nature

https://doi.org/10.1038/s41586-020-2157-4

Construction of a human cell landscape at single-cell level

Xiaoping Han, Ziming Zhou, Lijiang Fei, Huiyu Sun, Renying Wang, Yao Chen, Haide Chen, Jingjing Wang, Huanna Tang, Wenhao Ge, Yincong Zhou, Fang Ye, Mengmeng Jiang, Junqing Wu, Yanyu Xiao, Xiaoning Jia, Tingyue Zhang, Xiaojie Ma, Qi Zhang, Xueli Bai, Shujing Lai, Chengxuan Yu, Lijun Zhu, Rui Lin, Yuchi Gao, Min Wang, Yiqing Wu, Jianming Zhang, Renya Zhan, Saiyong Zhu, Hailan Hu, Changchun Wang, Ming Chen, He Huang, Tingbo Liang, Jianghua Chen, Weilin Wang, Dan Zhang & Guoji Guo

Cell atlases

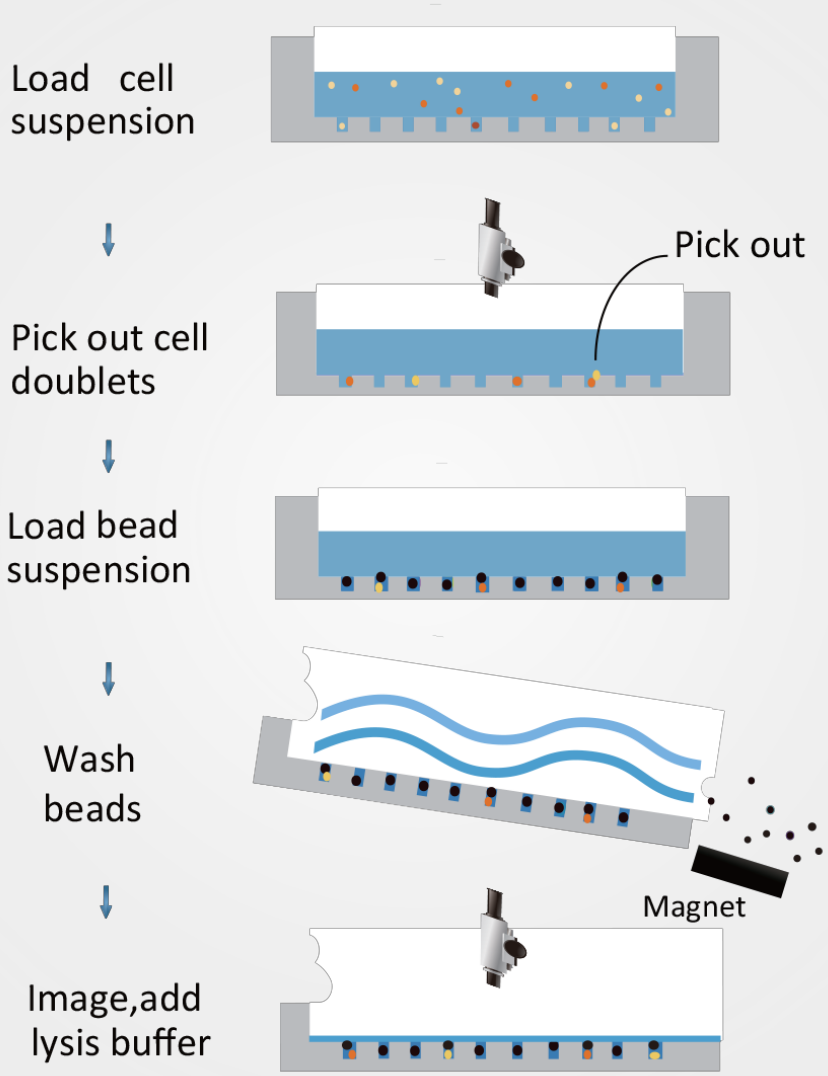
Resource

Cell

Mapping the Mouse Cell Atlas by Microwell-Seq

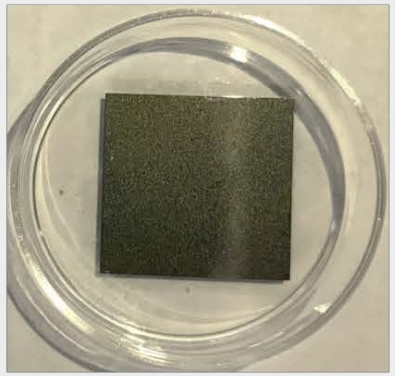
Xiaoping Han,[1,12,13,*] Renying Wang,[1,12,13] Yincong Zhou,[2,12,13] Lijiang Fei,[1,12,13] Huiyu Sun,[1,12,13] Shujing Lai,[1,12,13] Assieh Saadatpour,[11] Ziming Zhou,[1,12] Haide Chen,[1,12] Fang Ye,[1,12] Daosheng Huang,[1] Yang Xu,[1] Wentao Huang,[1] Mengmeng Jiang,[1,12] Xinyi Jiang,[1,12] Jie Mao,[3] Yao Chen,[4] Chenyu Lu,[5] Jin Xie,[6] Qun Fang,[7] Yibin Wang,[8] Rui Yue,[8] Tiefeng Li,[3] He Huang,[9,12] Stuart H. Orkin,[10] Guo-Cheng Yuan,[11] Ming Chen,[2,12] and Guoji Guo[1,9,12,14,*]

