

HUMAN
CELL
ATLAS

Benchmarking of Single Cell RNA Sequencing Protocols for Cell Atlas Projects

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Dec 10, 2019

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<https://github.com/elimereu>

Background



Cell Types



Dendritic cells

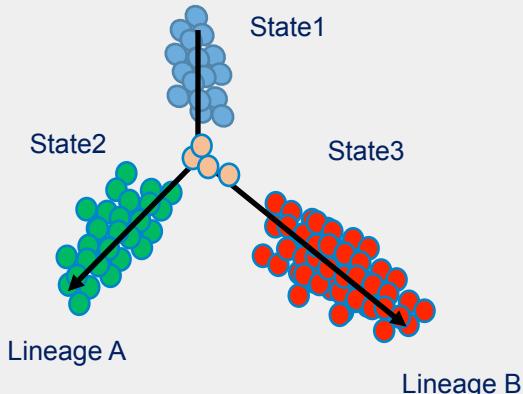


B cells



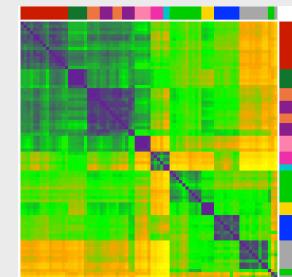
Endothelial cells

Cell States and lineages

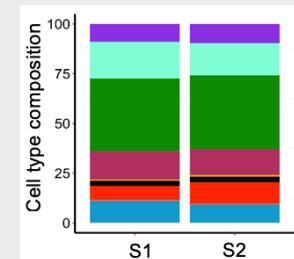


Evaluation

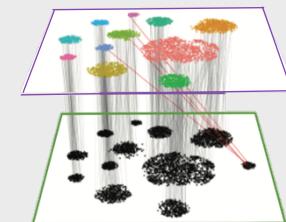
Reproducibility



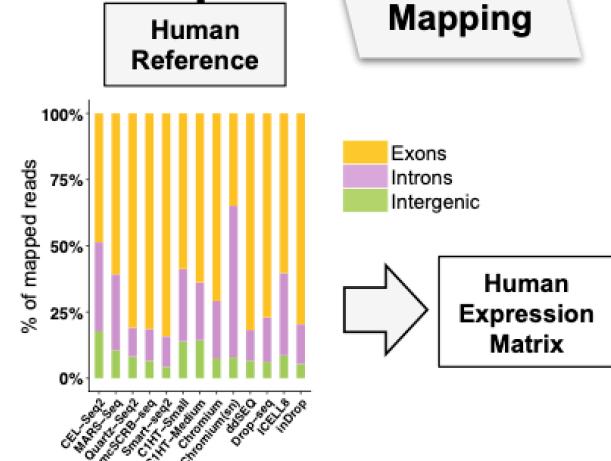
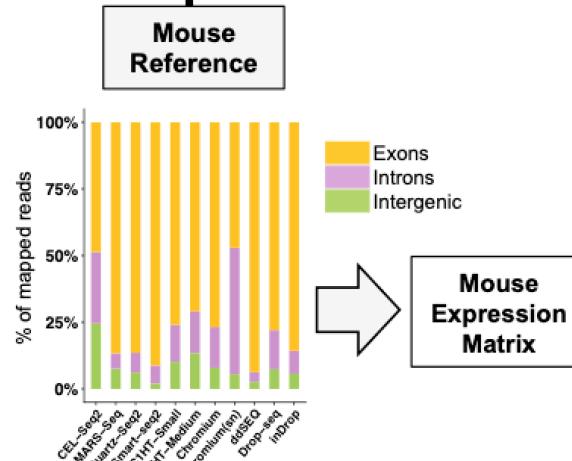
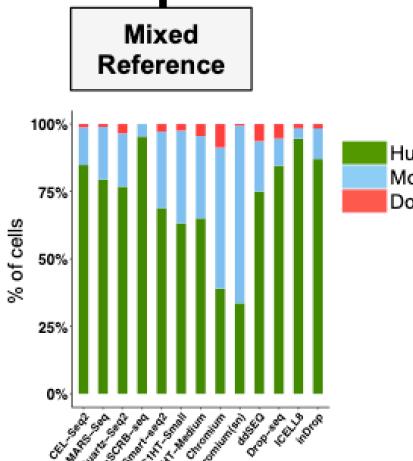
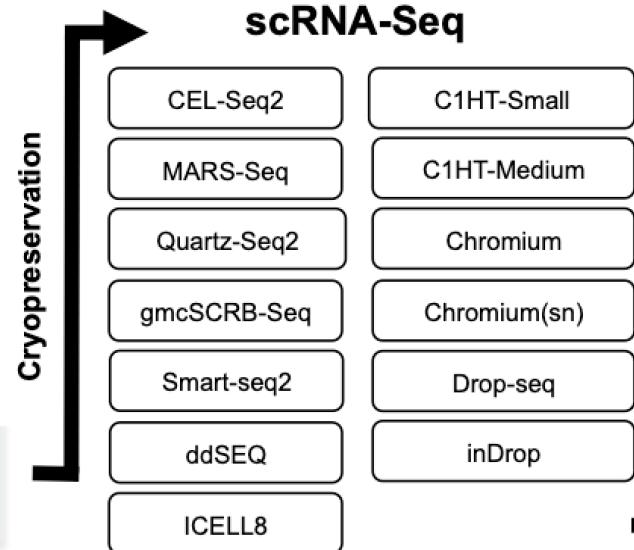
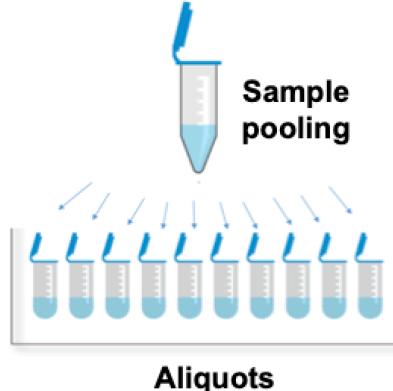
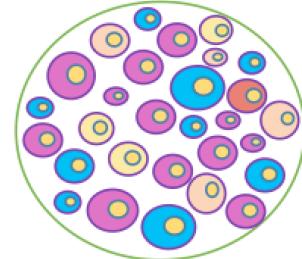
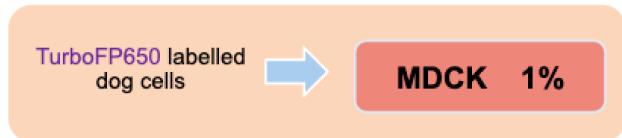
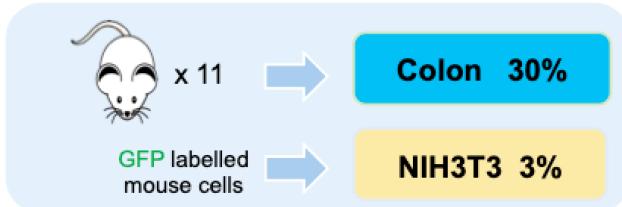
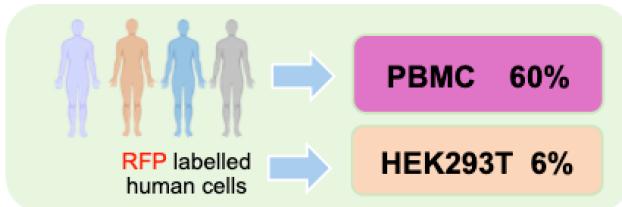
Integrity



Predictive values



Reference sample

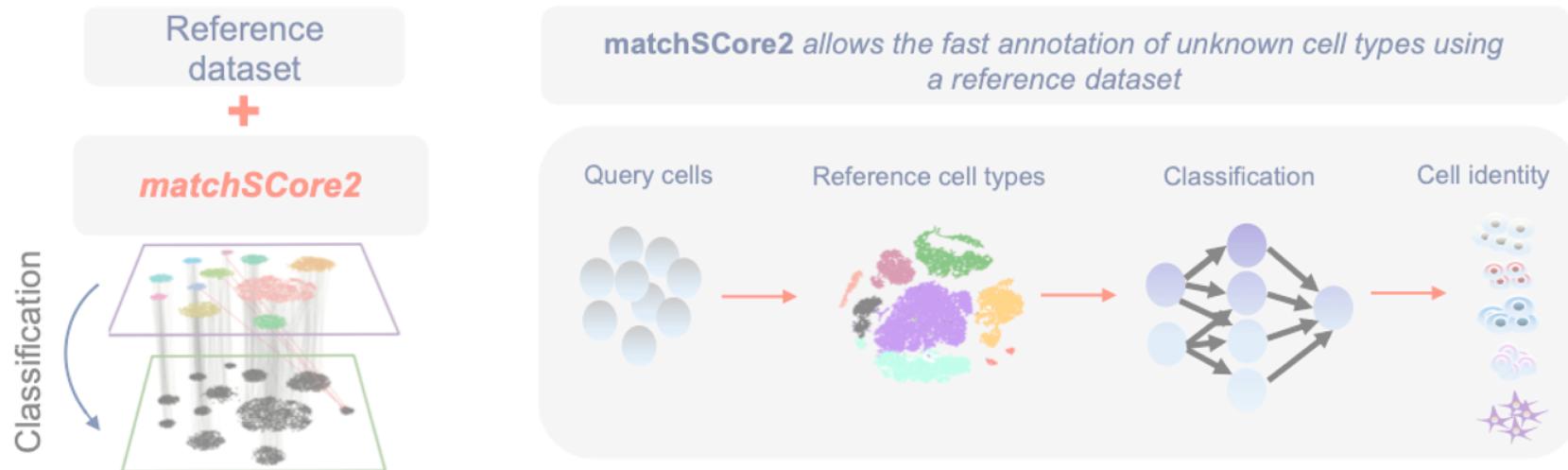
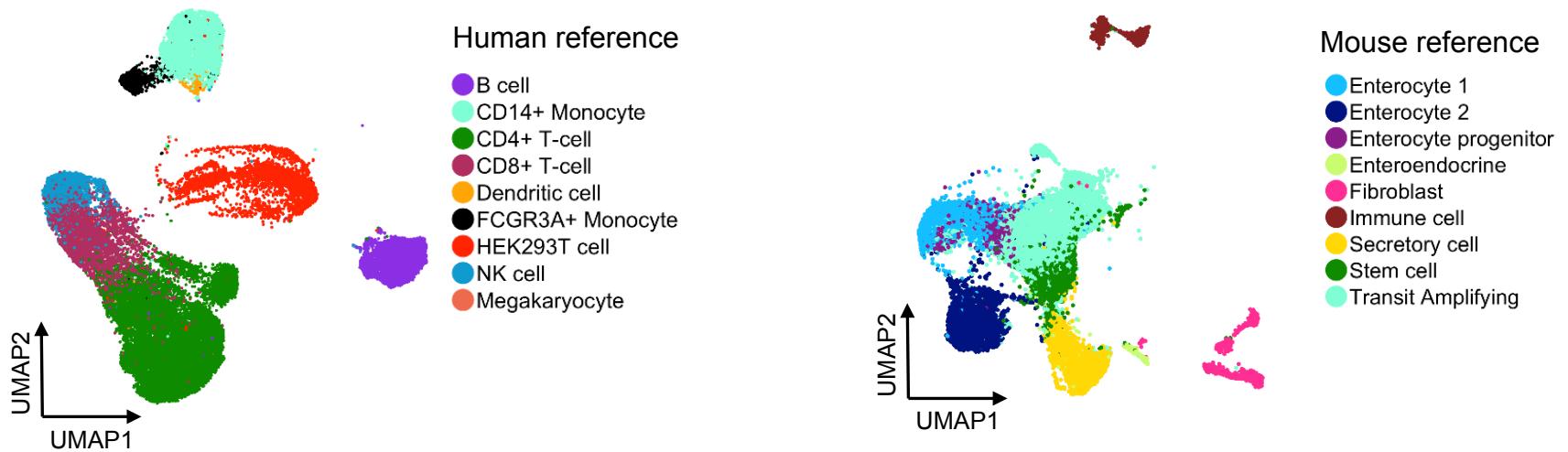


