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Upregulated C1qa signaling antagonizes glomerular health in aged kidneys

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Objectives: With age, the glomerulus, a crucial structure in the kidneys, can undergo structural changes that reduce its effectiveness in filtering waste products from the blood. This decline in function can lead to a decrease in kidney function and the development of age-related kidney diseases. Despite the importance of this research area, studying glomerular aging remains challenging due to technical limitations.

Methods: In this study, RNA-seq was applied to glomeruli isolated from young (2 months old), intermediate (12 months old), and old (24 months old) mice. This glomerular enrichment approach allowed us to explore the specific changes in glomeruli over time.

Results: Our results showed that the alterations in genes associated with immune system processes, innate immune responses, inflammatory responses, and chemotaxis were prominent between 12 months old and 24 months old mice. The classical complement pathway was the most prominent of all the upregulated complement pathways during aging. In particular, the genes for the classical pathway of complement 1 (C1) elements, including C1r, C1s, C1qa, C1qb, and C1qc, were all upregulated. Single cell RNA-seq data confirmed that these complement gene signatures were expressed in podocytes during aging, as determined by a deconvolution approach. In addition, immunostaining of C1qa was increased with age in human kidneys. To examine the role of C1qa in podocytes, a C1qa lentivirus was transduced into podocytes, resulting in increased levels of senescence markers, such as p16 and p21.

Conclusions: In conclusion, transcriptome data has advanced our understanding of the molecular mechanisms underlying glomerular aging and has provided evidence for the critical role of increased C1qa signaling in kidney aging.