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Effect of Lysophosphatidic Acid regulation on the aging kidney

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Objectives: Lysophosphatidic Acid (LPA) is a bioactive lysophospholipid that is present in all tissues. It has been reviewed that LPA could induce oxidative stress and inflammation. Oxidative stress is a major characteristic of aging which is a critical risk factor of renal dysfunction. Nuclear factor erythroid 2-related factor 2 (Nrf2), a transcription factor that regulates the expression of antioxidants, which could improve cell viability by reducing oxidative stress, is found to be decreased in the aging kidney. Also, LPA regulates the expression of Nrf2 has been reported. In this study, we evaluate the effect of LPA in the aging kidney by elucidating the potential LPA-Nrf2 signaling pathway.

Methods: Male 2- and 24-month-old C57/BL6 mice were used in this study. We measured histological change, oxidative stress, and aging-related protein expression in the kidneys.

Results: 24-month-old mice displayed increased albuminuria. Creatinine clearance decreased with aging. There were increases in mesangial volume and tubulointerstitial fibrosis in 24-month-old mice. There were also increases in autotaxin, LPAR1, PI3K, Akt, GSK3 β expression with aging and Nrf2, NQO1, HO1, SOD1, SOD2 were decreased in 24-month-old mice.

Conclusions: LPA signaling decreased antioxidants expression via down-regulating Nrf2. Targeting the LPA-Nrf2 pathway provides new evidence to decrease aging-related disease in the kidney.

Morphological changes in aging kidneys and the expression of LPA receptor 1 and Nrf2