Filtering

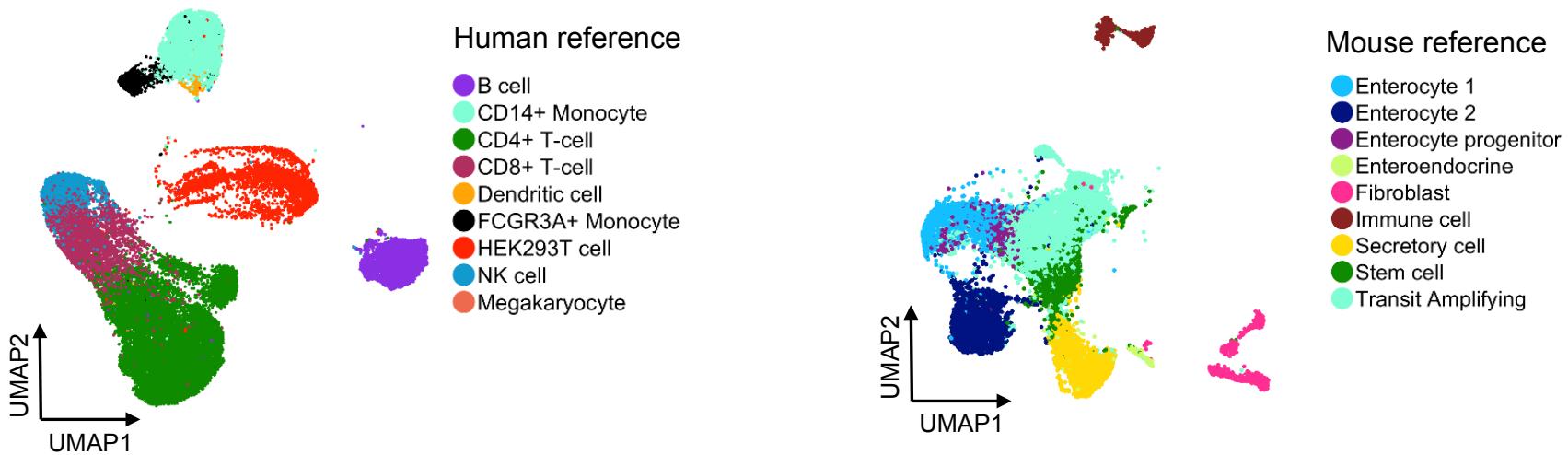
Mapping

Data Transfer

Reference datasets



Reference datasets



Reference
dataset



matchScore2

Classification

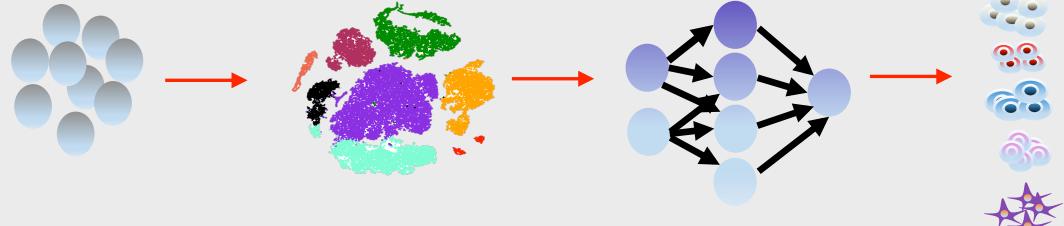
matchScore2 allows the fast annotation of unknown cell types using a reference dataset

Query cells

Reference cell types

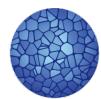
Classification

Cell identity



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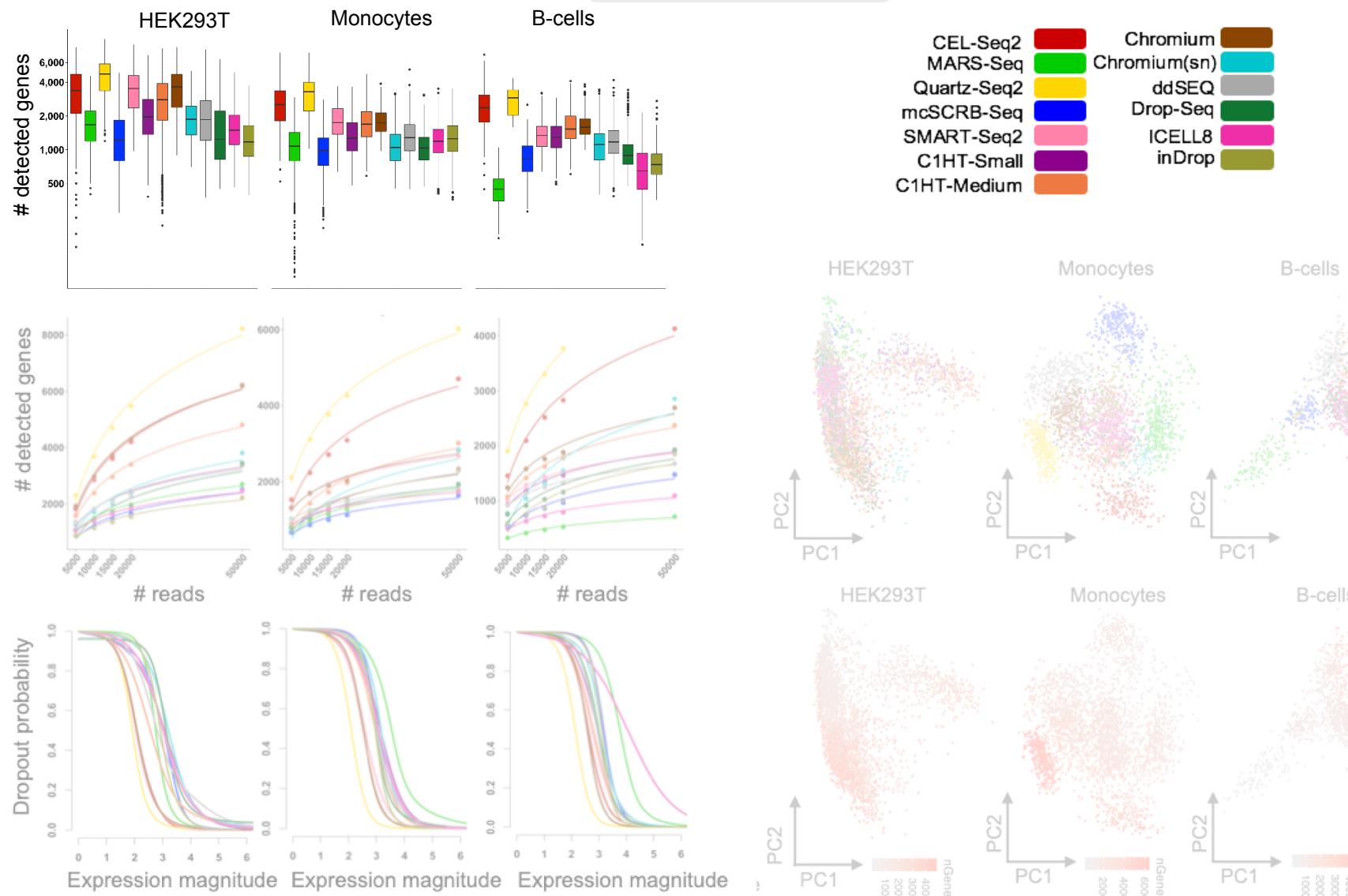
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Gene Detection



