Functional genomic laboratory

A single-cell lncRNA atlas unveils cell type- and age-specific expression of lncRNAs across kidney cell types

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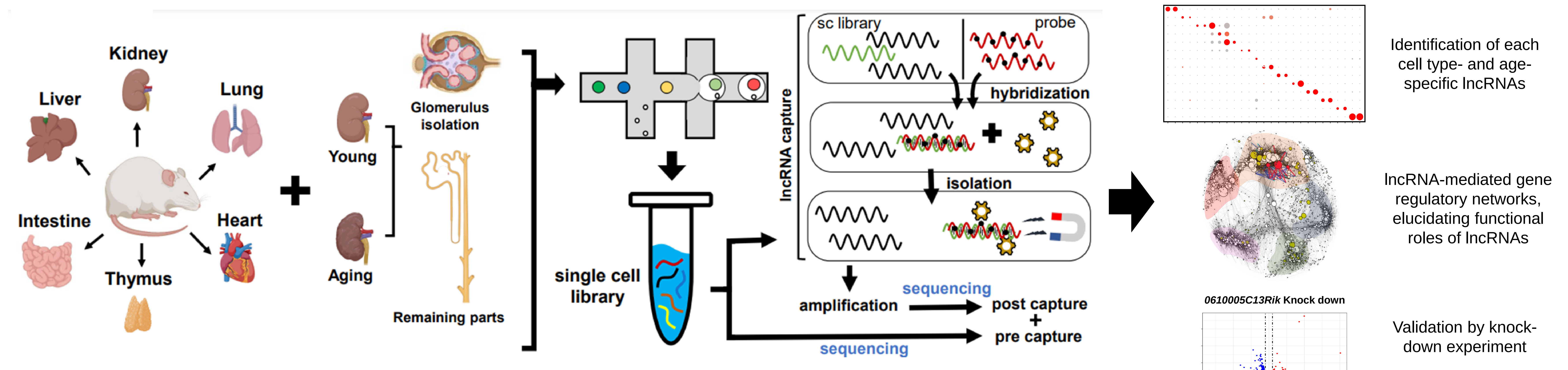
ABSTRACT

Long noncoding RNAs (lncRNAs) play versatile roles in the regulation of cell differentiation and homeostasis, influencing kidney aging and disease. However, the function of lncRNA remains poorly understood due to the lack of a reference map of lncRNA transcriptome in various cell types. In this study, we used a targeted single-cell RNA sequencing method to enrich and characterize lncRNAs in individual cells. We applied this method to various mouse tissues, including normal and aged kidneys. Through tissue-specific clustering analysis, we identified cell type–specific lncRNAs that showed a high correlation with known cell-type marker genes. Furthermore, we constructed gene regulatory networks to explore the functional roles of differentially expressed lncRNAs in each cell type. In the kidney, we observed dynamic expression changes of lncRNAs during aging, with specific changes in glomerular cells. These cell type– and age-specific expression patterns of lncRNAs potential roles in regulating cellular processes, such as immune response and energy metabolism, during kidney aging. Our study sheds light on the comprehensive landscape of lncRNA expression and function and provides a valuable resource for future analysis of lncRNAs.

INTRODUCTION



Identification of each cell type- and age-specific lncRNAs

lncRNA-mediated gene regulatory networks, elucidating functional roles of lncRNAs

