

## **Sulforaphane prevents age-associated cardiac, muscular, and skin dysfunction through Nrf2 signaling**

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Age-associated mitochondrial dysfunction and oxidative damage are primary causes for multiple health problems including sarcopenia, cardiovascular disease (CVD) and skin aging, all related with inflammation. Though the role of Nrf2, a transcription factor that regulates cytoprotective gene expression, remains poorly defined, it has shown beneficial properties in both sarcopenia and CVD. Sulforaphane (SFN), a natural compound Nrf2-related activator of cytoprotective genes, provides protection in several disease states including CVD and is in various stages of clinical trials, from cancer prevention to reducing insulin resistance and more recently in skin aging. Our studies aimed to determine whether SFN could present age related loss of function in tissues such as, heart, skeletal muscle, and skin, in 2- and 22-month-old C57Bl6 mice, and whether these alterations may relate to changes in the microbiome. The results revealed a significant drop in Nrf2 activity and mitochondrial functions, together with a loss of skeletal muscle, cardiac and skin function in the old control mice compared to the younger age group. In the old mice, SFN restored Nrf2 activity, mitochondrial function, cardiac function, exercise capacity, glucose tolerance and the antioxidant capacities of the skin, together with a significant reduction in reactive oxygen species and matrix metalloproteinase 9 levels. These alterations were accompanied by the restauration of the gut microbiome, with enrichment of bacteria known to be associated with an improved intestinal barrier function and the production of anti-inflammatory compounds.



Dr. Carvalho studies the underlying mechanisms that are in the origin of insulin resistance and diabetes and related complications, across the lifespan. She has discovered that low insulin receptor substrate-1 protein levels in adipose tissue are predictors of pre-diabetes. She investigates specific biomarkers and pathways that are associated with insulin action and metabolic dysfunction in insulin sensitive tissues, from bench to bedside. In addition, she has been evaluating how specific markers are important in tissue regeneration under diabetes conditions. Recently, she has started to investigate the effect of nutraceuticals to improve insulin action and metabolism, including essential amino acids and sulforaphane, among other. In the context of early insulin resistance development, inflammation, and aging.

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