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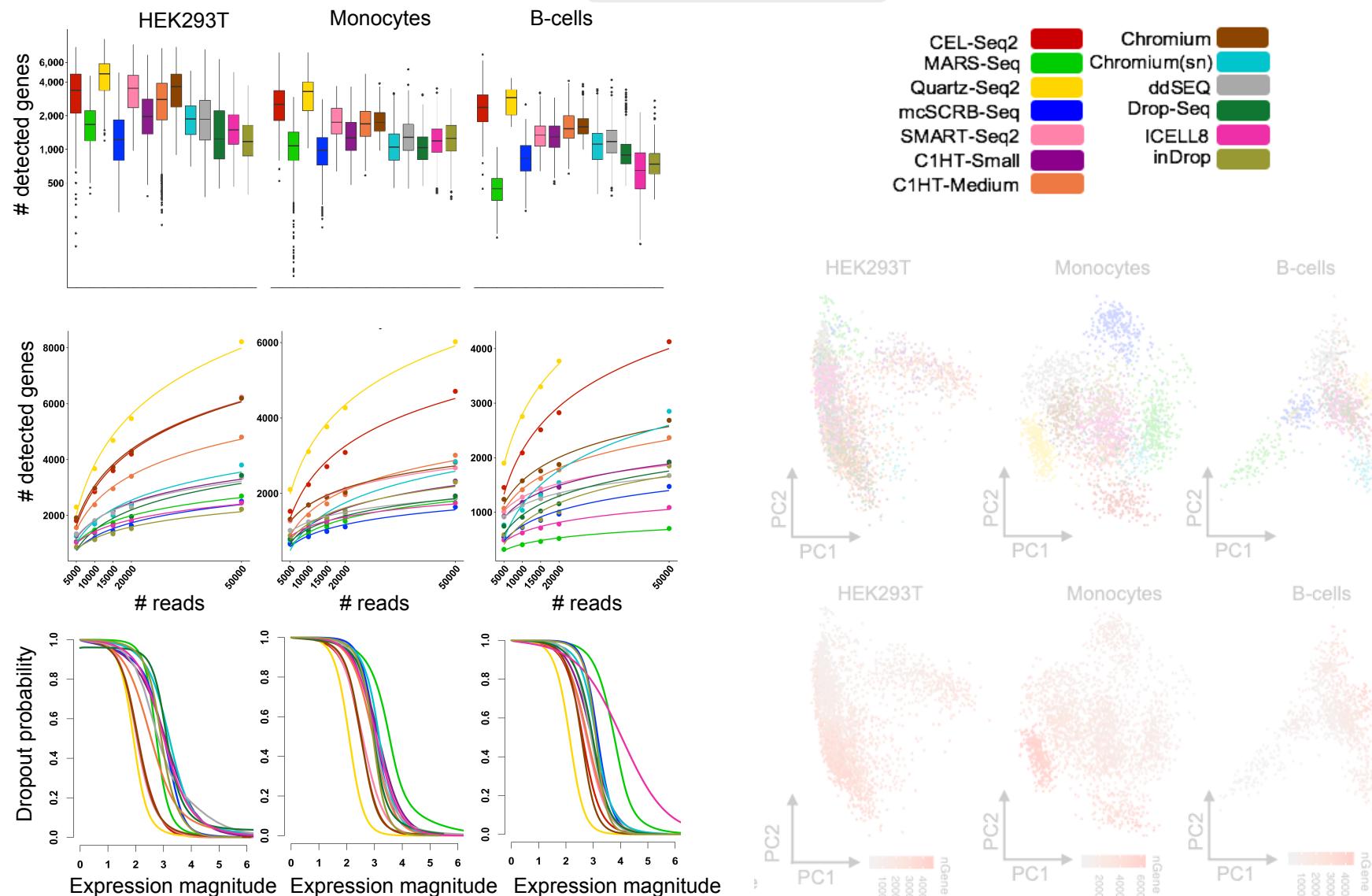
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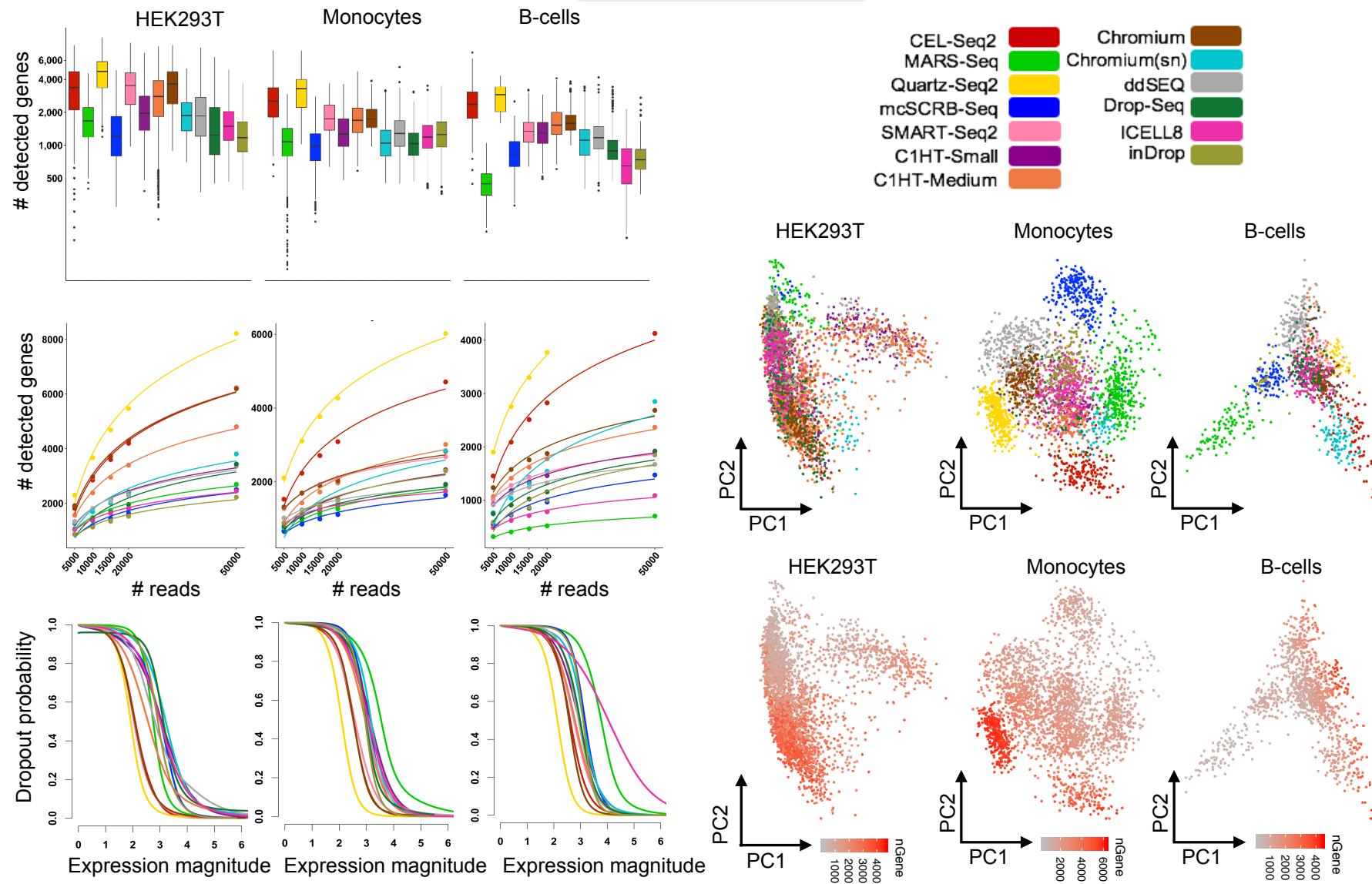
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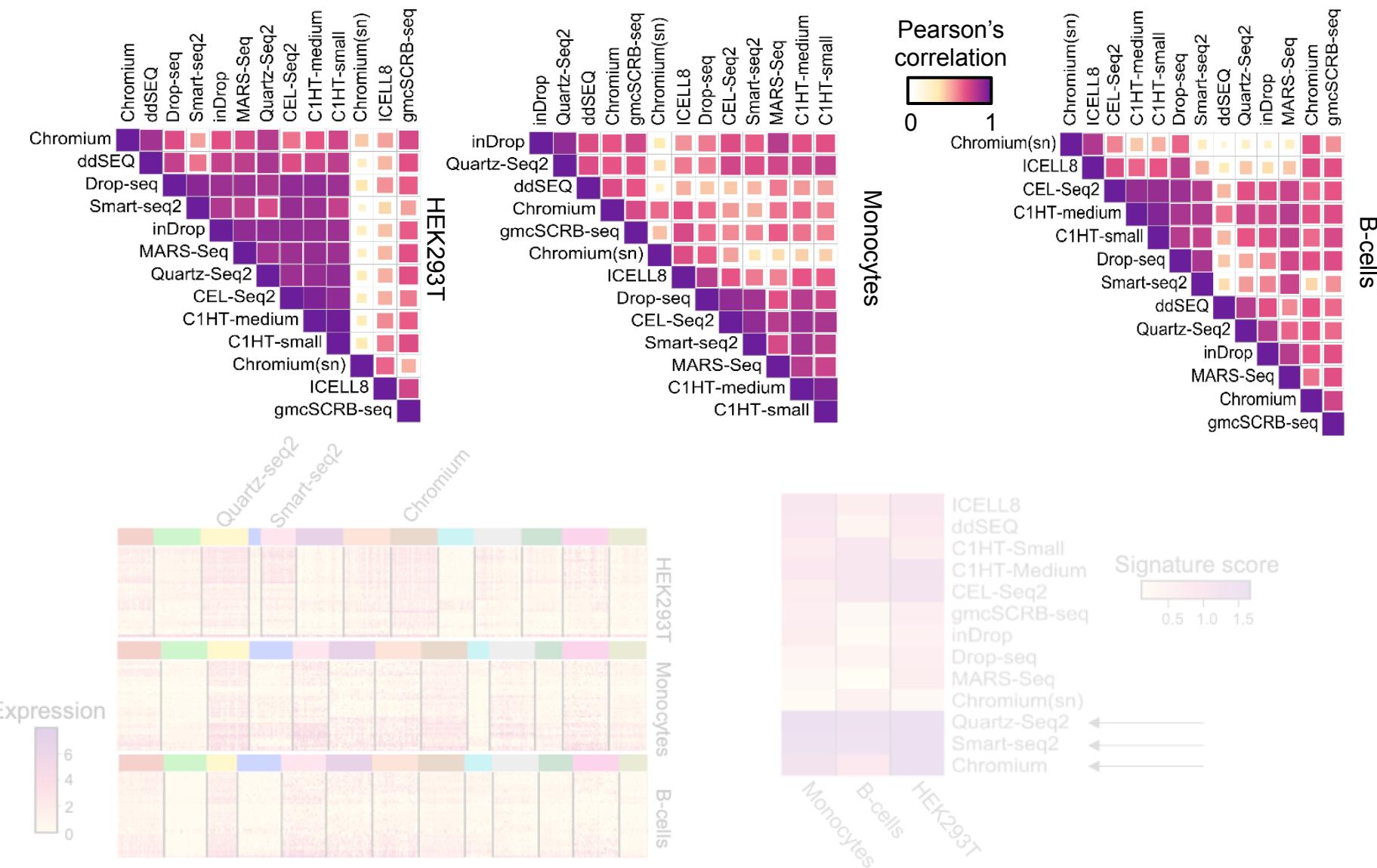
Gene Detection