Microwell-seq – a cost effective scRNA-seq method



Lai et al., 2017

Single cells are captured in a 28 µm well

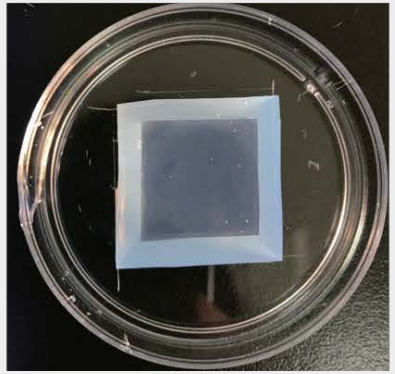


Silicon Wafer

Microwell

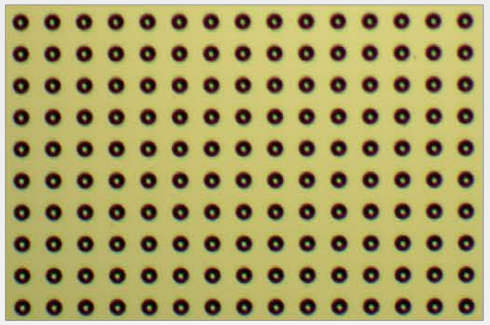
PDMS

Micropillar



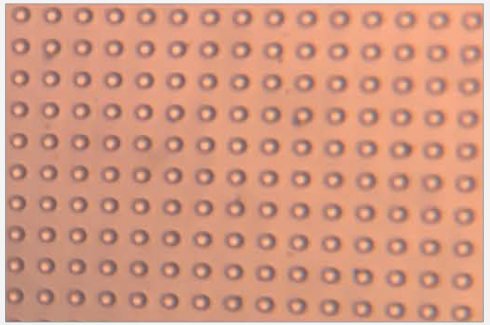
Agarose

Microwell



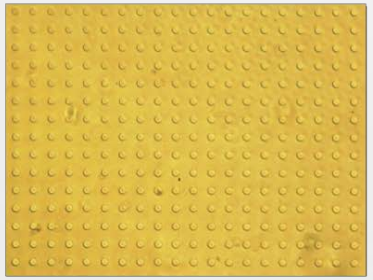
A silicon wafer (~20 by 20 mm) containing ~10,000 microwells was used as a template.

Polydimethylsiloxane (PDMS)was poured onto the silicon wafer(80 ℃, 5h) to create micropillars arrays.

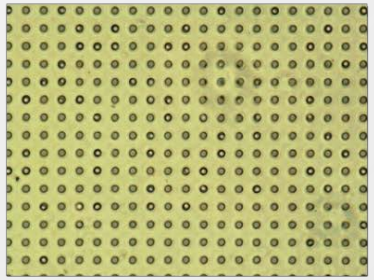


Agarose (5%) microwell arrays were cast from the PDMS micro-pillars array before each experiment.

