MGI DNBelab C4 based single-cell RNA sequencing for the fight against SARS-CoV-2

Pocket Single-Cell Lab combined with DNBSEQ™series genetic sequencers enables high-quality data for large-scale single-cell study in a cost-effective way

Highlights

Portable

- Length 205mm, Width 46mm, Height 57mm, Weight 200g
  Power-free, disposable, easy-to-use

Accurate

- Low multiplet rate and high gene detection sensitivity

One-stop

- Provide one-stop cell-omics platform from cell to single-cell analysis report

Introduction

The advance of single-cell trans-omics technology has offered incisive tools for understanding of systems biology. DNBelab Cell Omics Package, featuring proprietary DNBelab C Series Single-Cell Sample Preparation and DNBSEQ™sequencing technologies, is comprised of DNBelab C4 Pocket Single-Cell Lab, DNBelab C Series Single-Cell Library Preparation Set, and Single-Cell Analysis Suite, all as part of a portable, instant, and one-stop single-cell research workflow.

Here, we profiled the transcriptome of nine tissues/organs from a *Macaca fascicularis* monkey at single-cell resolution with DNBelab C4 system. The expression profile of SARS-CoV-2 receptor (*ACE2*) and its assistor (*TMPRSS2*) across 9 tissues/organs were examined. Taken together, our data constitute a unique resource which could aid the scientific community in the fight against SARS-CoV-2. From a wider perspective, this will also be instrumental for systematically comparative studies aimed at understanding physiological and pathophysiological differences between monkey and other species, in particular, human.

Figure 1. **The workflow from cell to data**

Case

Experimental Method

- **Collection of monkey tissues/organs**

Tissues/organs were isolated from a 6-year old female cynomolgus monkey. Whole tissues/organs including lung, kidney, pancreas, liver, brain, thyroid, parotid gland, aorta, and PBMCs were collected and reserved in liquid nitrogen.

- **Single-nucleus/cell suspension preparation**

Cell/nuclei were isolated as previously described (Liu et al., 2019) and then were resuspended with cell resuspension buffer at a concentration of 1,000 cells/μl for further single-cell library preparation.

- **Single-nucleus/cell RNA-seq**

The DNBelab C Series Single-Cell RNA Library Prep Set (MGI, #1000021082) was utilized as previously described (Liu et al., 2019; Zhu et al., 2020). Libraries were sequenced using 100bp paired-end sequencing on the DNBSEQ platform.

- **Single-cell RNA-seq data processing**

Sequencing data was processed using Single-Cell Analysis Suite, briefly, reads were aligned to *Macaca_fascicularis_5.0* genome using STAR (version 2.7.4a) (Dobin et al., 2013) and sorted by sambamba (version 0.7.0) (Tarasov et al., 2015). Cell versus gene UMI count matrix was generated using PISA (Han et al., 2020).

Result

The transcriptome profiling of nine tissues/organs at a single-cell resolution in monkey have been successfully profiled. We employed a high-throughput platform recently developed in-house, DNBelab C4, which is a scalable and cost-effective approach for microfluidic droplet-based approach. Except for PBMC sequencing, which was performed using cells in suspension, the sequencing for all the other tissues/organs was done using single-nucleus library preparations. We performed Uniform Manifold Approximation and Projection (UMAP) on the 215,334 cells/nuclei and identified 44 major clusters by performing unbiased graph-based Louvain clustering as shown in Figure 2.

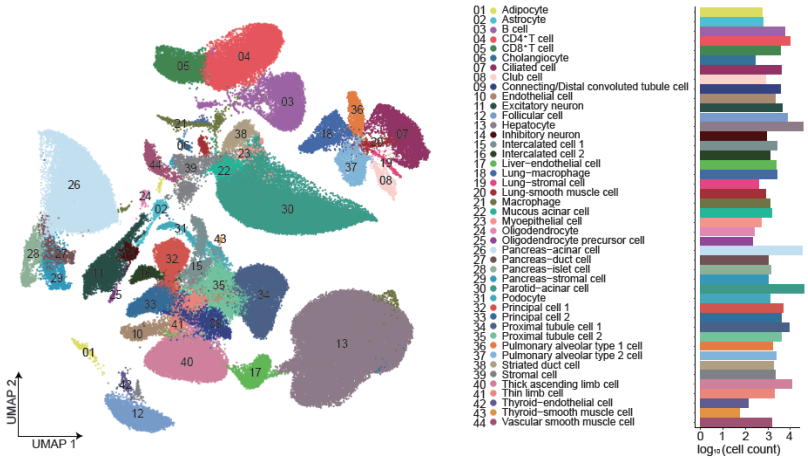

Figure 2. Construction of single-cell atlas across nine tissues/organs of a *Macaca fascicularis* monkey