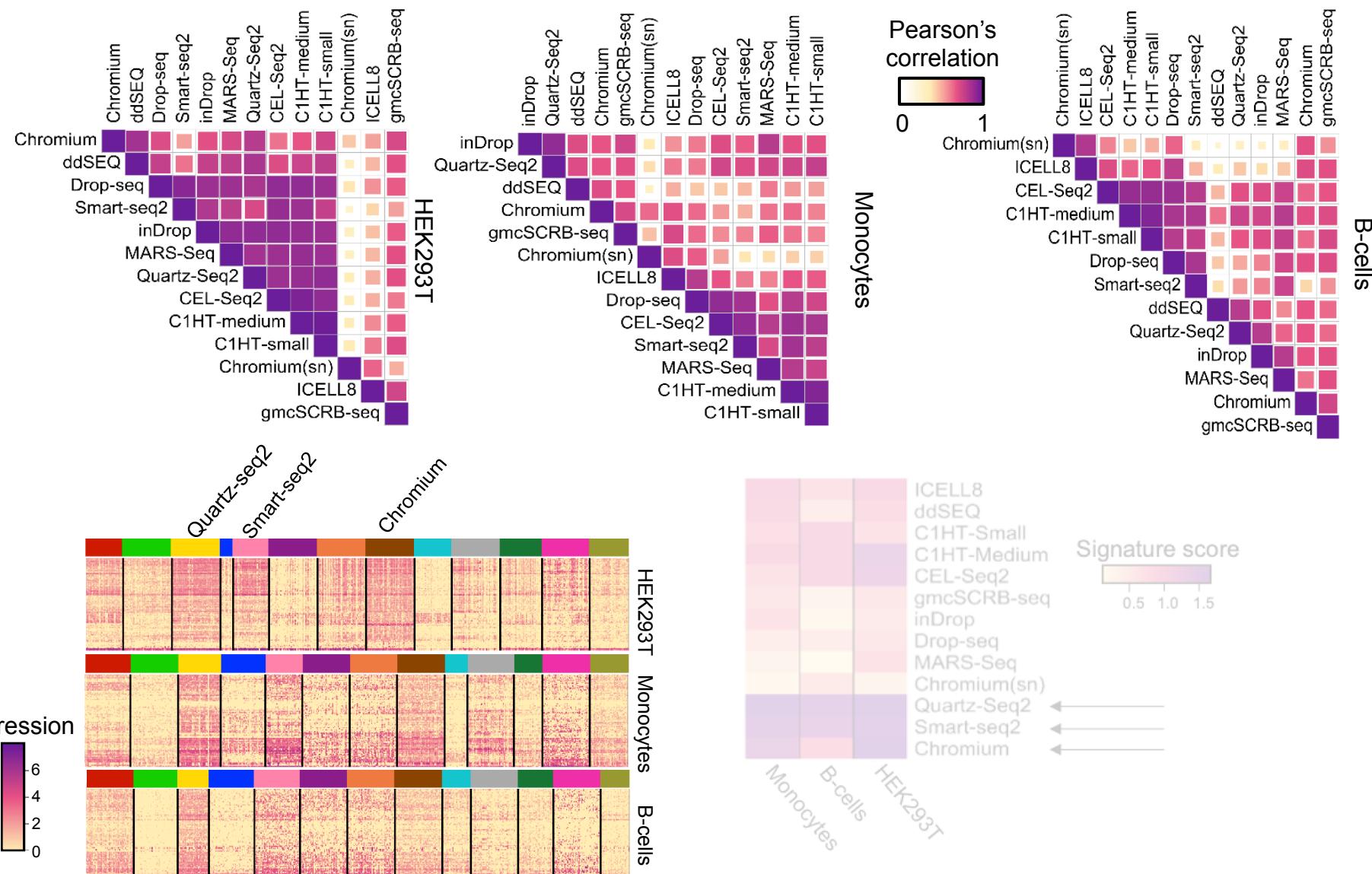
Gene Detection



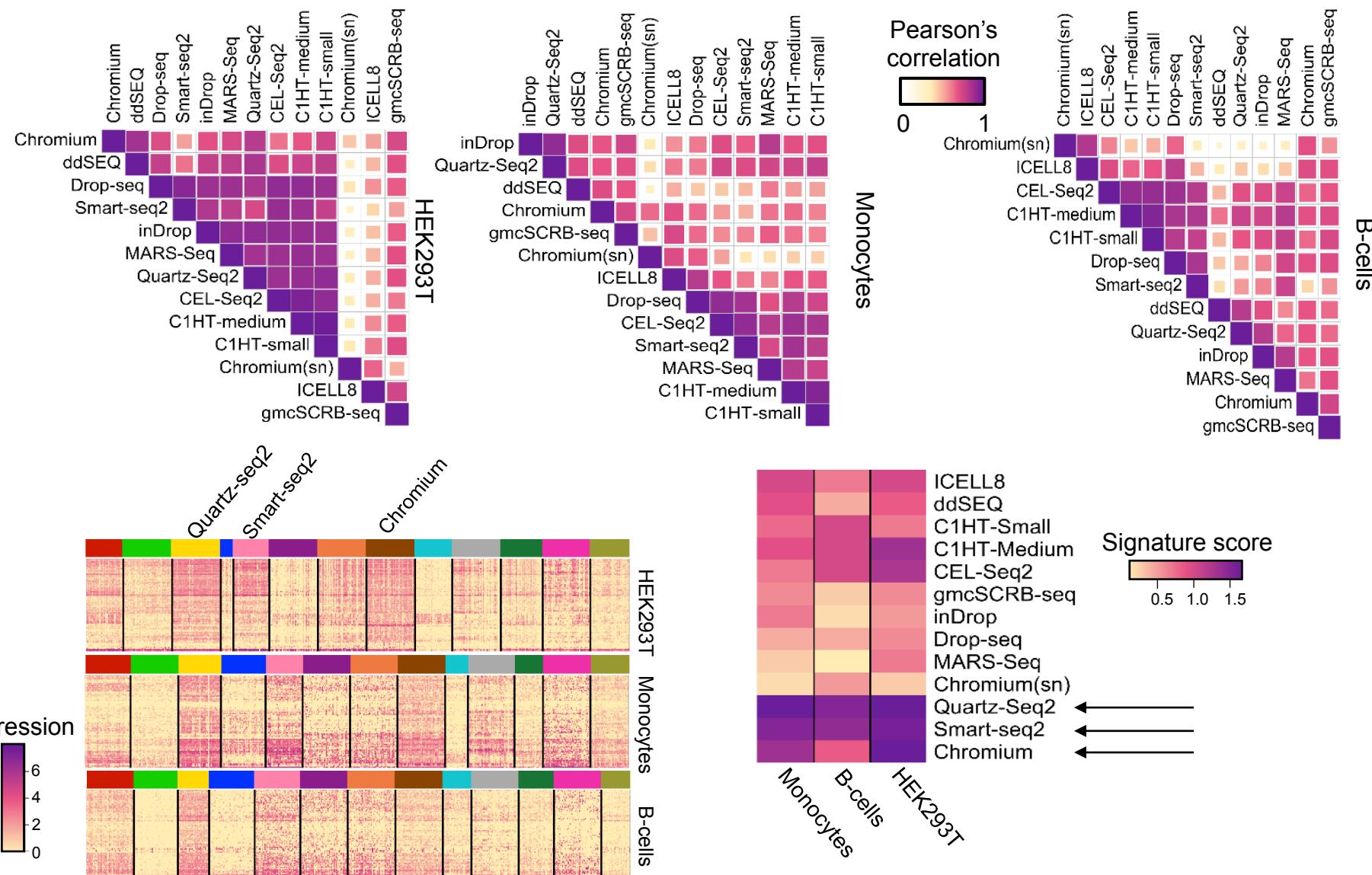
Correlation of gene expression levels



Correlation of gene expression levels

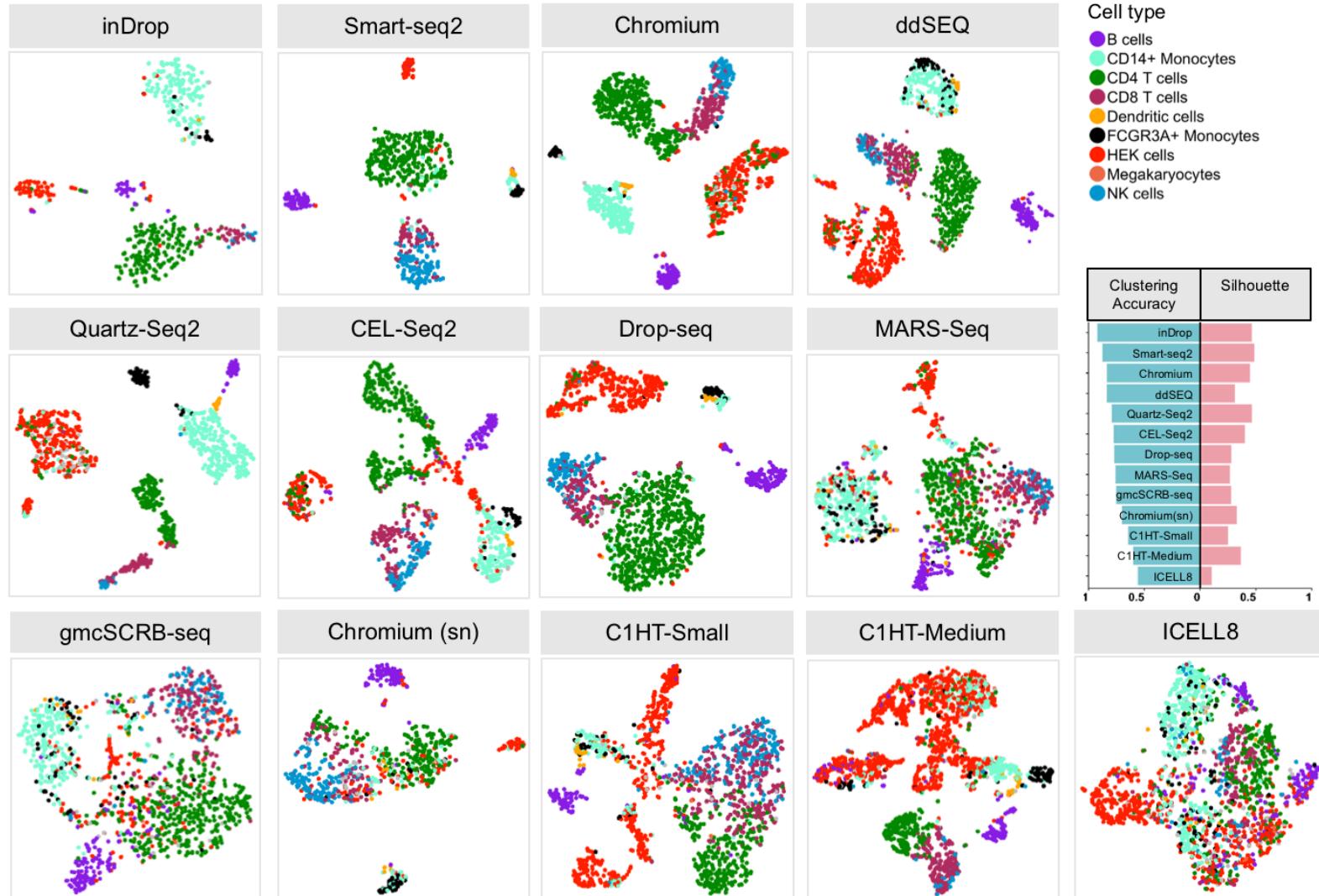


Correlation of gene expression levels



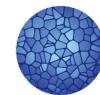
Human Clustering

order →