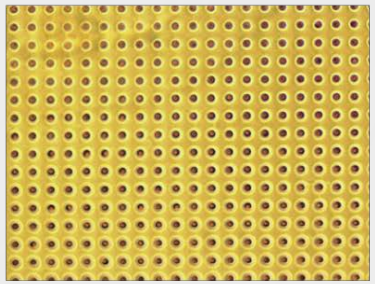
Empty



Cell



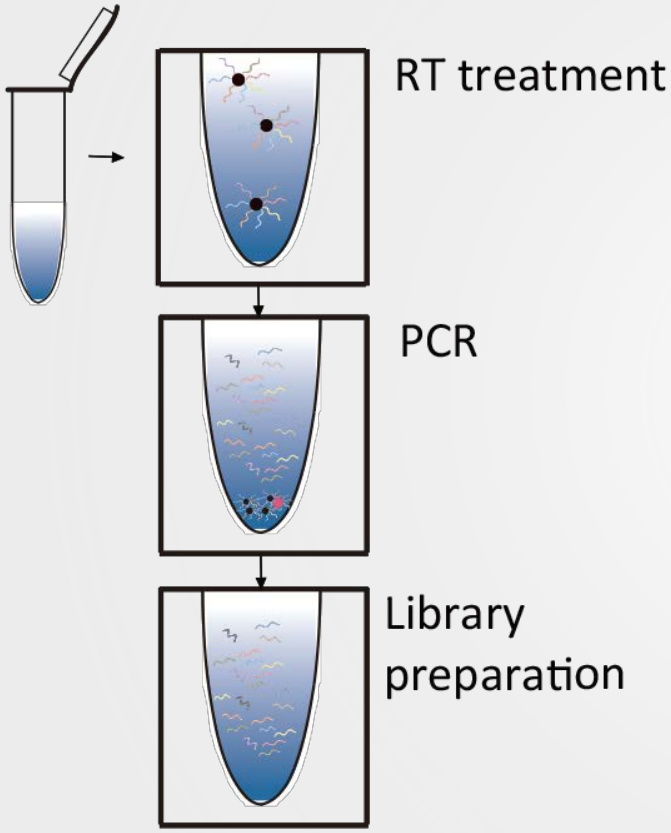
Magnetic Bead + Cell

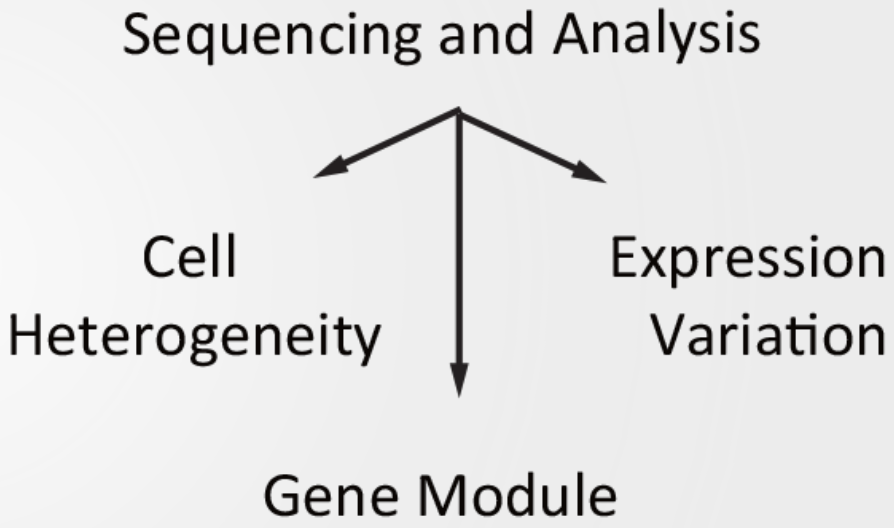


Lai et al., 2017

Lai et al., 2017

Single cells are captured in a 28 µM Microwell

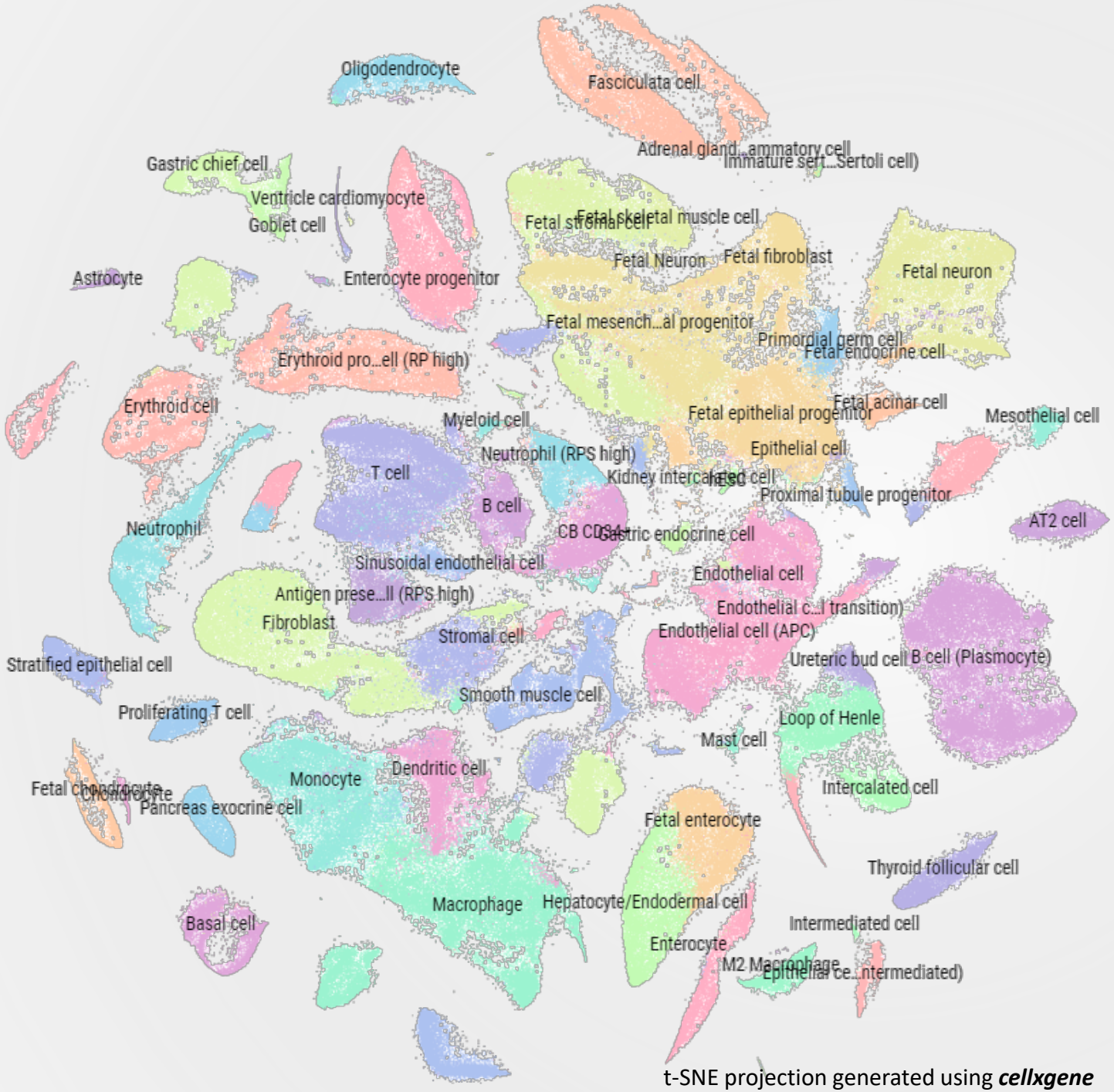




Lai et al., 2017

