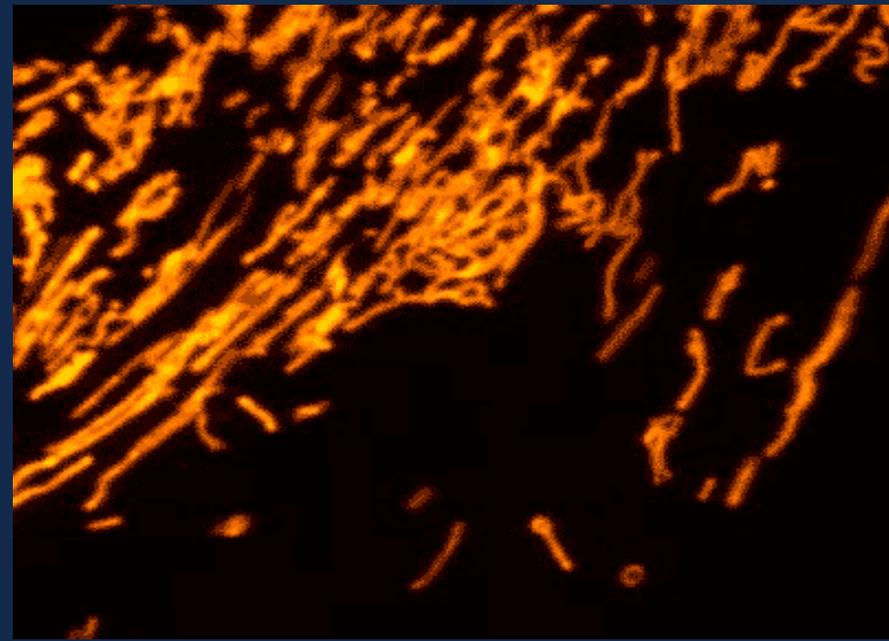
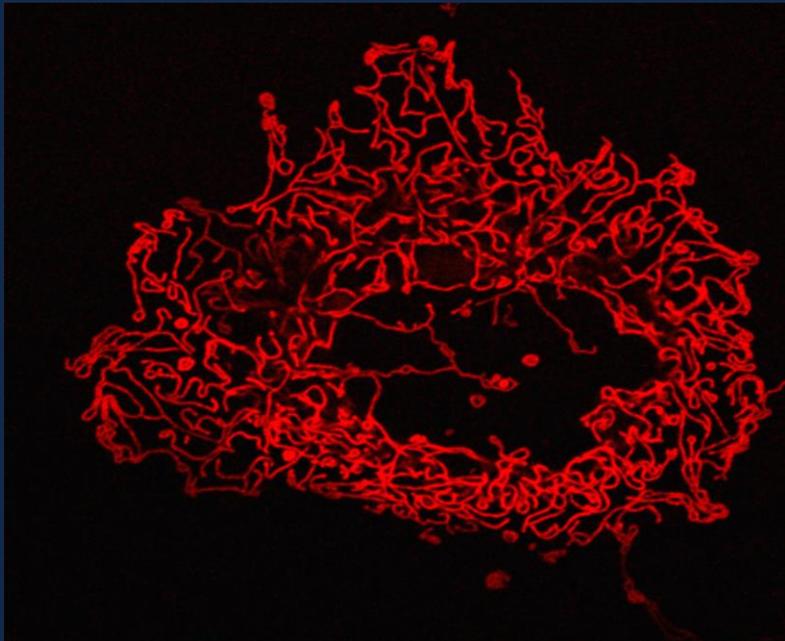


Mitochondrial Dysfunction

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Disclosures

-Current Funding

R01 AG054523 (PI)