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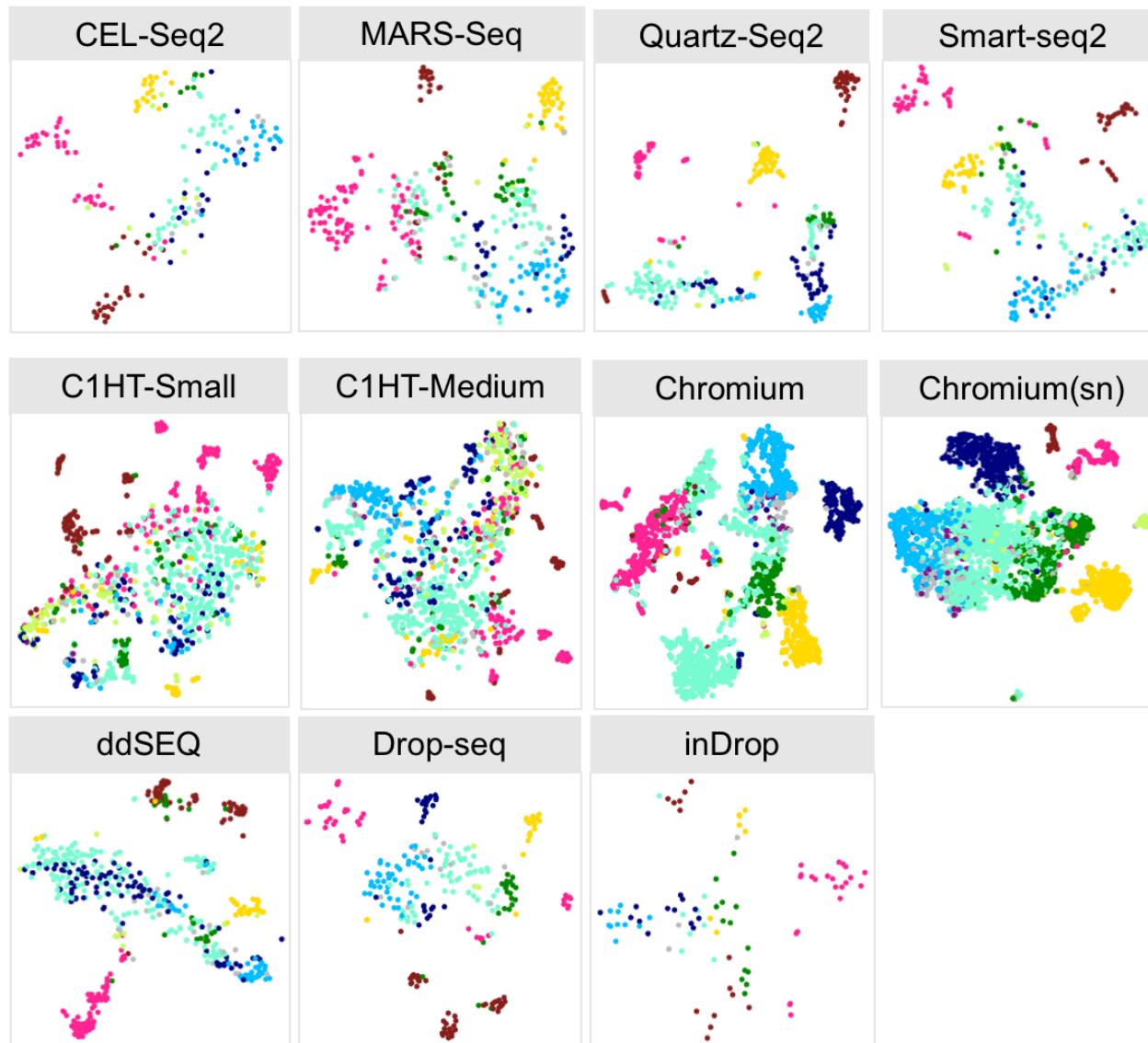
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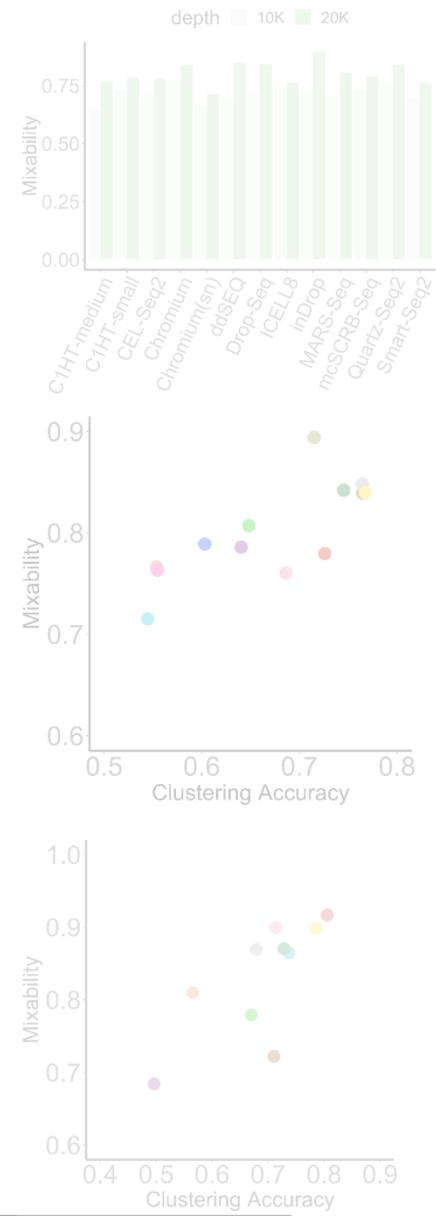
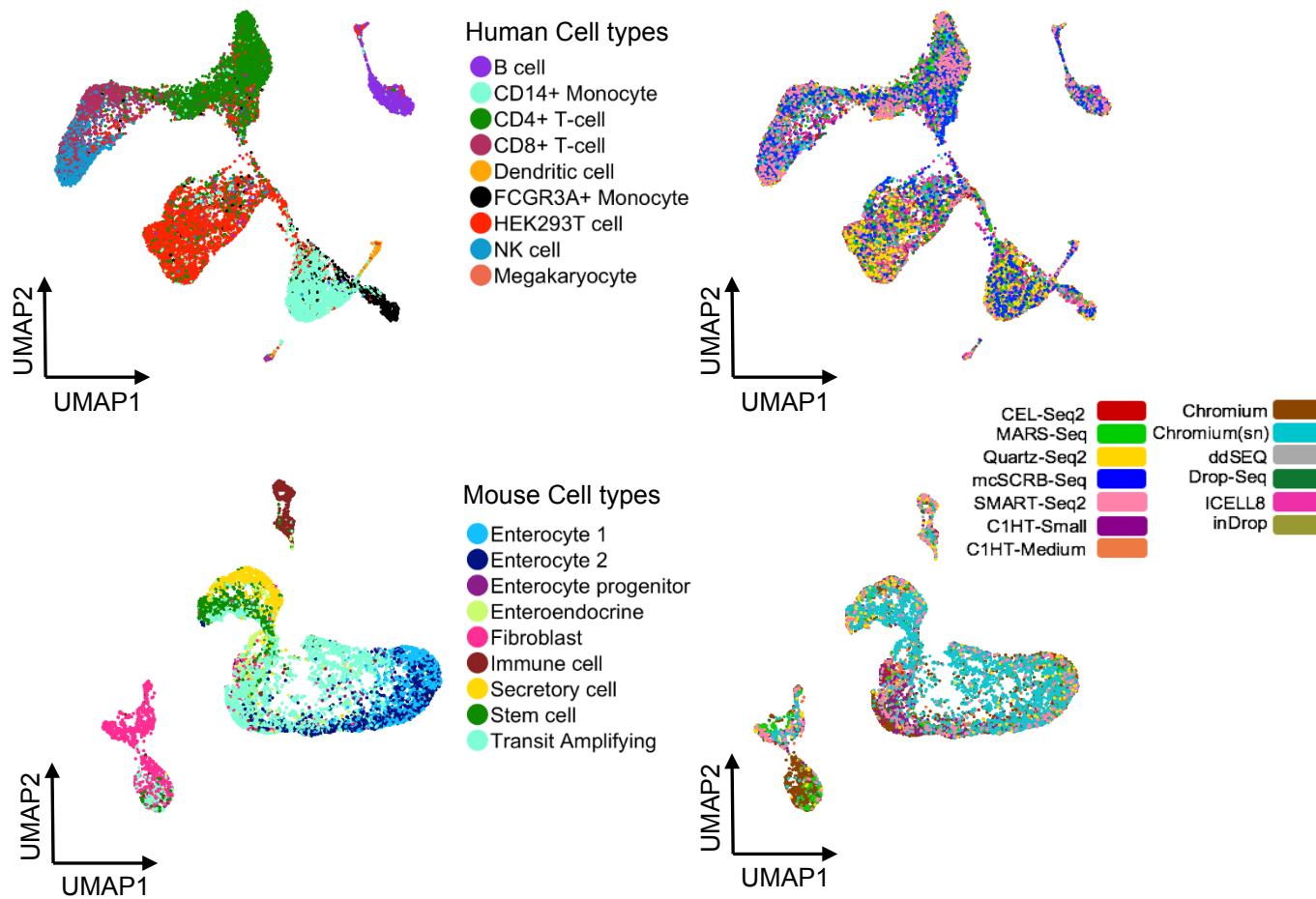
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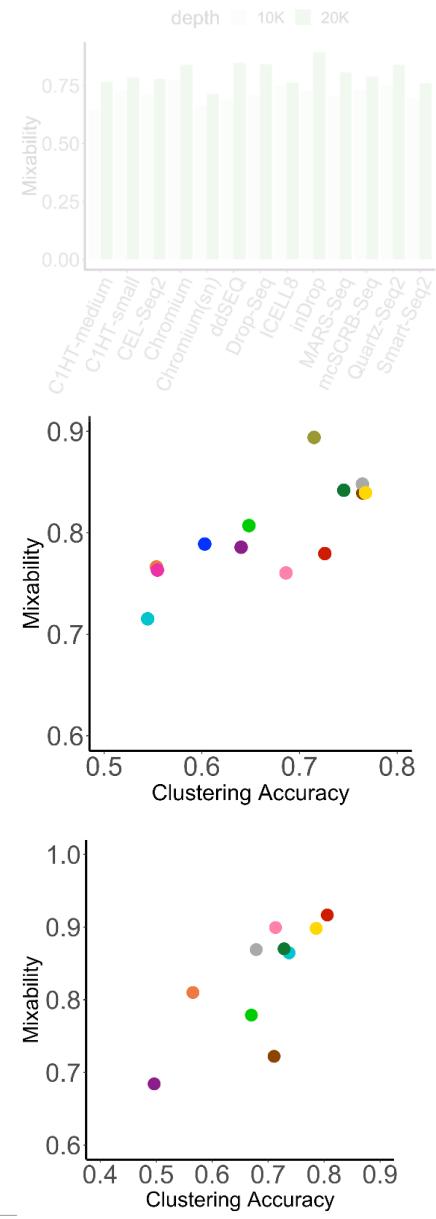
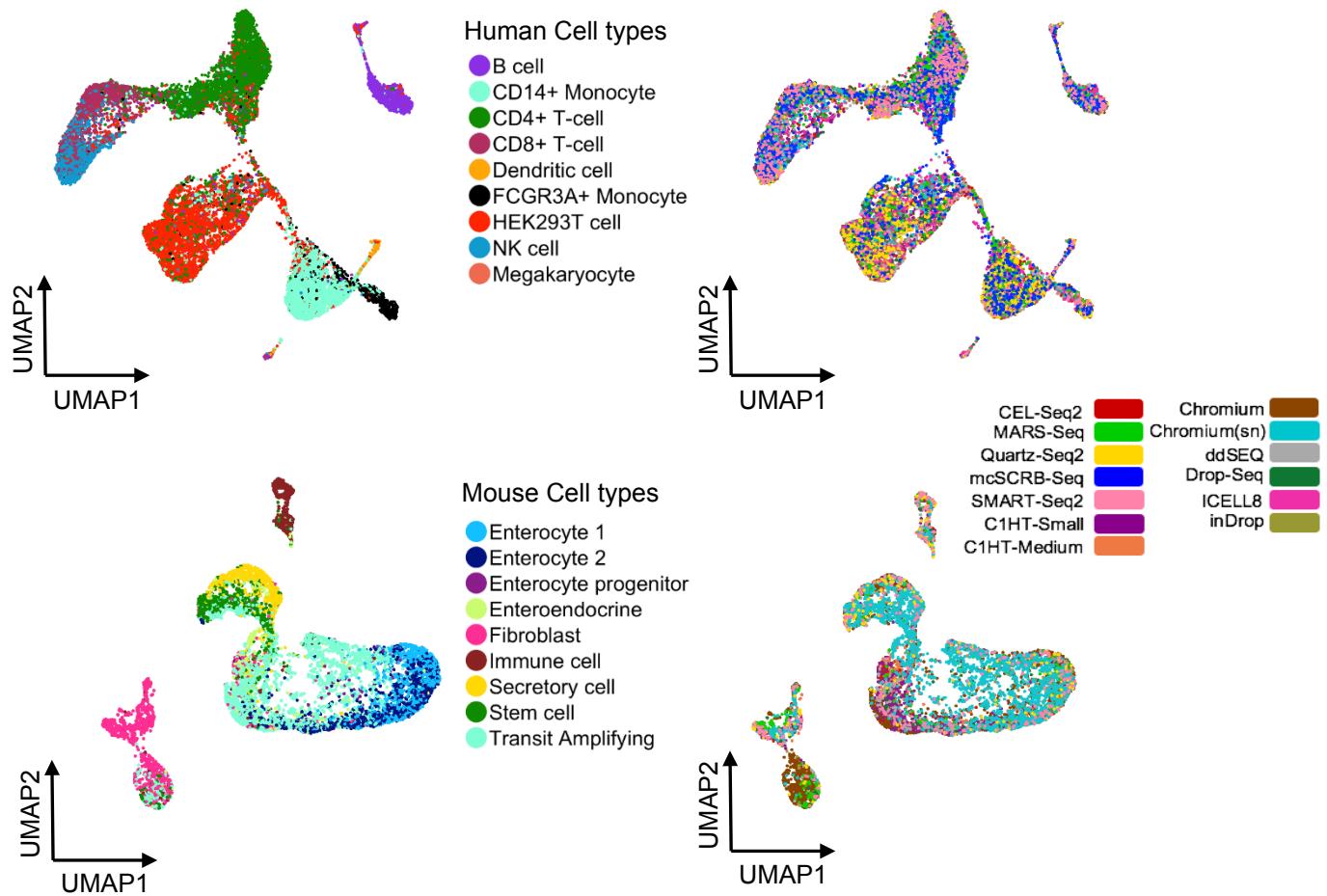
Mouse Clustering



