Autophagy as a central “longevity” pathway

James P White, PhD
Assistant Professor
Department of Medicine
Duke Molecular Physiology Institute
Fellow-Duke Aging Center
Disclosures

• Current Funding
  – K01AG056664

• Other Financial Relationships: NONE

• Conflicts of Interest: NONE
Cellular proteostasis.
Healthy and aged proteostasis.

Courtney L. Klaips et al. J Cell Biol 2018;217:51-63
Autophagy and Aging

Gelino and Hansen. 2012 JCEP
NIID

Pathological and Physiological Functions of Autophagy

Cell Death

Neurodegenerative Diseases

Type II Diabetes

Fatty Liver

Infectious Diseases

Aging

Cancer

Innate Immune System

Cardiomyopathy

etc...
Different types of autophagy

Modulation of pathogen recognition by autophagy

Ji Eun Oh and Heung Kyu Lee
The role of autophagy across the Osteo and Soft Tissues
Impaired proteostasis during skeletal muscle aging

Raquel Fernando\textsuperscript{a}, Cathleen Drescher\textsuperscript{a}, Kerstin Nowotny\textsuperscript{a}, Tilman Grune\textsuperscript{a,b,c,d}, José Pedro Castro\textsuperscript{a,b,e,f}.

Redox changes lead to the loss of proteostasis and function in the skeletal muscle during aging.

Skeletal muscle

Unfolded protein

Proteasomal activity

Free a.a.

Proteostasis

Native protein

E3 ubiquitin ligases function

Protein polyubiquitination

Autophagy

Young - Healthy muscle

ROS/damage

Proteasomal activity

Aggregation

E3 ubiquitin ligases function

Protein polyubiquitination

Autophagy

Redox cellular disruption

Loss of proteostasis

Old - Dysfunctional and sarcopenic muscle
Role of the Inflammation-Autophagy-Senescence Integrative Network in Osteoarthritis

Claire Vinatier*, Eduardo Dominguez*, Jerome Guicheux**, and Beatriz Caramés*
Autophagy in bone: Self-eating to stay in balance

Valérie Pierrefite-Carle, Sabine Santucci-Darmanin, Véronique Breuil, Olivier Camuzard, Georges F. Carle
Questions to consider..

• Are autophagy-inducing drugs legitimate anti-aging therapeutic targets?
• Is autophagy a cell-autonomous process or can a “signal” from distant tissues induce autophagy?
• Does caloric restriction/exercise secrete factors to promote proteostasis/autophagy?
Thank you

- White Lab
  - Akshay Bareja, PhD
  - David Lee, PhD

- William Kraus, MD
- Kim Huffman, MD, PhD
- David Bartlett, PhD
- Gurpreet Baht, PhD
- Deb Muoio, PhD
- Virginia Kraus, MD, PhD

- Ken Schmader, MD
- Harvey Cohen, MD

NIH - K01AG056664