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Genomic background analysis of recovery phase after ischemic/reperfusion injury stage in aging kidneys with mice model

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Objectives: Vulnerability and incomplete recovery from acute kidney injury is considered as one of the main reasons for high prevalence of kidney dysfunction in aging kidney. This study aimed to identify novel diagnostic and prognostic targets for aging kidney through genome-based investigation.

Methods: Analysis of RNA sequencing (RNA-seq) data of kidneys were performed with Illumina's HiSeq 2000 at 4 weeks after unilateral ischemic/reperfusion injury (IRI) for 45 minutes in 2 and 18-month-old C57BL/6 male mice. Comparison with baseline genomic expression were examined by utilizing public RNA-seq data (GSE121330). Differently expressed genes (DEGs) between old and young groups were retrieved through t-test. P-value and fold change of DEGs were obtained, and visualized with volcano plot and heatmap. We performed 'PathfindR' R package for enrichment analysis.

Results: Sixty DEGs of kidneys changed after IRI significantly with distinct characteristics between old and young mice (satisfied with p-value < 0.001 and |fold change| >2.5) were identified, and 51 of them were manifested in old mice. Fifty one genes including Car15, Fxyd2 and Slc17a1 significantly upregulated, whereas nine genes including Mmp12, Dcn, and Arntl were downregulated in old mice. GO enrichment network analysis based on 1,587 DEGs with cut-off value of p < 0.001 meaning significant difference between young and old mice kidneys in recovery phase after IRI revealed that biologic processes such as spliceosome and viral carcinogenesis, which were closely associated cell proliferation, were demonstrated to be downregulated significantly at four weeks after IRI in old mice.

Conclusions: Our study demonstrated a resource of gene profiles in the recovery phase of aging kidneys after IRI, which may be utilized as potential therapeutic targets.