Validation by knock-down experiment

RESULTS

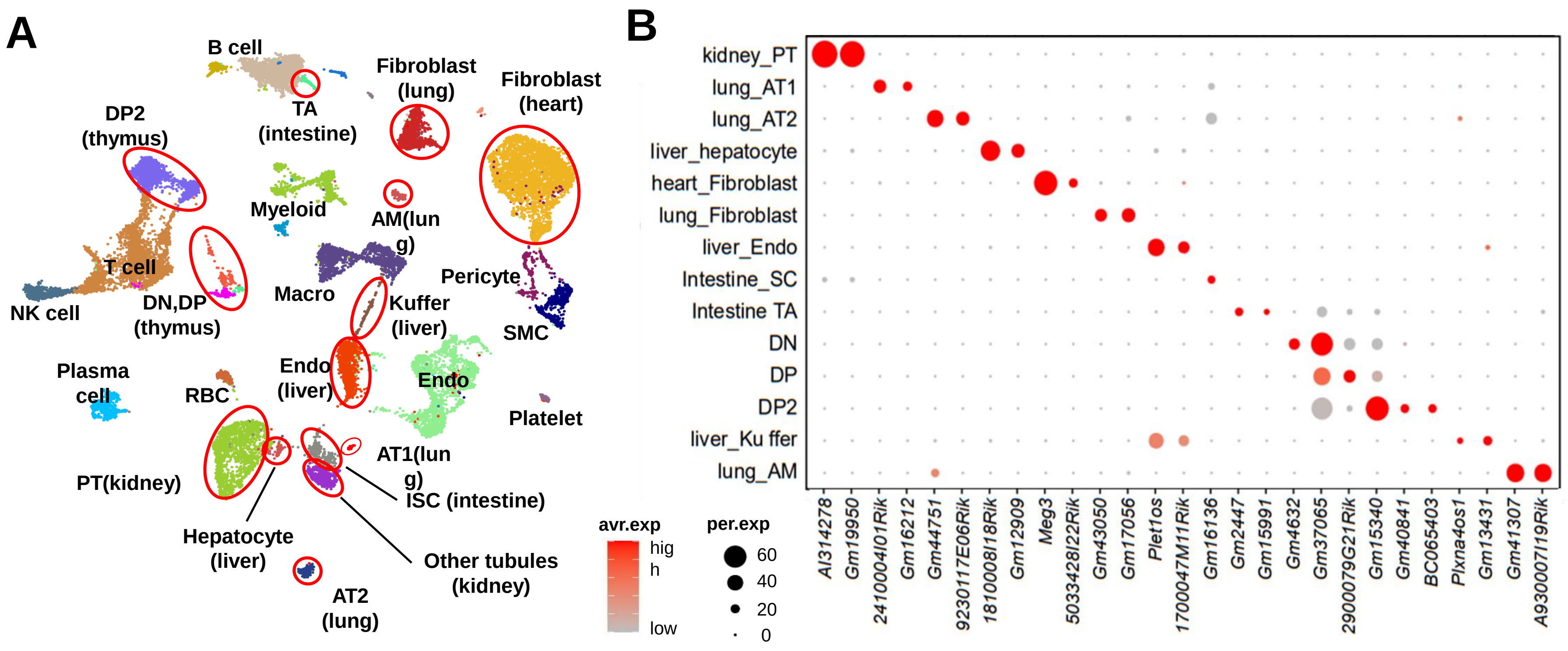


Fig 1. Targeted scRNA-seq enabled the detection of cell-type specific lncRNAs in six tissues.
A. The UMAP plot displays 31 cell clusters. Tissue-specific cell types are indicated by red circles
B. The heatmap illustrates differentially expressed lncRNAs in each cell type.

