Kanika Sharma

**University of Nebraska Medical Center
Omaha**

Lifetime Overexpression of Skeletal Muscle Nrf2 Attenuates Aging-induced Cardiac Dysfunction

Abstract:

This study delves into the influence of the Nrf2-Keap1 antioxidant defense system on heart tissue, mirroring its well-documented role in skeletal muscle (SkM) tissue. Redox homeostasis, plays a pivotal role in adapting to stress. Despite its significance, the protein targets of redox regulation in SkM remain largely unexplored. Leveraging prior research on SkM proteomic profiles in Nrf2 or Keap1 gene deletion models, this investigation employs label-free quantitation techniques to scrutinize the global expression profile of the heart. The analysis unveils significant alterations in 741 proteins in Aging Keap1 KO vs Aging WT (186 downregulated and 555 upregulated), and 784 proteins in Aging WT vs Young WT (335 downregulated and 449 upregulated). These proteins are implicated in crucial Oxidative signaling pathways, including Calcium Signaling, Nrf2-mediated oxidative stress response, oxidative phosphorylation, detoxification of ROS, and Cardiac signaling pathways such as Cardiac hypertrophy signaling, cardiac conduction, and dilated cardiomyopathy signaling pathways. Moreover, our findings illuminate potential molecular pathways and protein targets influenced by SkM Nrf2 upregulation, extending beyond skeletal muscle tissue to impact cardiac function. This investigation provides insights into the broader implications of Nrf2-mediated antioxidant defense mechanisms in preserving cardiovascular health and underscores the intricate crosstalk between skeletal muscle and cardiac tissues in response to oxidative stress.