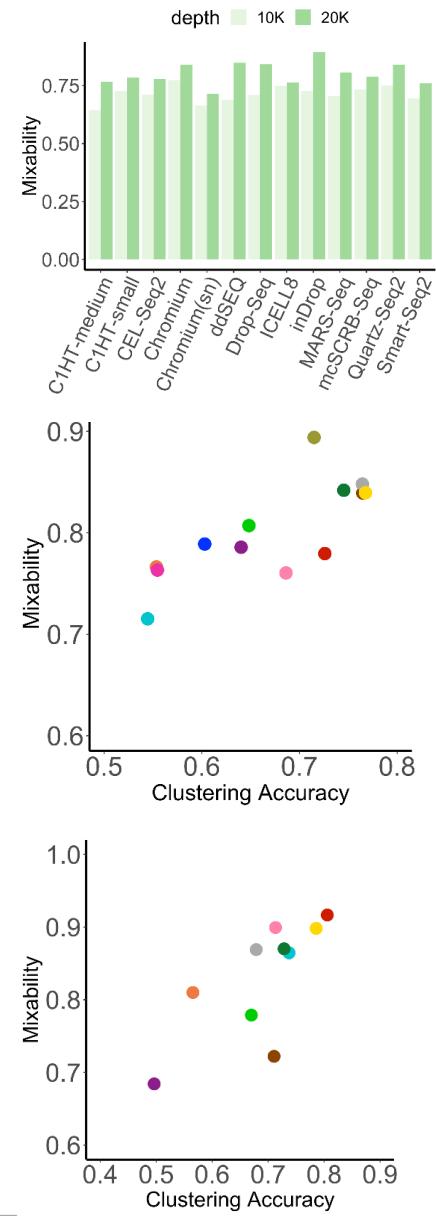
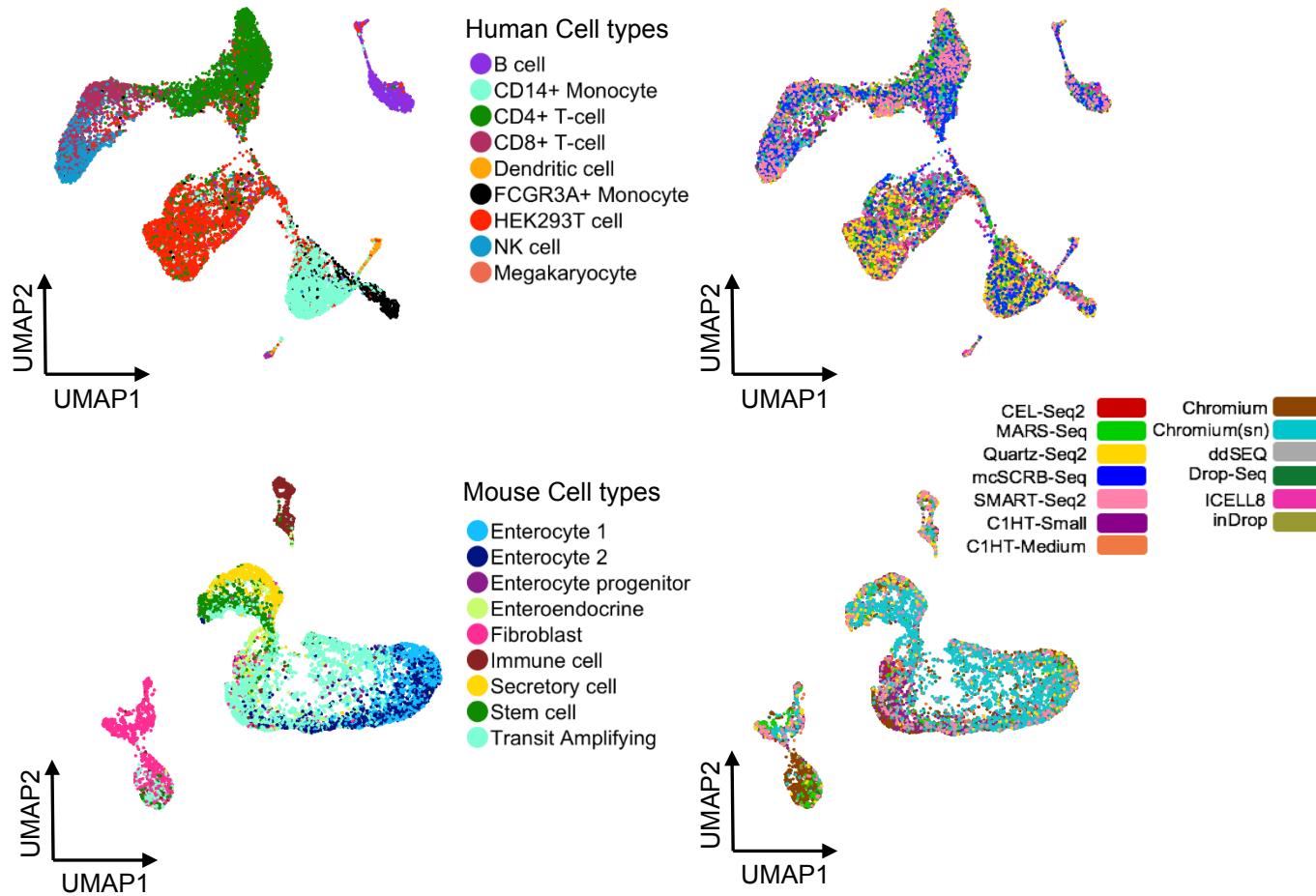
Integratability



