

Single-Cell Sequencing & Artificial Intelligence: Bringing Kidney Transplantation to the Digital Age & Beyond

Abstract

Kidney allografts carry a high risk of rejection that is difficult to predict pre-transplantation. Single-cell RNA sequencing (scRNA-seq) technology allows us to distinguish between cells that are morphologically identical but genetically and functionally distinct, based on active gene transcription. It can provide physicians with a much more detailed analysis of patient and donor specifics, increasing chances of successful transplantations.

scRNA-seq will require high-throughput analysis technologies and artificial intelligence (AI) programs to compile and interpret massive amounts of data to actionable states (Figure 1). Here we outline some of the major strides taken in kidney pathology and transplantation through the use of scRNA-seq and AI.

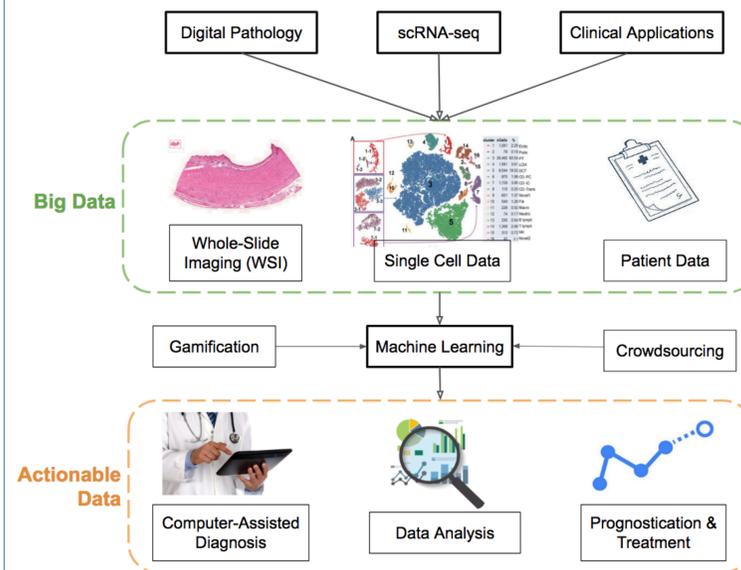


Figure 1: Bringing kidney medicine into the digital age with the help of scRNA-seq and artificial intelligence.

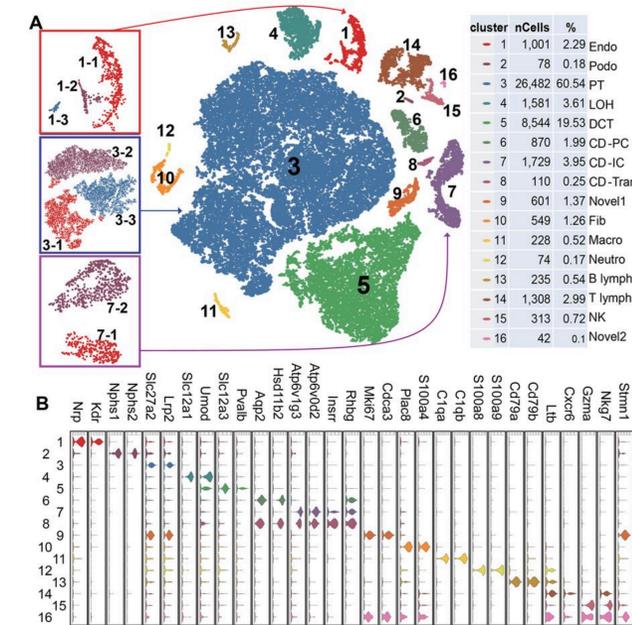


Figure 2: scRNA-seq in mouse kidney cells reveals 16 cell types (A) with variant marker gene expression (B)⁵.

Conclusion

scRNA-seq has exponentially developed in the past 8 years, signaling the start of an era in which researchers are able to identify and detect numerous new cell subtypes, subtle pathological mechanisms, and low-level gene expression at a cellular level. In conjunction with WSI and other mass data collection methods, new technology is producing 'big data', which can be efficiently analyzed by AI programs.

Renal transplantation today is uncertain and imprecise. Allograft rejection can be greatly reduced with detailed information on gene expression, precision phenotypes, and patient risk factors. scRNA-seq and AI will change how we conceptualize heterogeneous disease and gene expression, and create a better outlook for renal transplantation patients.

Introduction

Current biopsy analysis tools, used to assess the viability of allografts, are long overdue for a technology able to identify subtle cell-to-cell variations (such as in gene expression and protein signaling). Following the trends observed in analogous systems¹ we predict that scRNA-seq studies will double the number of classified kidney cell subtypes from 26 to 52.

A new wave of research has emerged, combining the skillsets of medical experts and computer scientists by using methods such as digital pathology, gamification, and crowdsourcing to improve clinical outcomes. With the help of large scale single-cell projects² and AI for data collection and mining, we can begin to understand how kidney medicine will evolve in the Digital Age. Transplant prognostication will likely increase in accuracy, giving physicians more time and information to decrease chances of rejection.

Clinical Applications

ML in Predicting Allograft Survival:

It is difficult to predict kidney transplant outcomes based on the extensive and diverse factors in the donor and recipient history. A recent study³ applied ML to large-scale retrospective data, finding that early acute rejection (within 1 year) and 3-month serum creatinine levels were important risk factors for long-term graft survival.

Whole Slide Image Analysis:

Because human pathologists and ML systems make different mistakes⁶, computer-assisted diagnosis could greatly improve histopathology classification. The ability to examine sub-visual features presents the opportunity for precise disease characterization and prognostication.

scRNA-seq in Mouse Kidney Cells:

A 2017 study⁴ determined 18 genes in mouse mesangial cells to be integral for endothelial homeostasis, most of which showed altered expression in several human glomerulopathies. Another study⁵ identified 3 novel renal cell types (Figure 2), and demonstrated that specific kidney diseases are linked to specific cell types.

Gamification in Medicine:

In addition to gamified learning in medical education, gamification has generated many novel discoveries in computational biology via crowd-sourcing. Examples include the creation of ML algorithms for image analysis⁷ and predictions of protein folding structures.

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