Background: In patients with mitochondrial myopathy (MM) due to single-large scale mitochondrial DNA (mtDNA) deletions, levels of mutation are typically undetectable in satellite cells (SC) despite their high abundance in mature muscle. In healthy muscle, quiescent SC can be activated through heavy resistive muscle contractions to participate in myofiber hypertrophy and repair. In MM with muscle SC devoid of mutation, SC activation may induce transfer of wild-type (wt) mtDNA templates, restoring a more normal mitochondrial genotype and improving oxidative capacity, as previously reported (Taivassalo et al., 1999). Objective: In patients with single-large scale mtDNA deletions, to determine the ability of resistance exercise training (RT) to increase strength, activate SC and improve mitochondrial genotype and muscle phenotype. Methods: 8 female patients (39+9 yrs) with characterized mtDNA deletions underwent 12 weeks of supervised high-intensity leg RT (3x/week, 80% maximal weight lifted 1 time, 1RM). At baseline and post RT: exercise testing was performed to determine peak muscle strength (1RM) and capacity for oxygen utilization (VO2) and extraction (a-vO2diff); muscle needle biopsies were obtained to determine: activation of SC (NCAM immunoreactivity); myofiber regeneration (neonatal-myosin immunoreactivity); % deleted relative to wt-mtDNA; and proportion of cytochrome oxidase negative (COX-) fibers. Results: The RT protocol was sufficient to increase quadriceps muscle strength (15%, p<.01). Within trained muscle, increases from baseline (p<.05) in NCAM and neonatal myosin-positive staining suggest RT-induced SC activation and muscle regeneration. An average 30% decrease in the overall proportion of COX- fibers (p<.05), increase in intermediate COX-staining fibers (p=.06) along with 7% fall in mutant-mtDNA suggest shifting of wt-mtDNA from SC to mature muscle following RT. Furthermore, increases in muscle O2 extraction (p<.03) may underlie improved peak VO2 (6%, p=.06). Conclusions: Preliminary findings of improved muscle oxidative capacity and strength support the potential of RT-induced SC gene transfer as a treatment paradigm for certain MM patients.

Keywords: Mitochondria, Chronic Diseases, Muscle Damage