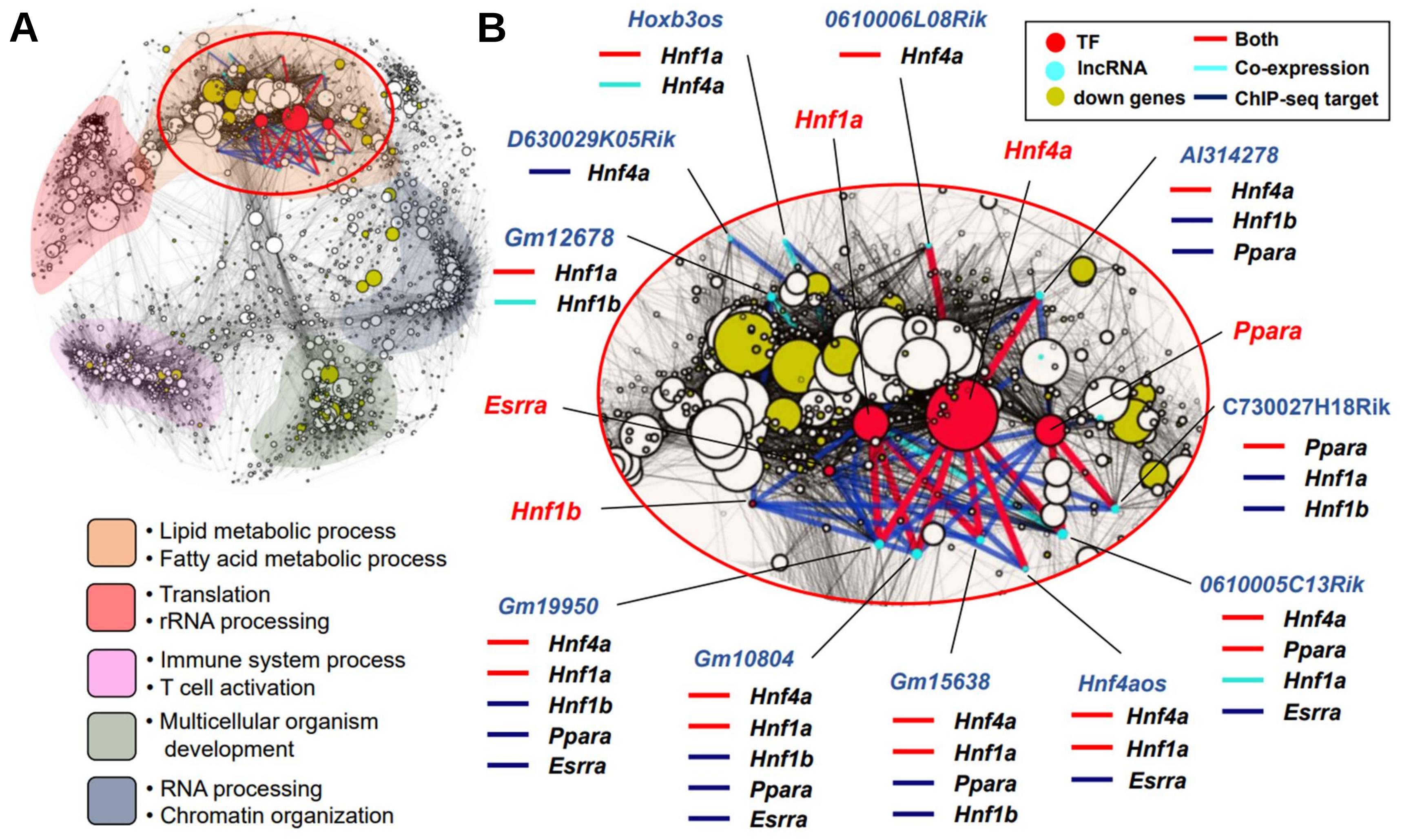


Fig 2. Gene regulatory network (GRN) analysis of lncRNAs and transcription factors in the kidney.
A. Gene regulatory networks between lncRNAs, transcription factors, and highly correlated genes in the kidney. **B.** Highlighting of a gene regulatory network involved in kidney tubule functions (orange color network).

