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P.L. Mechanism of training-induced mitochondrial biogenesis: A possible involvement of reactive oxygen species

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Training-induced adaptation of the skeletal muscle was rigorously studied in mid-1960' through 1970'. Gollnick PD, Holloszy J and Saltin B were the most influential exercise physiologists. Investigations in these days revealed that the most important physiological feature of endurance training-induced adaptation was an increased oxidative enzyme activity of the skeletal muscle. The increased oxidative enzyme activity is a reflection of augmented mitochondrial biogenesis. From the 1990' and thereafter, research efforts have been directed to elucidate mechanisms of the training-induced mitochondrial biogenesis. However, the mechanism has not yet been fully elucidated.

Recently, Gomez-Cabrera et al. (2008) published their research which indicated that reactive oxygen species (ROS) produced during endurance training played a critical role for training-induced mitochondrial biogenesis. However, later studies including ours reported divergent results.

Further studies are definitely needed to determine if ROS is involved in the endurance training-induced mitochondrial biogenesis.

S.L. Molecular mechanisms of unloading-mediated muscle atrophy and development of its countermeasures

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Skeletal muscle atrophy caused by unloading is characterized by both decreased responsiveness to myogenic growth factors (e.g. IGF-1, insulin) and increased proteolysis. Here we show that unloading stress led to skeletal muscle atrophy through the induction and activation of the ubiquitin ligase Cbl-b. Upon induction, Cbl-b interacted with and degraded the IGF-1 signaling intermediate IRS-1. In turn, loss of IRS-1 activated the FOXO3-dependent induction of atrogin-1, a dominant mediator of proteolysis in atrophic muscle. Forced Cbl-b expression was sufficient to induce IRS-1 ubiquitination and atrophy in rat tibialis anterior muscle. Cbl-b-deficient mice were resistant to unloading-induced atrophy and loss of muscle function. Furthermore, a penta-peptide mimetic of tyrosine^{608}-phosphorylated IRS-1 inhibited Cbl-b-mediated IRS-1 ubiquitination and strongly decreased Cbl-b-mediated induction of atrogin-1. Our results indicate that the Cbl-b-dependent destruction of IRS-1 is a critical dual mediator of both the growth refractory and proteolytic arms of the atrophic response. Inhibition of Cbl-b-mediated ubiquitination may be a new therapeutic strategy for unloading-mediated muscle atrophy.

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