Identification and Functional Characterization of SASP Factors Involved in the Progression of Chronic Kidney Disease: Toward the Realization of Healthy Longevity

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This study aimed to identify senescence-associated secretory phenotype (SASP) factors that play central roles in the progression of chronic kidney disease (CKD) and to elucidate their regulatory mechanisms and pathological significance at the molecular level. CKD is closely linked to accelerated aging, in which SASP factors secreted by senescent cells induce inflammation and fibrosis, leading to kidney functional decline; however, the upstream regulatory pathways remain poorly understood.
In this study, we focused on the transcriptional axis connecting aging and metabolic regulation, the MondoA–Rubicon/TFEB pathway, and demonstrated that the decline of MondoA promotes mitochondrial dysfunction and cellular senescence through Rubicon-dependent autophagy dysregulation and inactivation of the TFEB–PGC1α pathway. Furthermore, these alterations enhanced the secretion of SASP factors, driving the transition from acute kidney injury (AKI) to CKD through sustained inflammation and fibrosis.
These findings present a new molecular framework that integratively explains CKD progression through the disruption of autophagy, mitochondrial, and metabolic homeostasis, thereby paving the way for the development of therapeutic strategies based on the modulation of cellular senescence.