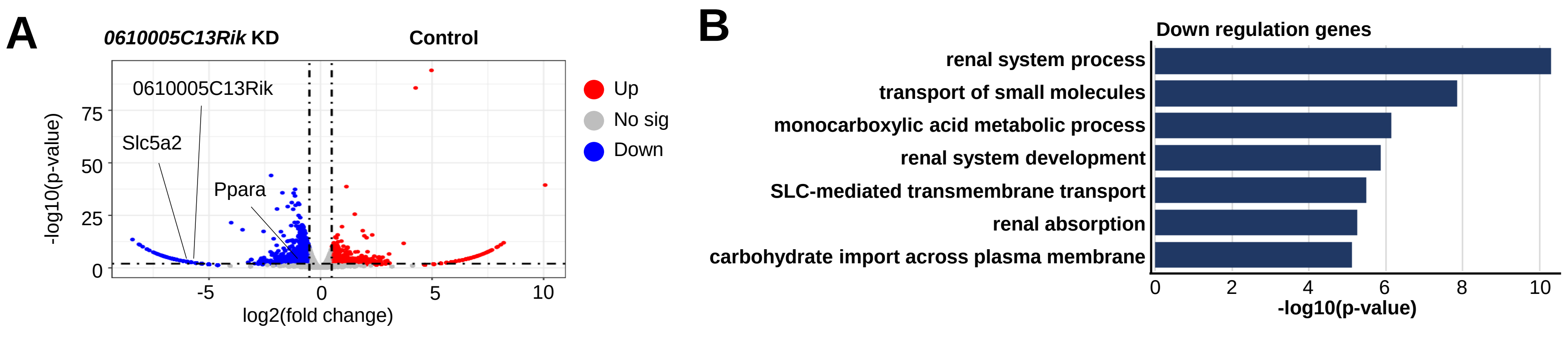


Fig 3. Validation of connectivity by 0610005C13Rik knock-down experiment
A. Down-regulated (blue) and up-regulated (red) genes following the 0610005C13Rik knockdown using siRNA. **B** Gene ontology enrichment analysis of downregulated genes.

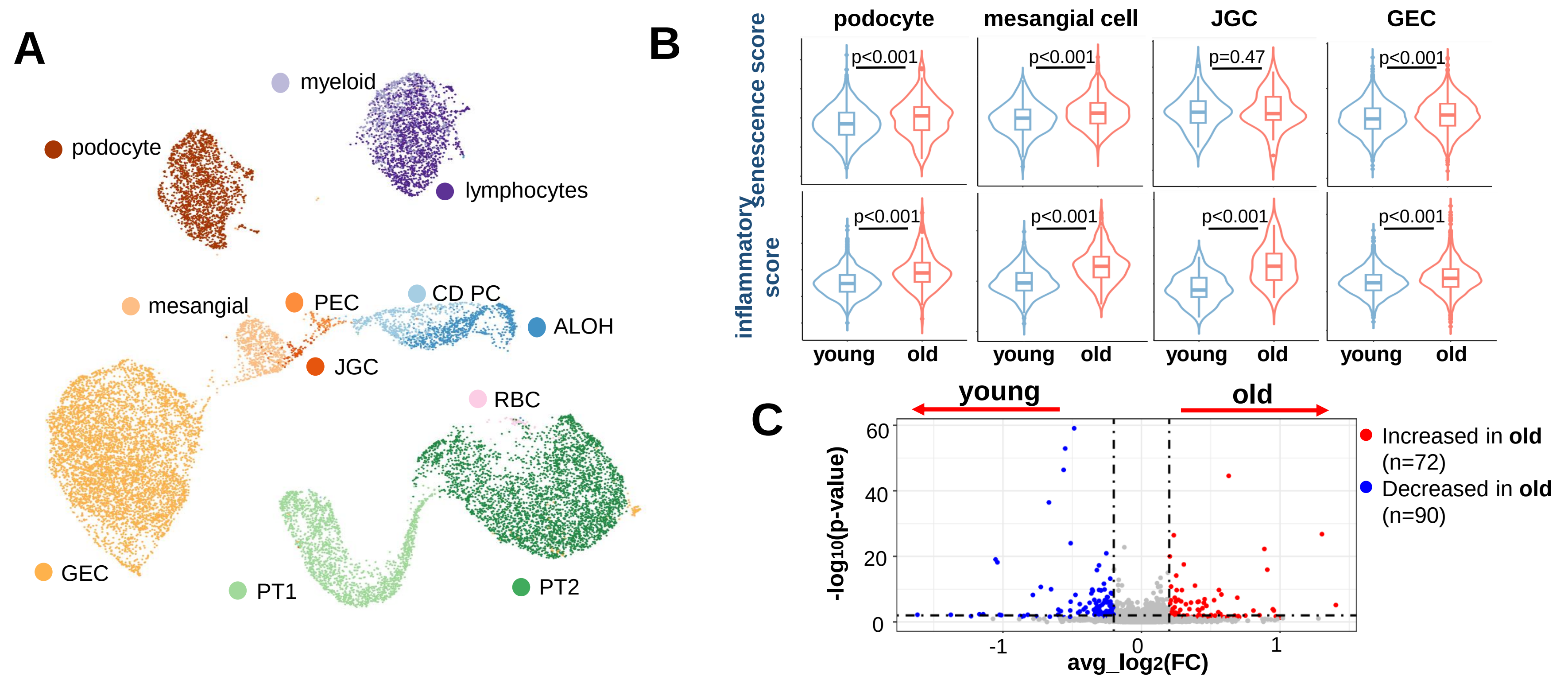


Fig 4. Comparison between young and old in various kidney cells.
A. UMAP visualization of 24 cell clusters. **B** Violinplot showing senescence and inflammatory scores in four glomerular cell types **C.** Volcano plot representing age-specifically expressed lncRNAs between young and old in all cell types.