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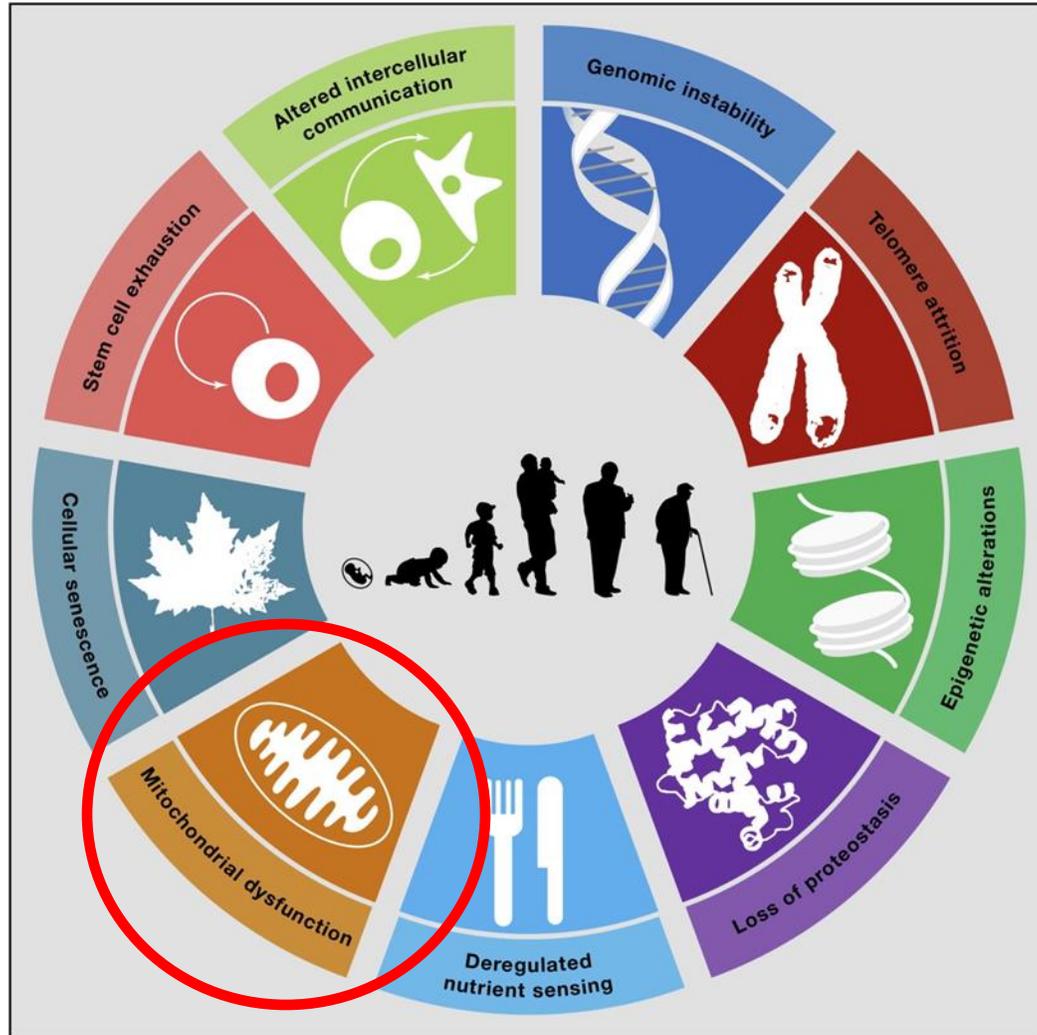
U01 AG060897 (co-PI)

R21 AG051077 (PI)

