conditions recycles used and damaged proteins, organelles, and other cell structures. This can result in an imbalance between protein production and degradation that is likely linked to muscle aging.

There may also be other ways that reduced autophagy may contribute to both muscle loss and muscle weakness during aging. In order to maintain muscle strength, muscle cells must get rid of the intracellular garbage that accumulates over time. In the case of muscle cells, this garbage includes old organelles such as mitochondria and endoplasmic reticuli, clumps of damaged proteins, and free radicals, all of which can become cytotoxic over time.

By recycling mitochondria, muscle fibers boost energy production and preserve muscle function. If muscle fibers fail to clear these potentially dangerous entities, they will become smaller and weaker. Sure enough, in a study from Marco Sandri's group at the University of Padova in Italy, mice whose skeletal muscles lacked one of the main genes that controls autophagy, Atg7, had profound muscle loss and age-dependent muscle weakness.[7]

Autophagy can promote degradation en masse for a large number and variety of substrates, enabling cells to quickly and efficiently generate recycled basic building materials in the face of

a wide range of nutritional deficiencies. Additionally, autophagy is the only pathway that is capable of degrading entire organelles, either randomly or in a targeted fashion—a critical process for maintaining homeostasis in the complex landscape of the eukaryotic cell.

Autophagy and Cellular Homeostasis

Today, autophagy is recognized as a critical process for maintaining cellular homeostasis, as well as for responding to stressors, such as nutrient deficiency, which may potentially compromise cell survival. When a cell is exposed to such stressors, autophagy, which occurs constitutively at low levels to balance the constant synthesis of biomolecules, is strongly upregulated. This upregulation increases sequestration and degradation of portions of the cell, releasing macromolecules back into the cytosol to power essential metabolic reactions and generate energy.

The contribution of autophagy to cellular health under both normal and stress conditions implies important physiological and pathological roles for this tightly regulated and precisely orchestrated process.

> ***Given the role of autophagy in physiology, it's not surprising that dysregulation of the process is tied to a number of pathologies, ranging from infectious diseases to neurodegenerative disorders to cancer.***

Autophagy Mitochondrial Homeostasis and Muscle Loss

Mitochondrial homeostasis is critical for proper neuronal function. **Neurons use mitophagy to selectively eliminate damaged mitochondria** that are not only inefficient at producing ATP, but also generate high levels of reactive oxygen species (ROS), which promote protein and lipid oxidation and DNA damage, causing further cellular dysfunction.

Mitochondria, the powerhouses of muscle, affect muscle loss. To work efficiently, skeletal muscle needs a sufficient number of fully functional mitochondria. These organelles represent around 5 percent to 12 percent of the volume of human muscle fibers, depending on activity and muscle specialization (fast-twitch versus slow-twitch). And research suggests that abnormalities in mitochondrial morphology, number, and function are closely related to the loss of muscle mass observed in the elderly.

In 2013, David Glass of Novartis and colleagues found that markers of mitochondrial metabolism pathways were significantly downregulated as rats aged, and this correlated with the onset of sarcopenia.[5] **Although the findings are merely correlative, the timing and near-perfect relationship between decline in mitochondrial gene expression and the onset of sarcopenia provides strong evidence that mitochondrial dysfunction may be driving sarcopenia.** The expression of genes and production of proteins that regulate mitochondrial fission and fusion—processes that maintain mitochondrial volume and function—also dropped, suggesting that mitochondrial dynamics are also perturbed during muscle aging.

As with muscle stem cell decline, the underlying cause of poor mitochondrial health may be gene regulation. In 2016, Alice Pannérec and her colleagues from Nestlé Institute of Health **Sciences** and Manchester Metropolitan University in the UK examined the transcriptomes of rat and human muscle and found that susceptibility to sarcopenia in both species was closely linked to deregulation of gene networks involved in mitochondrial processes, regulation of the extracellular matrix, and fibrosis, the formation of excess connective tissue in a muscle caused by the accumulation of extracellular matrix proteins.[6]

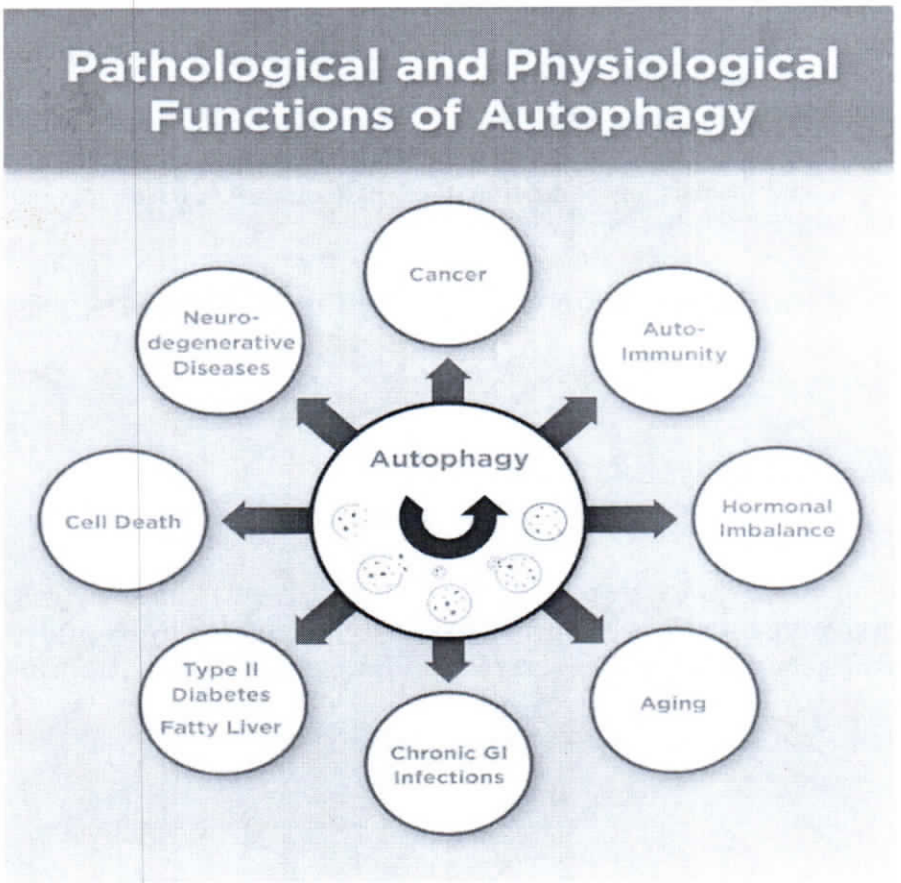
Credit. Much of this information was reported in *The Scientist*: March 2018

Questions?

mikeclark@seekingperfecthealth.com

512.736.5033

Autophagy's predominant role is cytoprotective, as is highlighted by its protective function in several neurodegenerative disorders, such as Huntington's disease (HD) and Parkinson's disease (PD).



Genetic Expression