Construction of a human cell landscape through microwell-seq

- Generation of extensive human cell atlas
  - All mayor human organs (60 tissue types)
  - Adult and fetal stages
  - 7 types of cell cultures (e.g. iPSC, embyroid bodies)



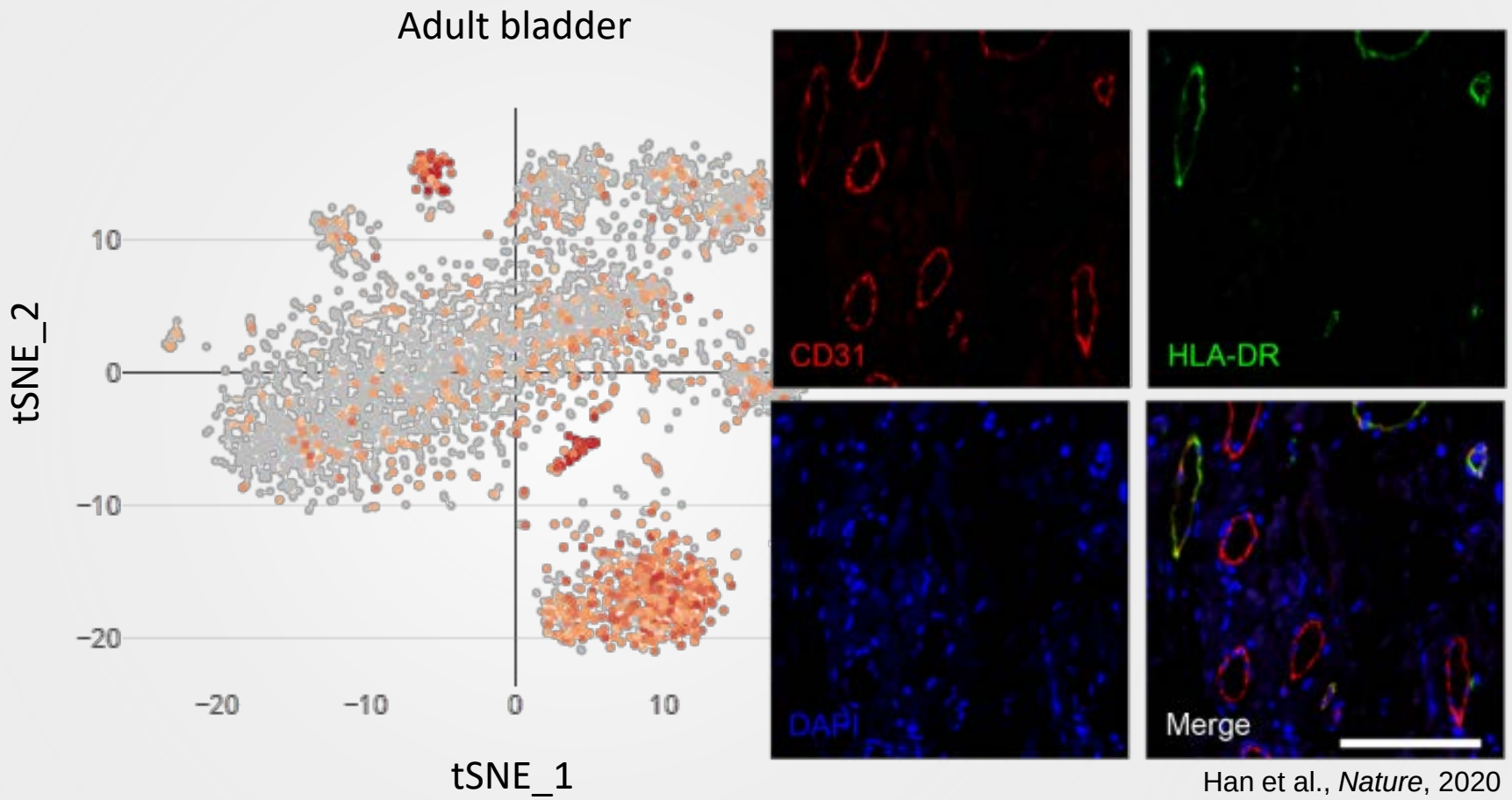
- 702.968 single cells passed QC
- 102 major clusters
- 843 cell-type subclusters

