The comprehensive single-cell atlas of mouse kidney with regional information

Abstract

The kidney is a highly heterogeneous organ, it is estimated that it has about 40 functionally different cell types. Single-cell RNA sequencing is a powerful technology for detecting cell types in highly complex tissues. However, no single study has comprehensively identified all cell populations residing in the kidney. For example, glomeruli are the functional units of the kidney, but they account for only about 1% -1.5% of the volume. Most whole kidney single-cell or single-nucleus RNA sequencing datasets do not include components of the glomeruli. Another exception is the neuron components, whose cell bodies are located paravertebrally and its axons extend into the kidney through renal hilus. However, their expression is largely unknown, especially their interactions with other renal components, through which they participate in the regulation of renal function. In this study, we used cutting-edge integration algorithms to integrate information from five sequencing datasets and generate a comprehensive single-cell atlas of mouse kidneys. Two of the datasets used micro-dissection to dissect different regions of the kidney for sequencing, and this regional information is also retained in this dataset. Using this dataset, we mainly explored the interactions between neurons and other renal components, and find that sensory neurons have more connections with other renal cells than sympathetic neurons but sympathetic neurons have stronger connections with those cells.

Introduction

Methods

Results

fastMNN integration better than other methods

First of all, we test the performance of the most used integration algorithms, which implemented in harmony1, Seurat2, batchelor3, and RICS4 R package respectively. Form comparison we find that fastMNN implemented in the batchelor R package is performed best than others, and harmony is in the second. Seurat and RISC performed worset both in integration performance and computational efficiency. fastMNN can clear bring similar cells together, such as VMSC and Pericytes from GSE129798 and GSE146912, but harmony failed to do this, such as afferent/efferent endothelial cells from GSE129798 and GSE146912 didn’t cluster together. However, Seurat and RISC even didn’t separate glia cells and neurons cells. Based on this clue, we choose fastMNN integration results for further analysis.

All cell’s canonical markers are detected in the integrated dataset

For ease the downstream marker detection and cell-cell communication analysis, we first partition cells into three different resolutions, for example at the first level immune cells from bone marrow and thymus are annotated as immune cells, at the third level all cell types are annotated to the highest resolution that can be identified in this dataset, such as T cells are divided into Cd4 positive and Cd8 positive T cells, proximal tubule epithelial cells are divided into PTS1, PTS2 and PTS3. But at the second level Cd4 and Cd8 T cells are in the T cell group and PTS1, PTS2 and PTS3 are in the proximal tubule cluster.

Cell-Cell communication

Discussion

Reference

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