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Functional compartmental RNA-seq analysis of the kidney according to aging

Ju-Young Moon, Su-Mi Kim, Dong-Jin Kim, Su-Woong Jeong, Jae-Hyung Lee, Sang-Ho Lee
Department of Internal Medicine, Kyung Hee University Hospital at Gangdong, Korea, Republic of

Objectives: RNA-Seq of the kidney is a comprehensive tool to understand the mechanism of kidney aging. The bulk RNA-seq of the aged kidney has been highly informative; however, it is limited to evaluating the averaged gene expression across various renal cell populations. In this study, we applied the RNA-seq for a location-specific manner of the young, adult, and old kidney to clarify the novel mechanism of kidney aging depends on functional compartments.

Methods: We performed RNA-Seq on glomeruli, tubules, cortex, and whole kidney samples from C57BL6 male young (two months, n=3), adult (12 months, n=3), and old (24 months old, n=3) mice. Glomeruli were isolated by magnetic beads method. After glomeruli isolation in the cortex, PDGFR-PE beads were used for removing interstitial cells and then remnant tubules were used for analysis. The paired-end raw reads were generated from the Illumina HiSeq system.

Results: In 36 samples, total 31,437 genes have at least one pair of reads. Intriguingly, the time expression pattern was different from each compartment. Glomeruli and tubules compartment showed early phase (from 2 to 12 months) expressional change while cortex and whole kidney showed late phase (from 12 to 24 months) expressional change. In the glomeruli, innate immune response, cell adhesion, iron transport, lipid metabolism, and cell migration were top statistically enriched biological process according to aging. Genes were highly expressed in tubules in the early phase were those with an innate immune system, adaptive immune response, antigen processing and presentation, chemotaxis, and cell surface signaling pathway.

Conclusions: RNA-seq analysis of the kidney showed significant pathway differences by functional compartment and early and late phase of aging. The present dataset provides a unique resource to understand gene expression and function in aging process of the renal functional compartment.