t-SNE projection generated using ***cellxgene***

Human landscape dataset can be used to…

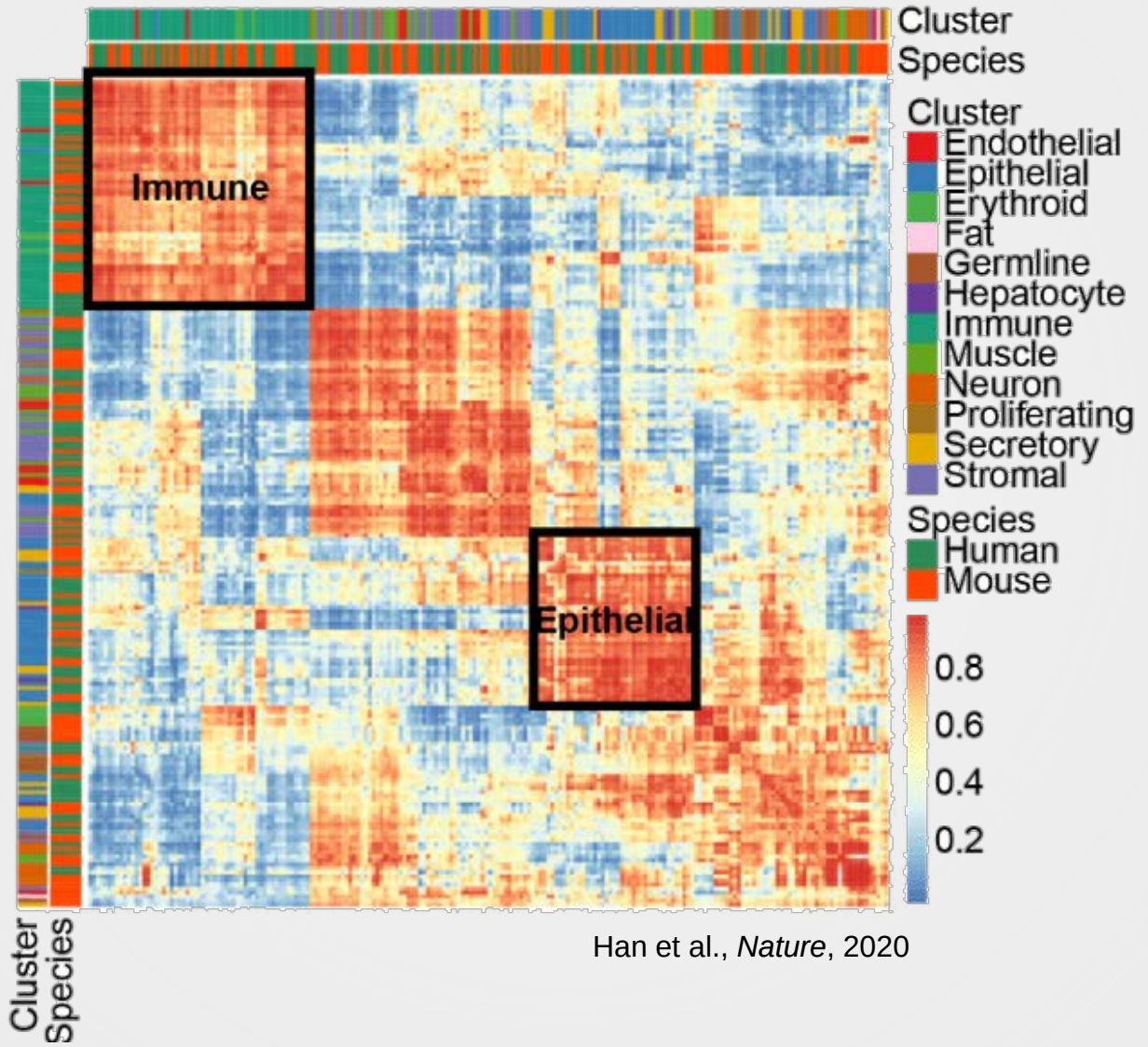
- study tissue heterogeneity and identify unknown cell types
- compare mammalian cell landscapes and identify conserved transcriptional networks
- study fetal to adult cell-type transitions