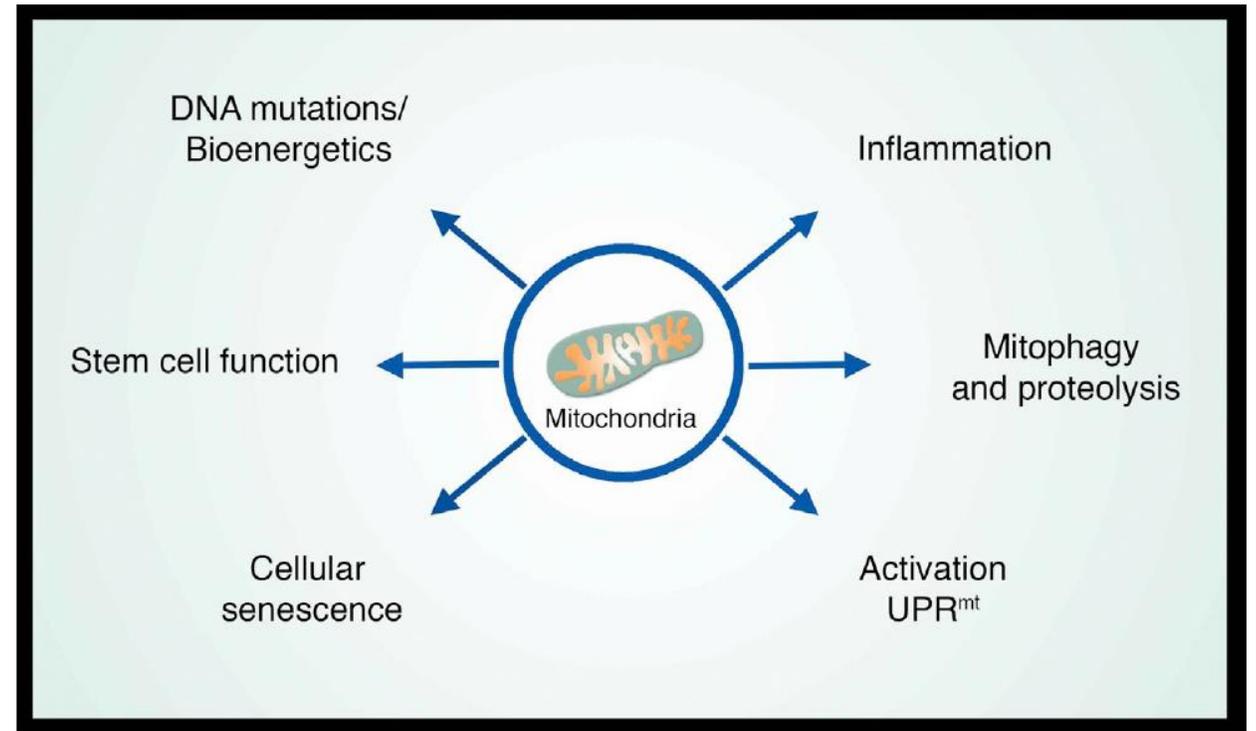
-Other Financial Relationships: none

-Conflicts of Interest: none

Hallmarks of Aging

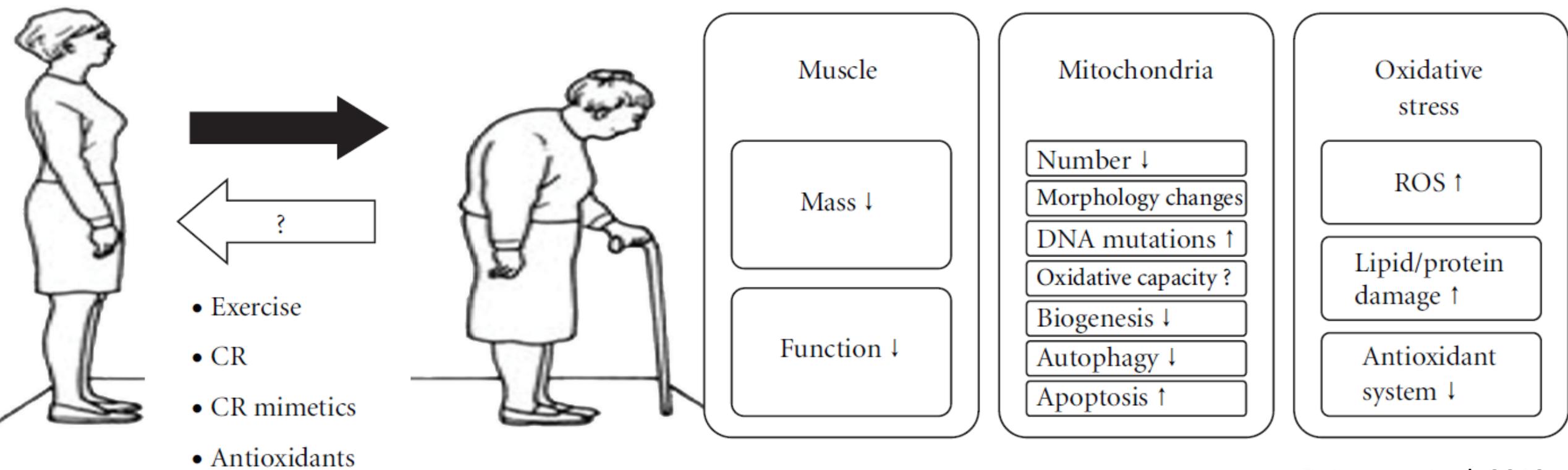


A Mitocentric View of Aging



Sun et. al. Molecular Cell 61, March 3, 2016

Lopez-Otin et. al. Cell 2013 153, 1194-1217



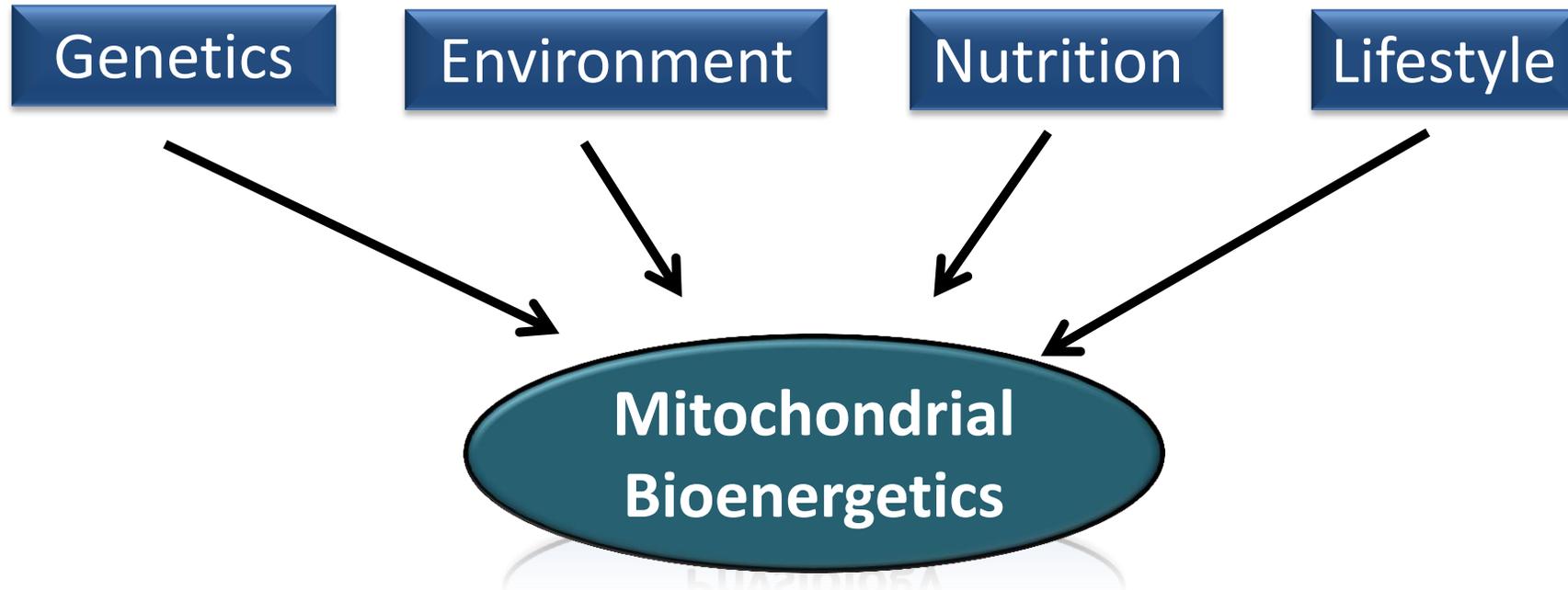
Peterson et. al. 2012

Human Bioenergetic Profiling

Precision Healthcare for Older adults

- Patient safety
 - Identifying whether an individual has the capacity to safely benefit from treatment
- Disease prevention
 - Presymptomatic identification of disease pathology
- Improved outcomes
 - Targeting mitochondrial function

Multiple factors underlie heterogeneity among older adults



The search for an integrative, cumulative, and measurable functional outcomes that can inform on patient heterogeneity

Approaches For Human Research

Invasive (biopsy based)

- +Detailed analysis (respirometry, enzyme activity)
- +Focused on tissue on interest
- +Gold Standard: nearly 200 publications examining human skeletal muscle (wiki-oroboros)