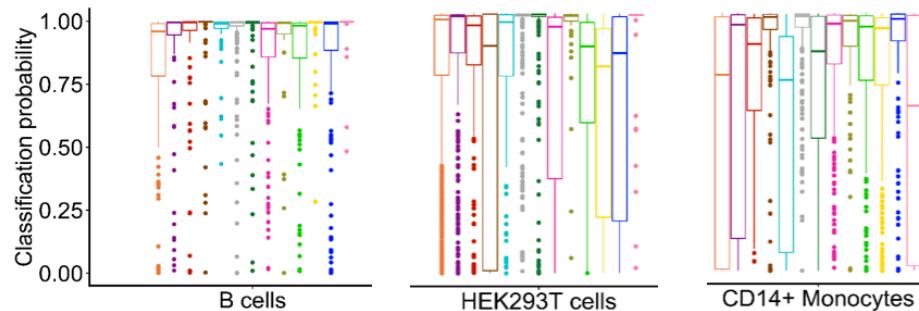
Integratability



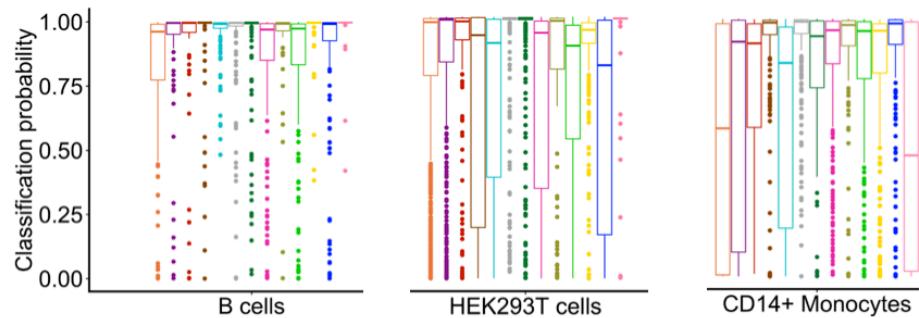
Integratability



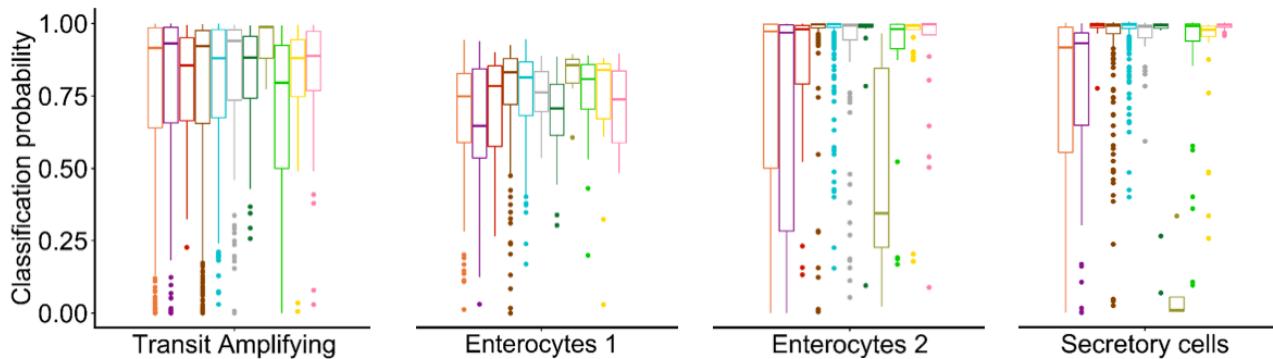
Mappability



Downsampled to 20K

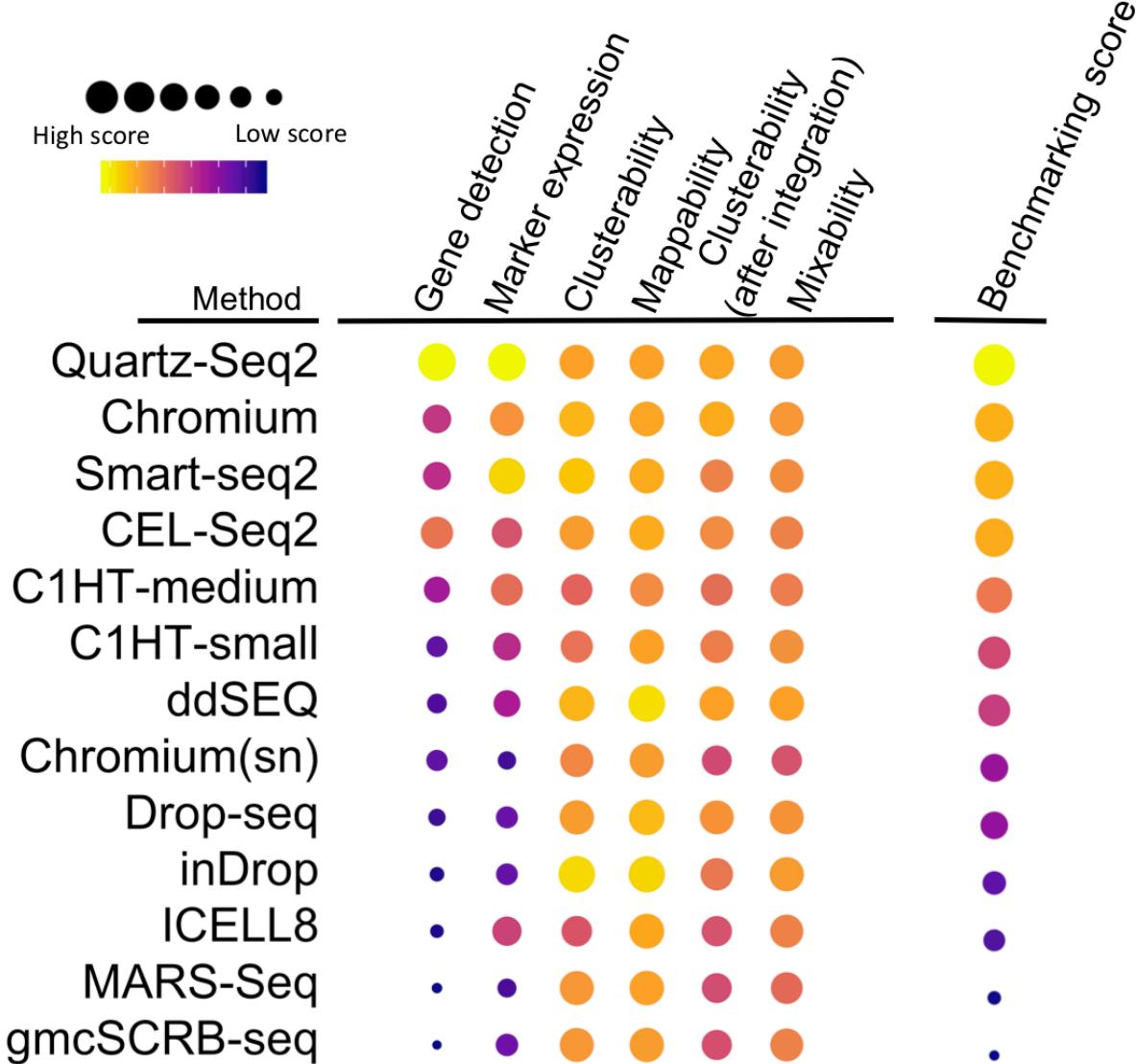


Downsampled to 10K

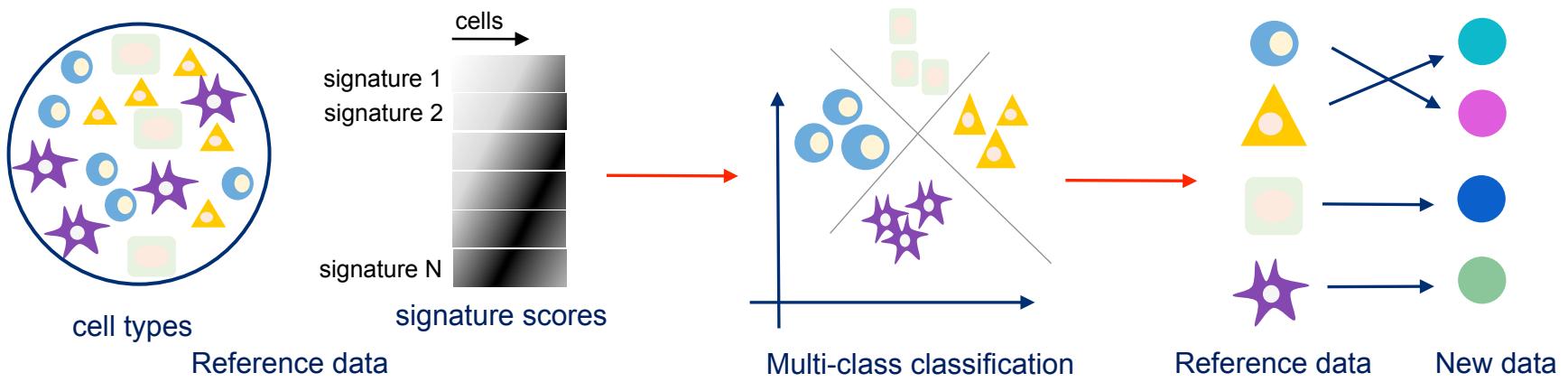


- C1HT-medium
- C1HT-small
- CEL-Seq2
- Chromium
- Chromium(sn)
- ddSEQ
- Drop-Seq
- ICELL8
- inDrop
- MARS-Seq
- Quartz-Seq2
- mcSCRB-Seq
- Smart-Seq2

Benchmarking scores



matchSCore2: comparing datasets at cell and gene level

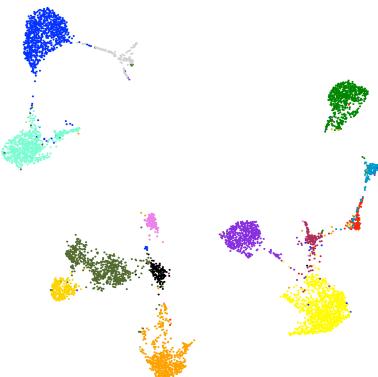


- *matchSCore2* facilitates the annotation task by leveraging large-scale reference data.
- *matchSCore2* trains a multinomial logistic model on the reference dataset.
- The main assumption of the model is that the number of cells N_k from each cell type and their proportions p_k are the parameters of a multinomial distribution
$$M \sim \text{multinom}(N = (N_1, \dots, N_m), p=(p_1, \dots, p_m)).$$
- The signature scores S_{jk} for the cell c_j and cell type T_k are used as predictors of the model.



matchSCore2: the lung atlas

OLD

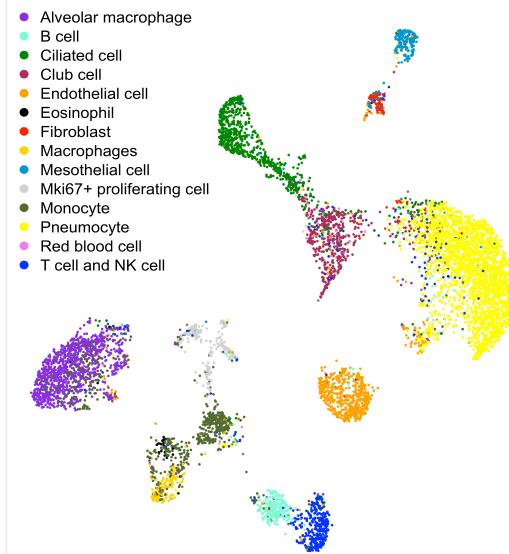


Reference cell types

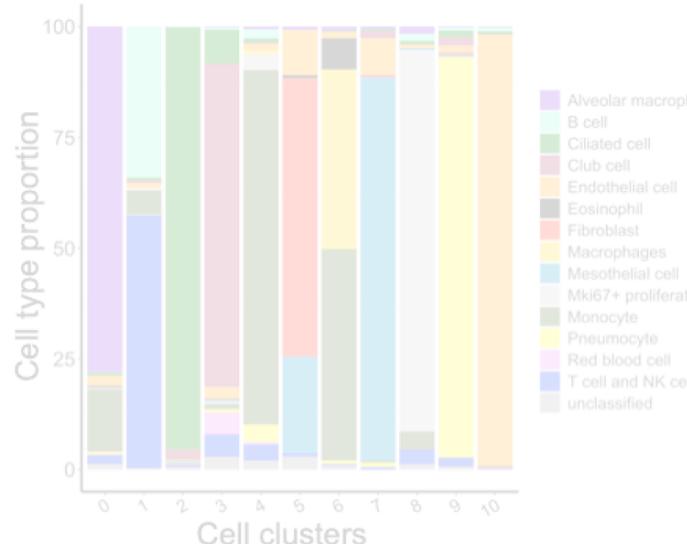
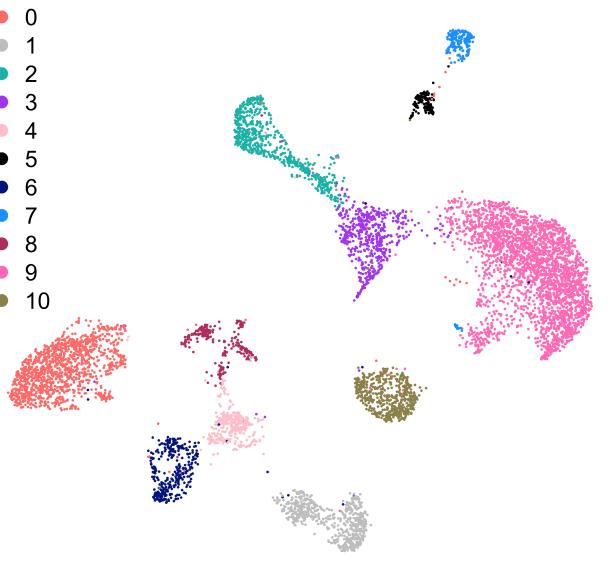
- Alveolar macrophage
- B cell
- Ciliated cell
- Club cell
- Endothelial cell
- Eosinophil
- Fibroblast
- Macrophages
- Mesothelial cell
- Mki67+ proliferating cell
- Monocyte
- Pneumocyte
- Red blood cell
- T cell and NK cell

YOUNG

matchSCore2



Clustering

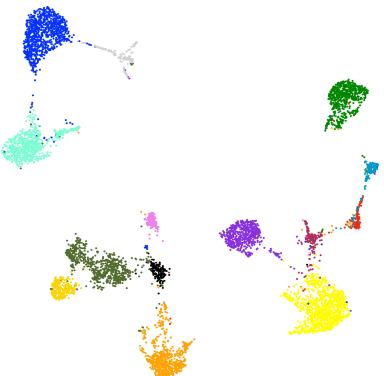


	OLD (reference)	YOUNG
T cell and NK cell	-0.01 0.46	0 0 0.09 0.01 0.02 0 0.01 0 0 0
Red blood cell	0 0.01	0 0.01 0.01 0 0.01 0 0 0 0 0
Pneumocyte	0 0	0 0.01 0.03 0 0 0 0 0 0 0
Monocyte	0.1 0.04	0 0 0.17 0.01 0.26 0.02 0 0 0.01
Mki67+ proliferating cell	0 0 0 0	0 0 0 0 0 0 0 0.65 0 0
Mesothelial cell	0 0	0 0 0.02 0.01 0.23 0.01 0.56 0 0 0.02
Macrophages	-0.07 0	0 0 0 0.1 0.01 0.31 0.01 0 0 0
Fibroblast	0 0	0 0.01 0.02 0 0.48 0.01 0.16 0 0 0.01
Eosinophil	0.1 0.02	0 0.01 0.06 0.01 0.1 0.01 0.01 0.01 0.01 0.01
Endothelial cell	-0.01 0	0 0 0.01 0.01 0.01 0.01 0.02 0 0 0.64
Club cell	0 0	0 0.02 0.58 0 0.02 0.01 0.02 0.01 0.03 0
Ciliated cell	0 0	0 0.03 0.03 0 0.01 0 0 0 0.01 0
B cell	0 0.27	0 0 0.1 0 0.04 0.01 0.01 0 0.01 0
Alveolar macrophage	0.05 0.01	0 0 0 0.03 0 0.07 0 0 0.01 0