Analysis of heterogeneity can reveal previously unknown cell types



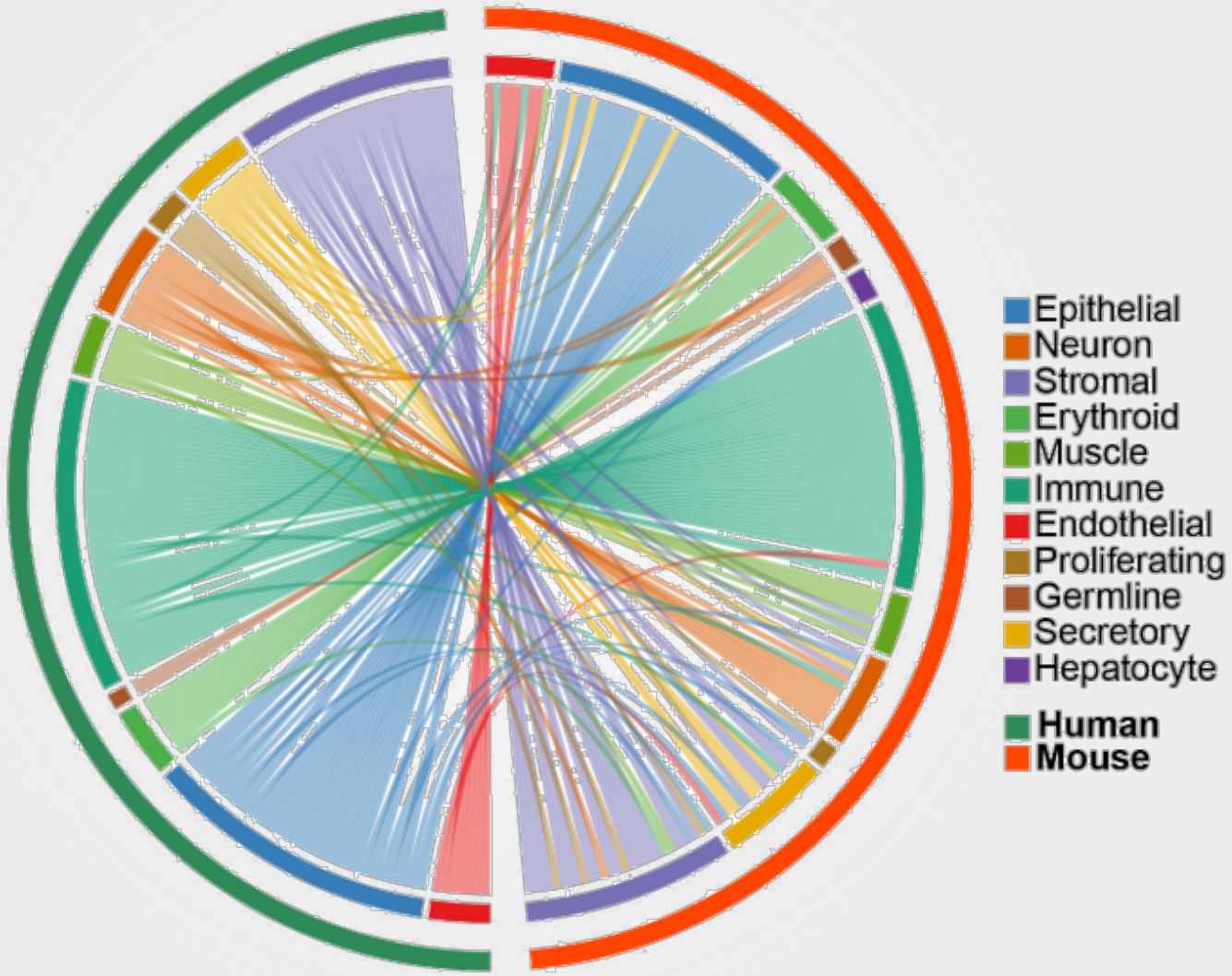
Han et al., *Nature*, 2020

Orhtologous gene expression among species can be studied



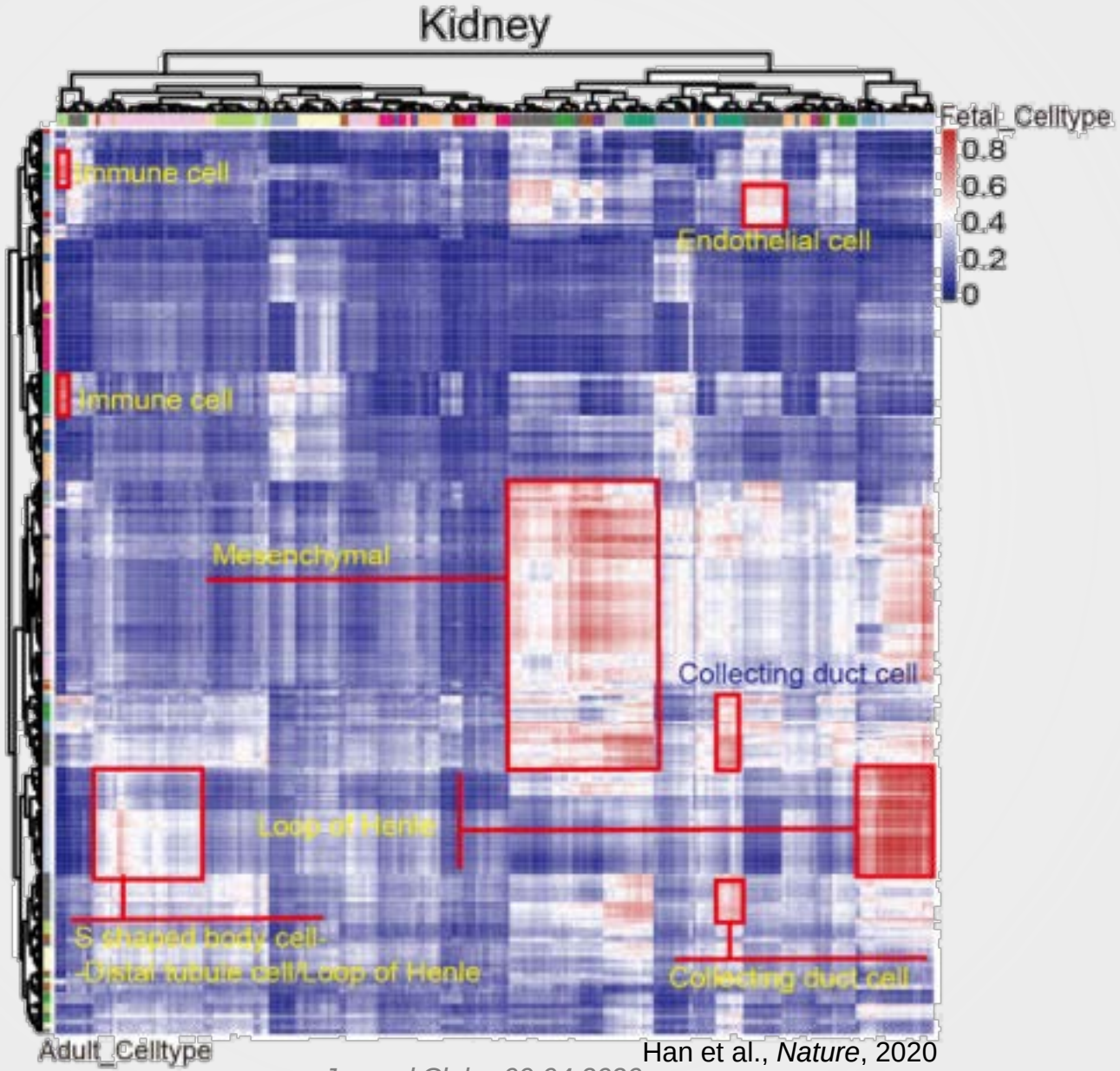
Han et al., *Nature*, 2020

Orhtologous gene expression among species can be studied



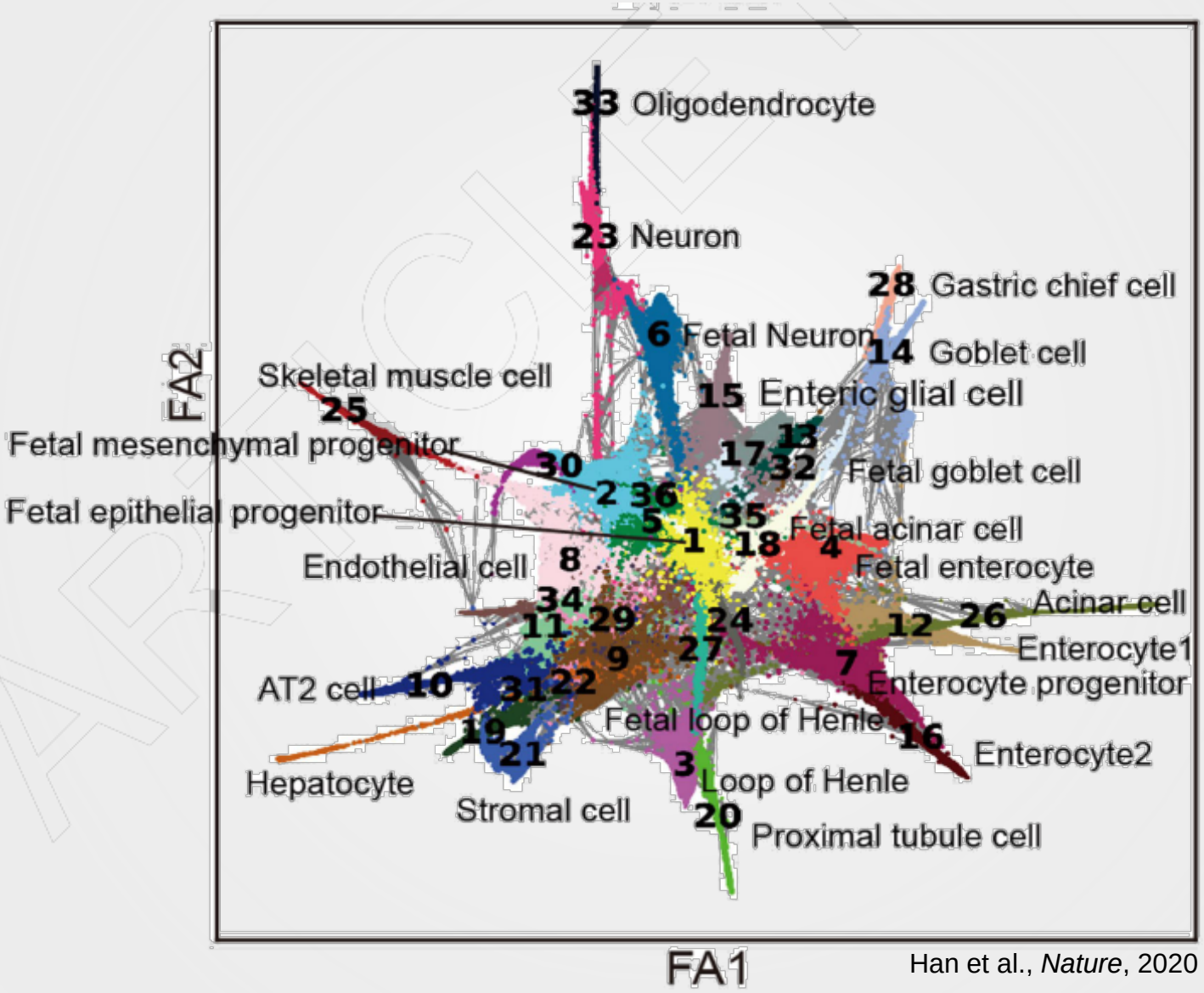
Han et al., *Nature*, 2020