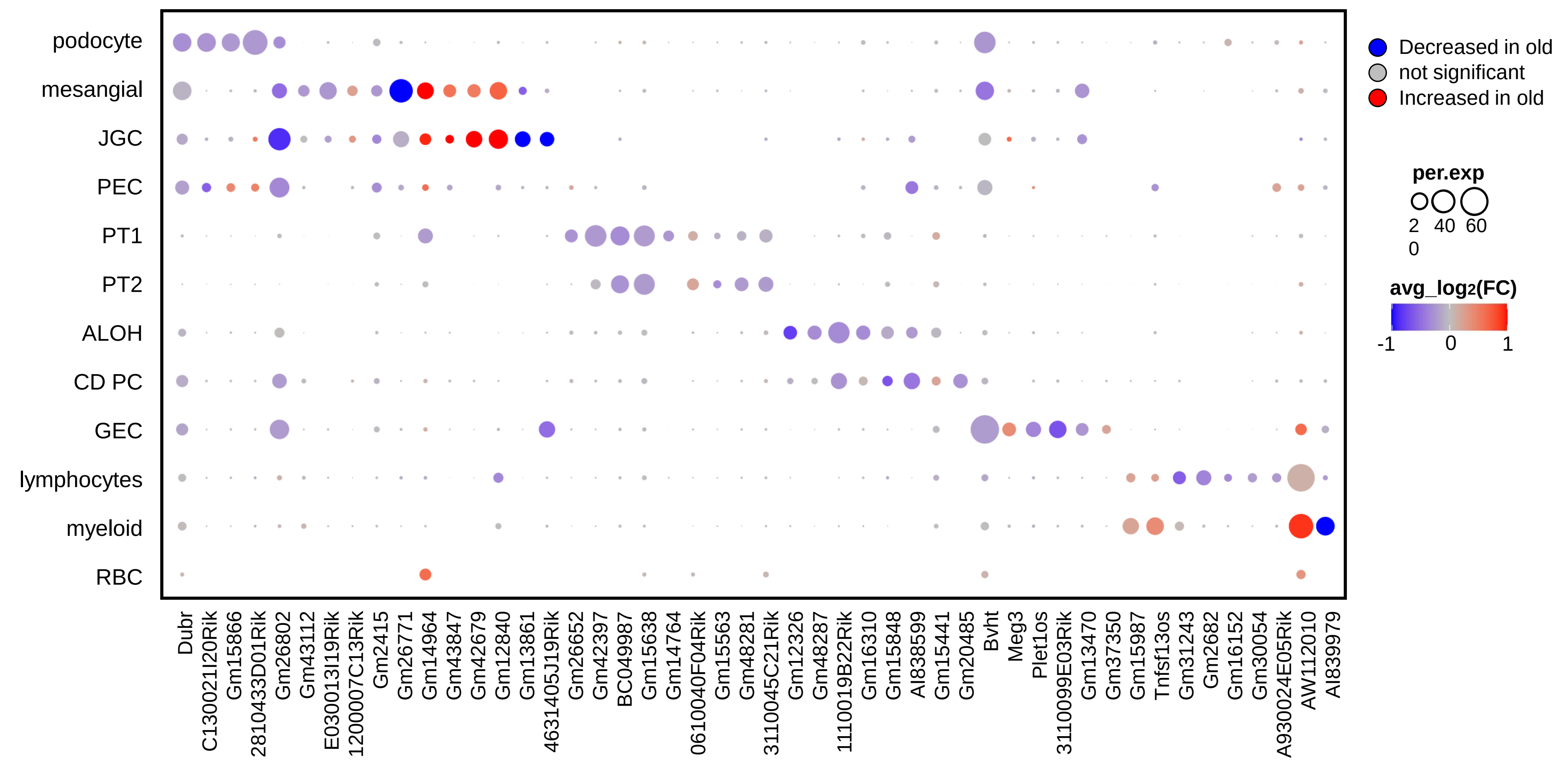


Fig 5. Exploring age- and cell type-specific expression of lncRNAs in glomerular cells.
Bubble plot showing age- and cell type- specific lncRNAs in each cell type.