matchSCore2: the lung atlas

OLD

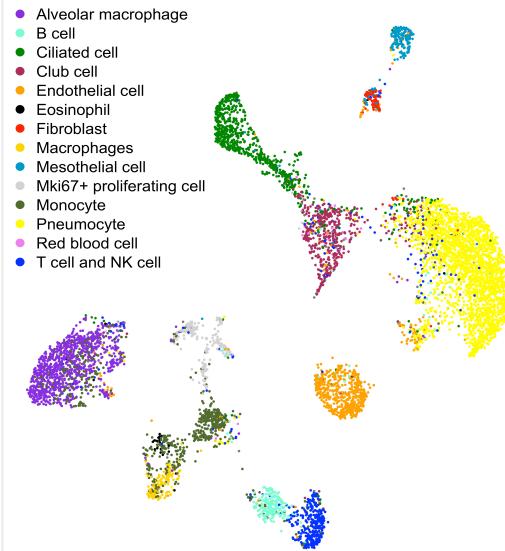


Reference cell types

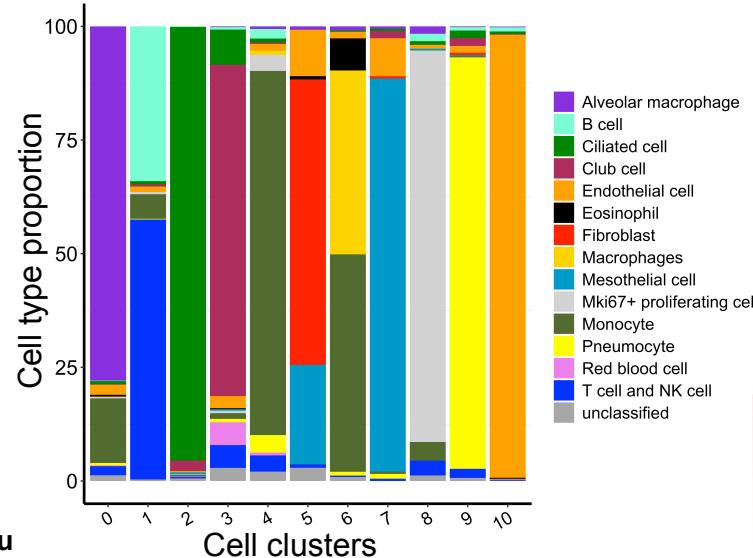
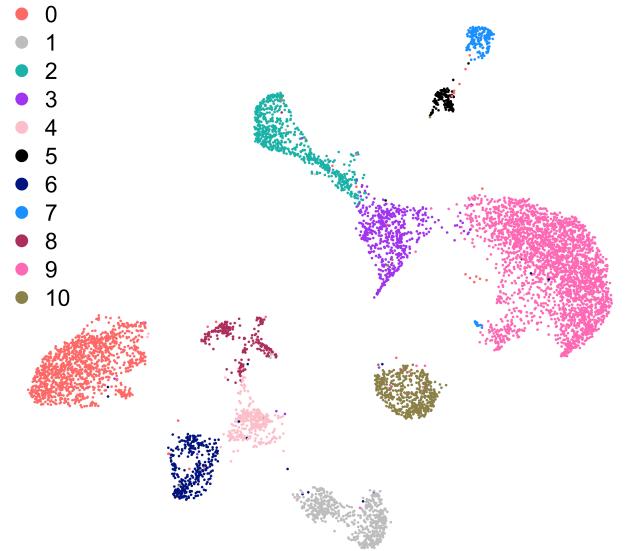
- Alveolar macrophage
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- Endothelial cell
- Eosinophil
- Fibroblast
- Macrophages
- Mesothelial cell
- Mki67+ proliferating cell
- Monocyte
- Pneumocyte
- Red blood cell
- T cell and NK cell

YOUNG

matchSCore2



Clustering



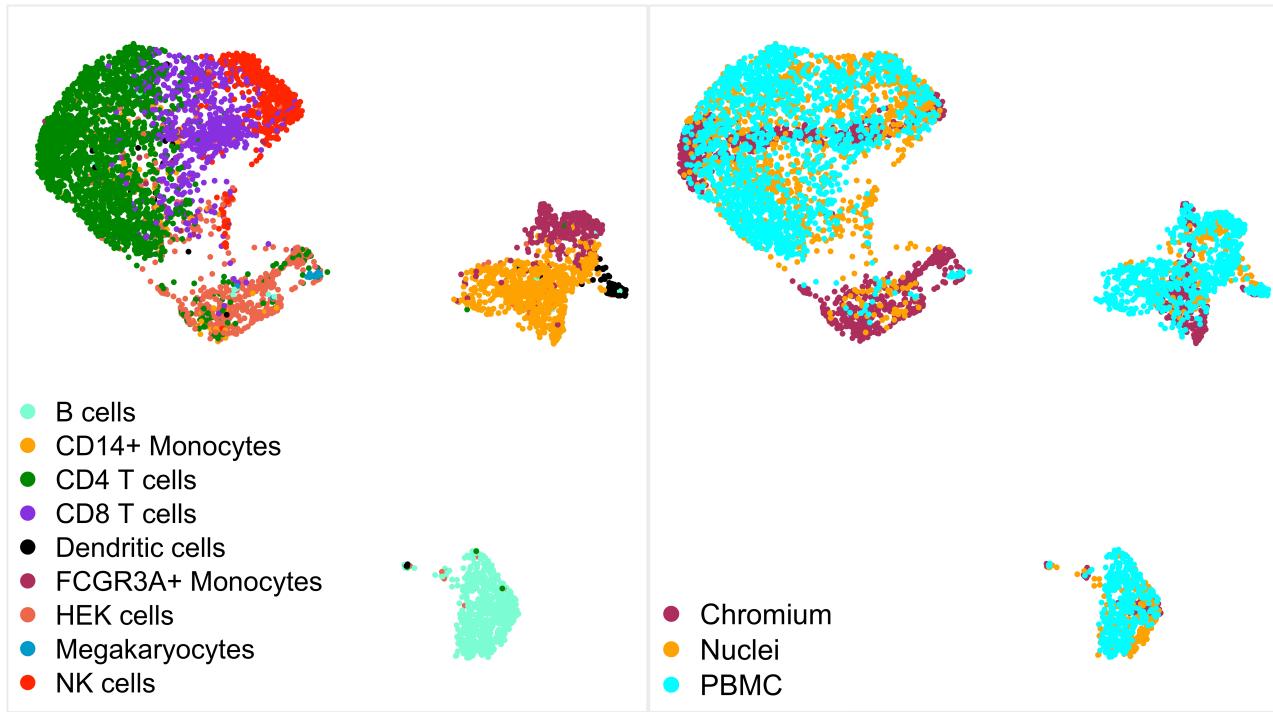
OLD (reference)

JI

	YOUNG										
OLD (reference)	0	1	2	3	4	5	6	7	8	9	10
T cell and NK cell	-0.01	0.46	0	0	0.09	0.01	0.02	0	0.01	0	0.01
Red blood cell	0	0.01	0	0.01	0.01	0	0.01	0	0	0	0
Pneumocyte	0	0	0.01	0.03	0	0	0	0	0	0.75	0
Monocyte	0.1	0.04	0	0	0.17	0.01	0.26	0.02	0	0	0.01
Mesothelial cell	0	0	0	0.02	0.01	0.23	0.01	0.56	0	0	0.02
Macrophages	0.07	0	0	0	0.1	0.01	0.31	0.01	0	0	0
Fibroblast	0	0	0.01	0.02	0	0.48	0.01	0.16	0	0	0.01
Eosinophil	0.1	0.02	0	0.01	0.06	0.01	0.1	0.01	0.01	0.01	0.01
Endothelial cell	0.01	0	0	0.01	0.01	0.01	0.01	0.02	0	0	0.64
Club cell	0	0	0.02	0.58	0	0.02	0.01	0.02	0.01	0.03	0
Ciliated cell	0	0	0.68	0.03	0	0.01	0	0	0	0.01	0
B cell	0	0.27	0	0	0.1	0	0.04	0.01	0.01	0	0.01
Alveolar macrophage	0.5	0.01	0	0	0.03	0	0.07	0	0	0.01	0

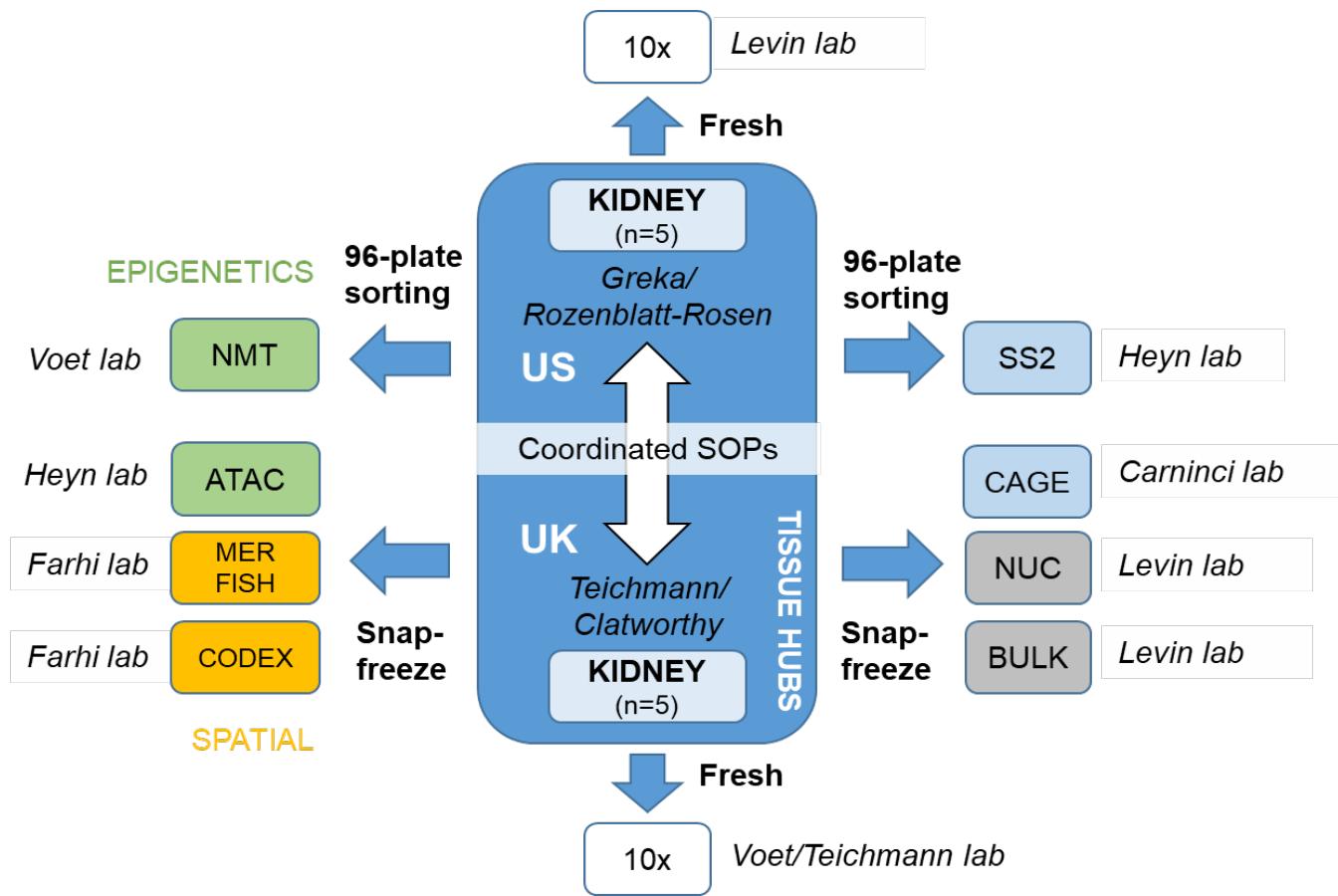


<https://github.com/elimereu>



- matchSCore2 combines datasets by using a SVD decomposition.
- The datasets are projected into a new common space of coordinates.
- This type of integration allows a direct comparison across cell types that are under different conditions (genotypes, treatments, diseased).

Developing *tools and standards* for the integration of ***multimodal*** HCA data in order to evaluate *performance, complementarity* and *replicability* of methods.



Acknowledgements

Single Cell Genomics Team

Atefeh Lafzi
Catia Moutinho
Holger Heyn

HCA consortium

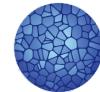
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Sagar	Lan T. Nguyen
Dominic Grün	Aviv Regev
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Stéphane C. Boutet	Swati Parekh
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Aik Ooi	Lucas E. Wange
Robert C. Jones	Johannes W. Bagnoli
Kelly Kaihara	Wolfgang Enard
Chris Brampton	Marta Gut
Yasha Talaga	Rickard Sandberg
Yohei Sasagawa	Itoshi Nikaido
Kaori Tanaka	Ivo Gut
Tetsutaro Hayashi	Oliver Stegle
Cornelius Fischer	



Thank you for your attention!



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