ESSR Journal Club

Covered Article: “Exercise Training-induced Regulation of Mitochondrial Quality” by Zhen Yan, Ph.D., Vitor A. Lira, Ph.D., and Nicholas P. Greene, Ph.D.  
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1. In his paper, Dr. Yan indicates that an important function of exercise is to increase mitochondria number (i.e., mitochondrial biogenesis). However, he argues that mitochondrial number per se is only part of the positive influences of exercise in muscle. What is the rationale for arguing that increasing mitochondria number as the sole mitochondrial outcome for exercise improvements, is an inadequate strategy for improving muscle performance outcomes?

2. What are some of the biological markers that have been used to identify mitochondrial biogenesis and mitochondrial function? What are the elements that can decrease mitochondrial function and “quality”? What are the two spatially distinct mitochondrial populations in skeletal muscle?

3. How does exercise (especially very intensive acute exercise) potentially contribute to obtaining “damaged” mitochondria? What other factors could lead to mitochondrial damage or dysfunction in skeletal muscle?

4. PGC-1α is considered to be a “master regulator” of mitochondrial biogenesis in several tissues including brown adipose and neural tissues. How does exercise alter PGC-1α to stimulate the transcription of the nuclear and mitochondrial encoded mitochondrial genes, and the replication of mitochondrial DNA? What is the evidence supporting that the induction of this co-activator of transcription factors is essential for promoting skeletal muscle mitochondrial biogenesis in response to exercise?

5. Dr. Yan identifies several important proteins that appear to have a role in regulation of PGC-1α-induced mitochondrial biogenesis. Discuss the roles of AMPK, Sirt1 and p38γ MAPK on signaling and regulation of PGC-1α changes in response to exercise. What are the differences by which acute and long-term exercise affect AMPK signaling? Is AMPK upstream or downstream of PGC-1α (i.e., does it regulate or is it regulated by PGC-1α)? Is the p38γ MAPK - PGC-1α regulatory axis functionally required for exercise-induced metabolic adaptations in skeletal muscle?

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6. Dr. Yan describes mitochondria are dynamic and not static structures. What is fission and fusion of mitochondria and what are the important proteins that regulate the processes of fission and fusion in the mitochondrial outer and inner membranes? In what ways does exercise impact fission and fusion of mitochondria in skeletal muscle? How does exercise-induced changes in PGC-1α affect mitochondrial fusion and fission?

7. Dr. Yan argues that mitochondrial damage is deleterious to normal function. Describe the general mechanism of autophagic removal of mitochondria (mitophagy), to maintain overall mitochondrial “health”. What role does exercise play in regulating mitophagy? What impact does aging in affect skeletal muscle mitophagy? Discuss the general roles of AMPK and mTOR in mitophagy.

8. Dr. Yan concludes his paper with a general hypothesis that remodeling of the mitochondrial network through fusion and fission, and elimination of damaged/dysfunctional mitochondria through mitophagy are important elements of exercise-induced adaptations in skeletal muscle. This provides a novel hypothesis, given that the dogma in the literature is largely that the main importance of exercise is to improve mitochondrial number (biogenesis), as a means to increase the muscle’s ability for oxygen consumption, produce energy and reduce fatigue. Do you think that fission/fusion/mitophagy would be equally important as mechanisms involved in adaption to exercise in young adults and elderly people? Speculate on the relative importance of mitochondrial biogenesis vs. mitophagy in muscles of healthy persons as compared to persons with cardiovascular or metabolic diseases, who might be prescribed exercise.