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Aging-related renal fibrosis was alleviated via conserving mitochondrial function in NLRP3 KO mice

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Objectives: Nod-like receptor family, pyrin domain containing-3 (NLRP3) activation in kidney diseases contributes to aggravating disease progression and fibrosis. However, the role of NLRP3 in renal aging is not clear. This study was designed to identify whether the NLRP3 KO mice could be protected from renal aging.

Methods: NLRP3 KO and counterpart wild-type (WT) mice were used at different ages (3 months, 12 months, and 24 months). Plasma, urine, and kidneys were collected.

Results: Plasma creatinine and blood urea nitrogen (BUN) increased with aging, while BUN was significantly decreased in NLRP3 KO old mice (24M) compared with WT old mice. NLRP3 ablation contributed to decreasing tubular vacuolization, tubulointerstitial fibrosis, and atypical autophagosomes with aging. In line with it, renal fibrosis markers, such as CTGF, and fibronectin were alleviated in RT-PCR tests. Immunoblot results showed that autophagy with mitochondrial biogenesis increased in old NLRP3 KO mice. In addition, phosphorylated AMPK and PGC-1α were increased in old NLRP3 KO mice. Transcriptional expression data using kidney RNA bulk sequencing showed augmentation of autophagy and mitochondrial biogenesis in old NLRP3 KO mice.

Conclusions: NLRP3 absence prevented aging-related renal fibrosis via maintaining renal mitochondrial biogenesis and autophagy.