Including fetal samples helps decipher cellular development



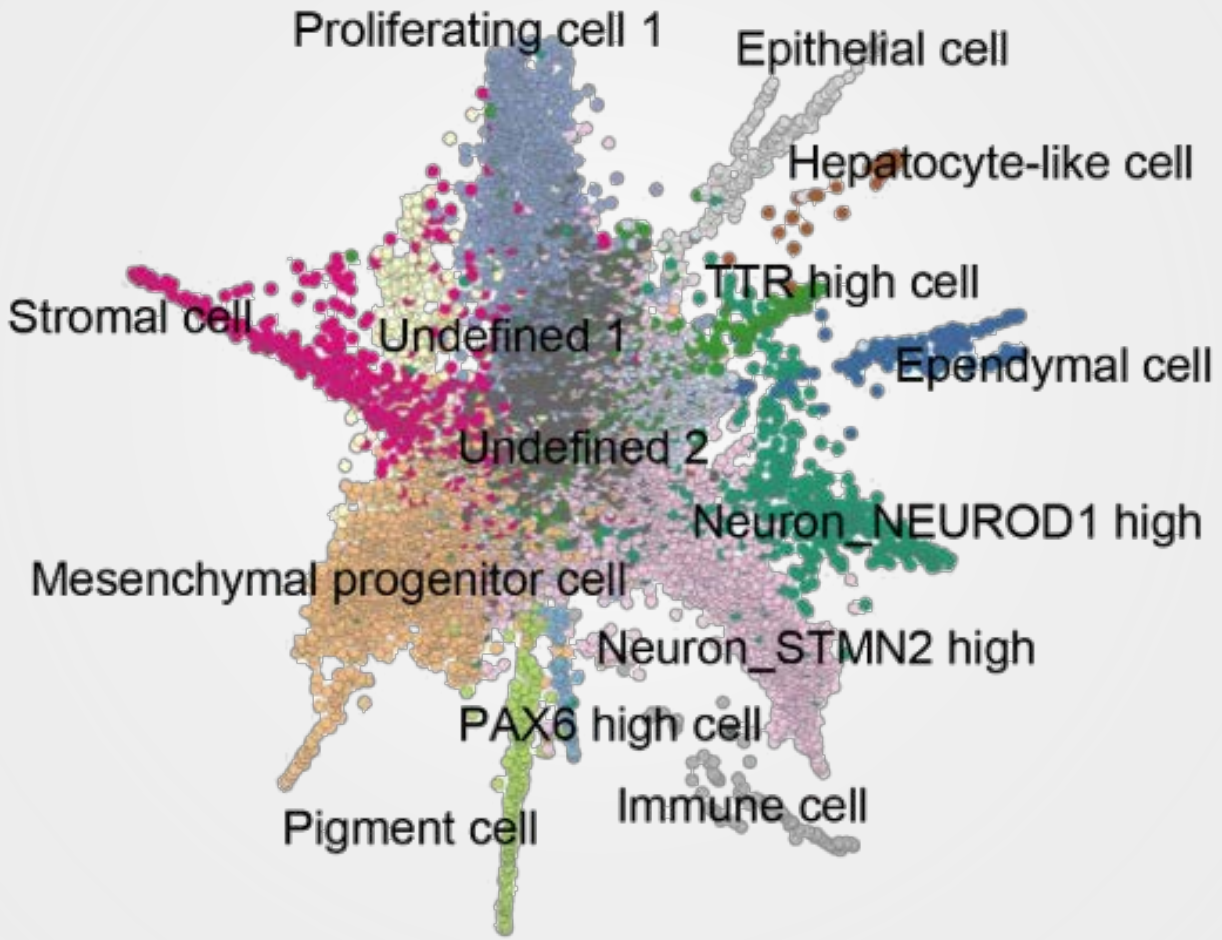
Han et al., *Nature*, 2020

Including fetal samples helps decipher cellular development



Han et al., *Nature*, 2020

Fetal plasticity is captured in iPSC to EB transition



Key findings

- identification of novel cell types and progenitors
  - MHC-II complex expressed in bladder and kidney
    - Novel immune function
- study conservation of transcriptional profile and cell types across species
- decipher fetal-adult transition
  - Fetal cells have high transcriptional plasticity, whereas differentiated cells have more stable transcriptome.

Outlook

- limitations in sequencing depth and cell number need to be overcome
  - Detection of rare cell types

- contribution to the international human cell atlas iniative