SIRT3: A Unique Potential Therapeutic Target for Sepsis-Induced Skeletal Muscle Atrophy

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Sepsis is an overwhelming immune response to an infection that accounts for 20-30 million hospital cases per year. One of the major issues surrounding this syndrome is the muscle atrophy of the skeletal muscle in the thoracic diaphragm. Due to the relationship between sepsis and low energy levels, my lab decided to focus on the mitochondria. Sirtuin 3 (SIRT3) a member of the mammalian sirtuin family, is associated with energy production, suppression of ROS levels in the mitochondria of skeletal muscle, & mitochondrial biogenesis. This study was designed to investigate the gene expressions of proteins associated with the inflammatory response, glucose & fatty acid metabolism, mitochondrial biogenesis, & protein degradation in response to the elimination of SIRT3 from the genome. The methodology for this experiment included the use of skeletal muscle from S3KO (SIRT3 knockout) mice & wildtypes (WT). A quantitative polymerase chain reaction (RT-qPCR) and a western blot were performed. It was hypothesized that the lack of SIRT3 would decrease the gene expression of genes associated with the inflammatory response (TNFa, IL-2, IL-6, SIRT1), mitochondrial biogenesis (TFAM), glucose & fatty acid metabolism (PGC1a, LCAD, AKT), and that it would increase the gene expression of genes associated with protein degradation (PPAR?, FOXO1, Atrogin1, MURF1, SREBP-1c). I concluded that while proteins associated with the inflammatory response, mitochondrial biogenesis, & glucose & fatty acid metabolism had higher gene expressions in WT, the lower gene expression of proteins associated with protein degradation in S3KO indicates that those proteins become less atrophic when SIRT3 is not present. Future research includes the investigation of MURF1 & Atrogin1 from a metabolic perspective.

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