NRF-2 and mitochondrial biogenesis

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Nuclear factor erythroid 2-related factor 2 (NRF-2) is a transcription factor regulating the gene expression of a diverse network of cytoprotective proteins, including antioxidant, anti-inflammatory, and detoxification enzymes. NRF-2 has an important role in the maintenance of cellular redox homeostasis by regulating the synthesis of glutathione, thioredoxin, and NADPH and by controlling the mitochondrial production of reactive oxygen species (ROS). Under conditions of stress, activation of NRF-2 counteracts increased ROS production *via* a number of pathways including the transcriptional upregulation of uncoupling protein 3 and heme oxygenase 1. NRF-2 influences mitochondrial biogenesis by maintaining the levels of nuclear respiratory factor 1 and peroxisome proliferator-activated receptor γ coactivator 1α, as well as by promoting purine nucleotide biosynthesis. Dietary components such as sulforaphane, curcumin, silymarin and resveratrol activate NRF-2 leading to increased cytoprotective responses and improvements in the overall health and survival of the cell. For example, broccoli-derived sulforaphane inhibits oxidant-mediated opening of the mitochondrial permeability transition pore and mitochondrial swelling. Exercise also activates NRF-2 leading to similar positive adaptations to the mitochondria, cell and organism. In summary, NRF-2 supports the structural and functional integrity of the mitochondria, and this role is particularly important under conditions of stress. As many chronic diseases have oxidative stress, inflammation, and mitochondrial dysfunction, NRF-2 activation is a promising therapeutic target for disease prevention and treatment.