Training-induced adaptation in skeletal muscle fatty acid oxidation: is mitochondrial biogenesis necessary or sufficient?

Arend Bonen, University of Guelph, Canada

It has long been accepted that i) the increase in fatty acid oxidation during a exercise is dependent on the increased delivery of circulating fatty acids to muscle, and ii) that exercise-training-induced fatty acid oxidation upregulation is largely attributable to mitochondrial biogenesis. These long-standing concepts were developed prior to recent recognition that fatty acid entry into muscle occurs via a highly regulatable, CD36-mediated transport mechanism. We examined the role of CD36 in muscle fatty acid oxidation under a) basal conditions, b) during exercise, c) in exercise-trained muscle, and d) in muscle in which CD36 was overexpressed without altering mitochondrial content and enzymes. Under basal conditions CD36-KO mice displayed reduced fatty acid transport and oxidation, but mitochondrial content and enzymes were comparable. Acutely exercised (78%VO_{2max}) CD36-KO mice exhibited markedly reduced rates of fatty acid transport and exercise duration, while muscle glycogen utilization was accelerated. Exercise-training provoked comparable increases in mtDNA and β-HAD in WT and CD36-KO muscles, but fatty acid oxidation was increased only in WT muscle. Overexpressing CD36 in WT sedentary muscle, to the same levels as was induced by training, upregulated fatty acid oxidation similarly to training, but without changes in mitochondrial biogenesis or enzymes. This work challenges the long-held, mitochondrial-centric understandings of the molecular mechanisms involved in the acute regulation and adaptation of fatty acid oxidation in mammalian skeletal muscle.