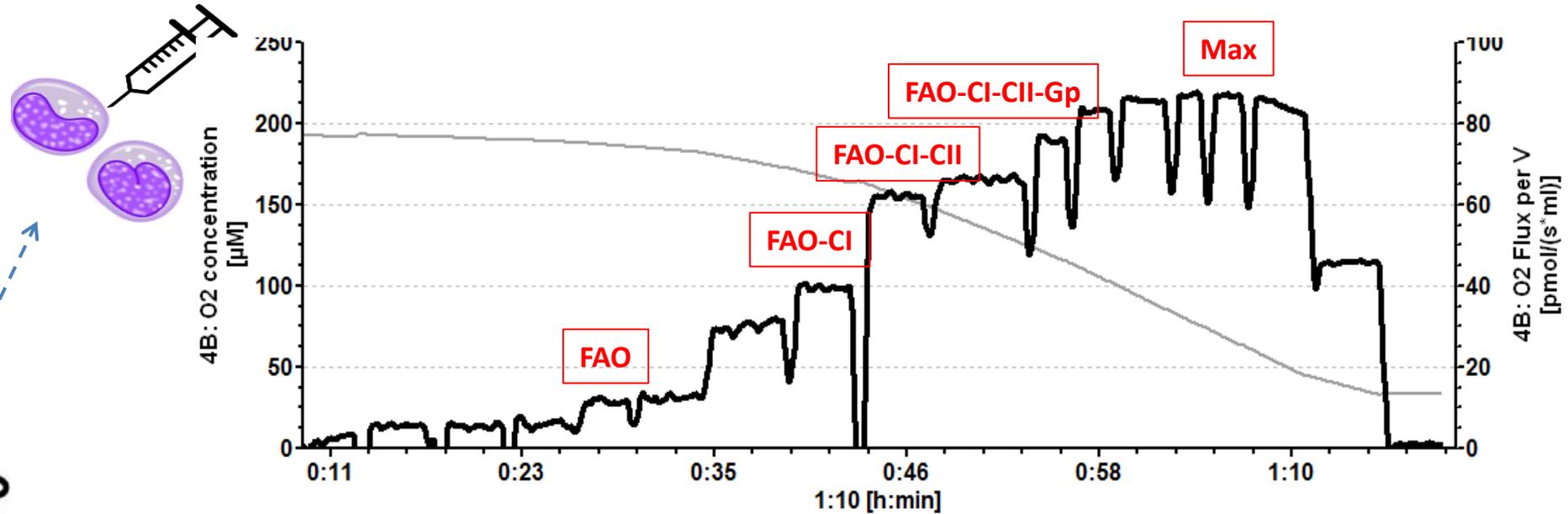
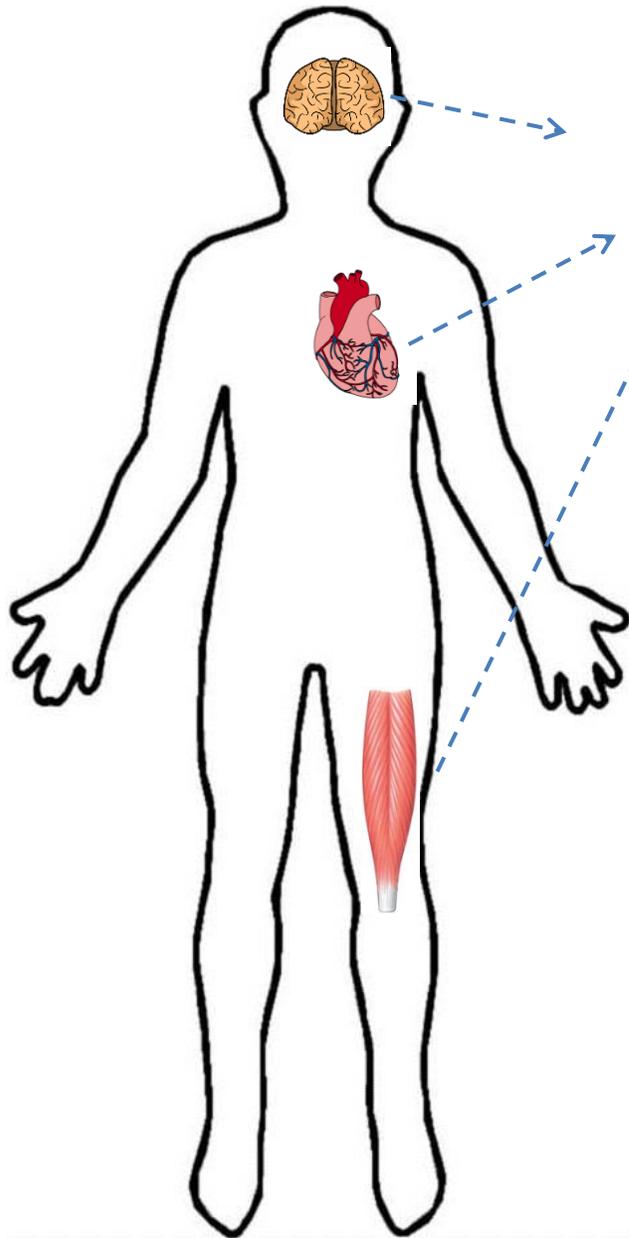
Minimally Invasive (blood-based)

