METABOLIC RESPONSES TO A HIGH FAT DIET IN SKELETAL MUSCLE OF RATS BRED FOR HIGH OR LOW ENDURANCE RUNNING CAPACITIES

Scott P. Naples

Dr. John P. Thyfault, Thesis Supervisor

ABSTRACT

Whole body aerobic capacity and mitochondrial oxidative capacity are linked and may play an obligatory role in the maintenance of metabolic function and protection against insulin resistance when challenged with a high-fat diet (HFD). The purpose of this study was to determine whether maintenance of insulin sensitivity after HFD is associated with a HFD-induced increase in skeletal muscle PGC-1α and PPARδ expression and increases in mitochondrial content and density. **Methods:** We previously reported a novel model in which rats were artificially selected over several generations to produce high and low capacity runners (HCR and LCR) with contrasting intrinsic aerobic capacities which were resistant or susceptible to the effect of a HFD on insulin sensitivity. HCR and LCR rats were divided into HFD or normal chow (NC) fed groups for 7 weeks. RT-PCR and western blotting were performed in red gastrocnemius skeletal muscle to examine PGC-1α and PPARδ, and transmission electron microscopy was used to characterize mitochondrial subpopulations. **Results:** Despite illustrating that inherent oxidative capacities of the HCRs and LCRs confer protection and susceptibility to insulin resistance when challenged with a HFD, between strain similarities and lacking HFD-induced alterations in mRNA and protein expression and mitochondrial content and density between HCR and LCR animals indicated that transcript expression is not predictive of protection against insulin resistance. **Conclusions:** These results suggest that other mechanisms besides mitochondrial content and size, fatty acid transcription factor expression are responsible for protection against HFD-induced insulin resistance.