

Skeletal Muscle Mitochondrial Subpopulation Response in a Type 2 Diabetic Mouse Model

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Dysfunctional mitochondria are central to the pathogenesis of type 2 diabetes mellitus. In skeletal muscle, two spatially distinct mitochondrial subpopulations exist. The interfibrillar mitochondria (IFM) which are situated between myofibrils and the subsarcolemmal mitochondria (SSM) which reside directly below the sarcolemma. The objective of this study was to determine how type 2 diabetes mellitus differentially affects distinct mitochondrial subpopulations in skeletal muscle. Db/db mice and littermate controls were sacrificed at 20 weeks of age and mitochondrial subpopulations were isolated from the gastrocnemius muscle. State 3 respiration in db/db mice was significantly lower in both IFM and SSM populations compared to respective controls leading to a decrease in RCR ratios ($P < 0.05$). Electron transport chain complex I and IV activities were significantly decreased in the diabetic IFM with no change in the SSM ($P < 0.05$ for both). Superoxide production was increased in the diabetic IFM, whereas there was no significant difference in the ($P < 0.05$) SSM. Increased lipid peroxidation was evident in the diabetic skeletal IFM, with no change occurring in the SSM ($P < 0.05$). These findings indicate that both mitochondrial subpopulations in the mouse gastrocnemius muscle are affected during type 2 diabetes mellitus, however, the IFM exhibit a greater dysfunctional profile.