- +Detailed analysis (respirometry, enzyme activity)
- +Circulating cells as surrogates capable of reporting in systemic bioenergetic capacity
- +Samples can be collected at multiple sites and shipped to a central facility for analysis

Non-Invasive

- Near-infrared spectroscopy (NIRS)
 - muscle oxygenation and hemodynamics
- phosphorus 31-(P31) magnetic resonance spectroscopy (MRS).
 - high-energy phosphate metabolites such as ATP and phosphocreatine (rest, exercise, recovery)

Blood-Based Bioenergetic Profiling



Premise: *Respirometric profiling of circulating cells reports on systemic bioenergetic capacity because these cells are continuously exposed to blood-borne factors that mediate mitochondrial function across multiple organs.*

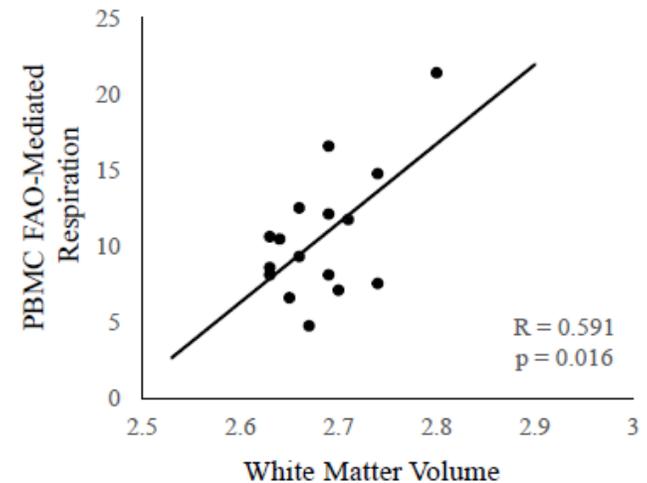
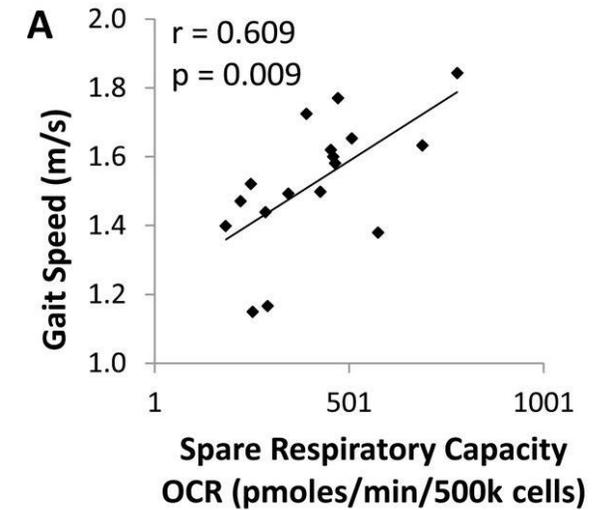
Mounting Evidence: Biomarker of Biological Age

-Gait Speed (J Geron. 2014)

-Muscle Strength, exSPPB, Muscle Quality, Inflammation (Exp. Geron. 2015)

-Brain Morphology and Cognitive Performance (Clin. Sci. 2018)

-Surgical outcomes, cognition, psychiatric health, inflammation, sepsis



Gaps in knowledge and high priority research areas that can be addressed with current approaches and new methodologies in development

-Identification of factors mediating age and disease related bioenergetic decline

-Appears to be systemic, but specific organs/tissues are differentially affected

-Defining mitochondrial health

-What is a healthy/normal bioenergetic profile?

-Should we focus on **maximal capacity** or **efficiency**

-The role of mitochondrial fuel utilization in aging and disease progression

-Substrate sensitivity and availability (e.g. glucose, fatty acids, ketones)

-Targeting mitochondrial function

-Optimizing behavioral Interventions

-e.g. to date, exercise is still the best intervention to combat sarcopenia

-Pharmacological and Nutraceutical

Acknowledgements

The Mito Team

Current

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