Age-Related Renal Injury

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The kidney is an organ that ages quickly compared with other organs. Expression of senescence markers reflects changes in energy metabolism in the kidney. Two important issues in aging are mitochondrial dysfunction and oxidative stress. Age-related oxidative damage occurs because of an increased rate of generation of oxidants, and reactive oxygen species (ROS) contribute to the accumulation of oxidative damage to cellular constituents. These events are controlled by the mitochondria, which play an important role in the control of senescence.

AMPK signaling inhibits the inflammatory response, which is mediated by several transcription factors that are the downstream targets of AMPK, such as SIRT1, PGC-1α, and FOXO factors. The responsiveness of AMPK signaling is also affected by aging. The loss of sensitivity of AMPK activation to cellular stress impairs metabolic regulation, increases oxidative stress, and reduces autophagic clearance. SIRT1 is expressed throughout the body, has broad biological effects, and can significantly affect both cellular survival and longevity during acute and long-term injuries by mechanisms that involve both oxidative stress and cell metabolism. It has been suggested that SIRT1 and AMPK regulate each other and share many common target molecules such as PGC-1α, FOXO, and NF-κB. The activation of AMPK and SIRT1 may allow for the concurrent deacetylation and phosphorylation of their target molecules, which may decrease or slow the effects of aging .

AMPK, and SIRT1 may protect against age-related renal injury and that the pharmacological targeting of AMPK-SIRT1 signaling molecules may prevent or reduce the pathological changes in the kidney associated with aging.