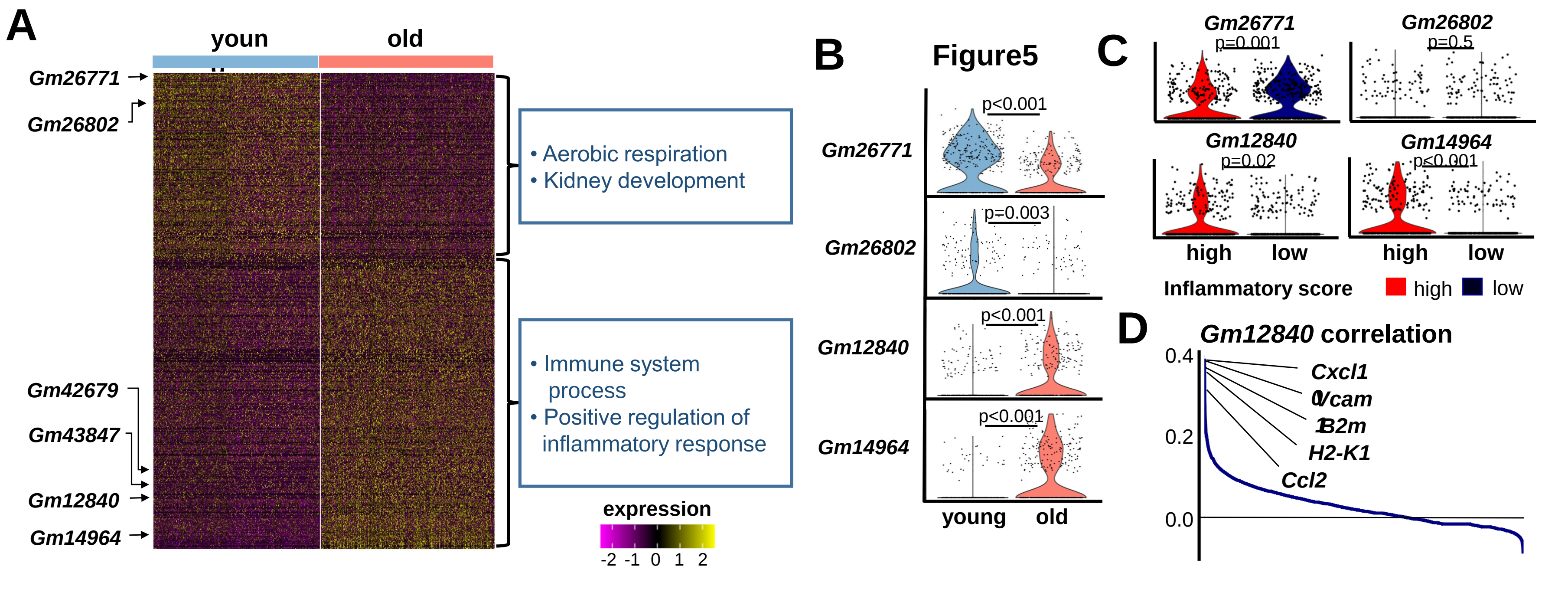


Fig 6. Characterization of age-specific gene expression and lncRNA dynamics
A. Heatmap showing age-specific gene expression in mesangial cells. **B.** Vlnplot showing age-specific lncRNAs in the mesangial **C.** Changes of lncRNA expression according to inflammation socre levels. **D.** Line plot showing the correlation with Gm12840.

REFERENCE

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2. Derrien T, Johnson R, Bussotti G, et al. The GENCODE v7 catalog of human long noncoding RNAs: analysis of their gene structure, evolution, and expression. Genome Res. Sep 2012;22(9):1775-89. doi:10.1101/gr.132159.111