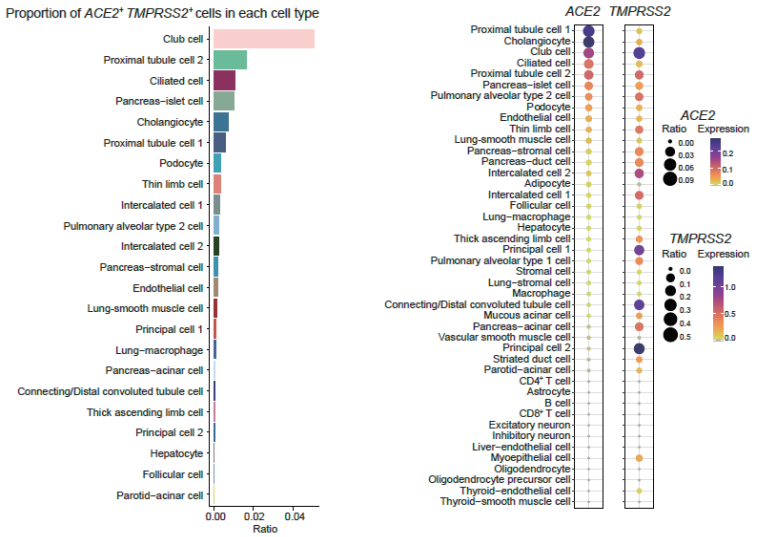

Figure 3. *ACE2* and *TMPRSS2* expression across 44 cell clusters in monkey

Further, we found that *ACE2* and *TMPRSS2* are expressed in a variety of cell types, mainly epithelial cells, within the nine monkey organs/tissues. High expression level of *ACE2* is not only found in lung epithelial cell but also in kidney, liver and pancreas, suggesting potential infect targets by SARS-CoV-2 (Figure 3).

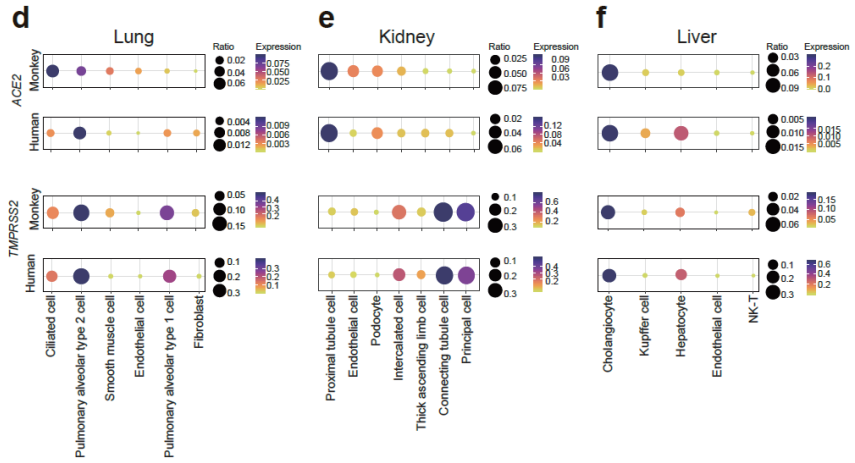

Figure 4. Comparative analysis of *ACE2* and *TMPRSS2* expression between monkey and human

IIn addition, *ACE2* showed distinct patterns among cell subtypes in lung, kidney and liver between the two species. As to *TMPRSS2*, it demonstrated similar expression pattern among cell subtypes in all three tissues (Figure 4). These different expression level of *ACE2* across cell types in the lung, kidney and liver in monkey and human raise the possibility that infection with SARS-CoV-2 in the two species will have different effects.

Conclusion

In the current application note, we introduced how DNBelab C4 was applied to build a single-cell transcriptome atlas. Combined with MGI DNBSEQ™series genetic sequencer, DNBelab C4 enables high-quality data for large-scale and high throughput single-cell study in a cost-effective way.

Ordering Information

Product	Specification	Item number
DNBelab C Series Single-Cell RNA Library Prep Set	16RXN	1000021082

*one kit will include one DNBelab C4 free of charge

Reference

1. Liu, C. et al. A portable and cost-effective microfluidic system for massively parallel single-cell transcriptome profiling. bioRxiv. 818450 (2019)
2. Zhu, L. et al. Single-cell sequencing of peripheral blood mononuclear cells reveals distinct immune response landscapes of COVID-19 and influenza patients. Immunity. S1074-7613(20)30316-2 (2020)
3. Dobin, A. et al. STAR: ultrafast universal RNA-seq aligner. Bioinformatics 29, 15-21 (2013)
4. Tarasov, A. et al. Sambamba: fast processing of NGS alignment formats. Bioinformatics 31, 2032-2034 (2015)
5. Han, L. et al. Single-cell atlas of a non-human primate reveals new pathogenic mechanisms of COVID-19. bioRxiv. 022103 (2020)

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