The effect of Retinoic acid isomers on mitochondrial in muscle cells

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Skeletal muscle is an important organ, critical for locomotion as well as the metabolic health of an individual. The mitochondria are organelles that drive the metabolic process, and dysfunction in mitochondrial turnover can lead to metabolic diseases such as obesity. Apart from exercise, a known stimulator of mitochondrial turnover, several supplements belonging to the retinoic acid family, known as the retinoic acid (RA) isomers, have been identified for their potential to stimulate mitochondrial turnover in adipose and liver tissue. The purpose of this study is to evaluate whether these RA isomers have the potential to promote mitochondrial turnover in muscle cells. Immature mouse muscle cells were grown and differentiated into myotubes to simulate mature muscle in an organism. These cells were then treated with either the RA isomers, or simulated exercise called contractile contractile activity (CCA; 4d, 3hrs/day), produced with an electrical stimulator. Samples were collected 21h after the last CCA and were analyzed for mitochondrial markers. Following treatment with either CCA or the RA isomers, mitochondrial markers COX I and COX IV protein levels tended to increase, as expected. Treatment of myotubes with the RA isomers resulted in an increase in PGC-1α expression; along with an increase in the import of mitochondrial transcription factor A (Tfam) into the mitochondria. RA isomers also induced strong increases in the expression of mitochondrial DNA-encoded COX I subunit, but not nuclear-encoded COX IV. There was no effect on the autophagy markers p62 or LC3 II with RA isomer treatment. Upon analysis, our data suggest that retinoic acid isomers can promote mitochondrial biogenesis, possibly via increased import of Tfam and subsequent stimulation of transcriptional activity of the mitochondrial genome. Thus, RA isomers may be useful adjuncts to contractile activity in stimulating mitochondrial biogenesis in muscle.