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Corresponding author(s):	Zhi Wei, Hakon Hakonarson

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Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see our <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

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For	all st	atistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.
n/a	Cor	nfirmed
	×	The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
X		A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
	×	The statistical test(s) used AND whether they are one- or two-sided Only common tests should be described solely by name; describe more complex techniques in the Methods section.
X		A description of all covariates tested
x		A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
	×	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
	×	For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted Give <i>P</i> values as exact values whenever suitable.
x		For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
x		For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
x		Estimates of effect sizes (e.g. Cohen's d, Pearson's r), indicating how they were calculated
	'	Our web collection an statistics for higherists contains articles an many of the points above

Software and code

Policy information about <u>availability of computer code</u>

Data collection

Provide a description of all commercial, open source and custom code used to collect the data in this study, specifying the version used OR stat that no software was used.

Data analysis

Python --- 3.7.6 h5py --- 2.9.0 Scanpy --- 1.4.4 Numpy --- 1.17.0 Sikit-learn --- 0.19.2 Pytorch --- 1.5

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The scRNA-seq datasets supporting this study are available publicly: 10X PBMC dataset (https://support.10xgenomics.com/single-cell-gene-expression/datasets/2.1.0/pbmc4k); mouse bladder cells (https://figshare.com/s/865e694ad06d5857db4b); worm neuron cells (http://atlas.gs.washington.edu/worm-rna/

docs/); human kidney cells (https://github.com/xuebaliang/scziDesk/tree/master/dataset/Young); Macosko mouse retina cells (https://scrnaseq-public-datasets.s3.amazonaws.com/scater-objects/macosko.rds); Shekhar mouse retina cells (https://scrnaseq-public-datasets.s3.amazonaws.com/scater-objects/shekhar.rds); CITE-seq dataset (https://github.com/canzarlab/Specter/tree/master/data); human liver dataset (https://github.com/BaderLab/scClustViz). All datasets can be found on GitHub: https://github.com/ttgump/scDCC/tree/master/data				
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All studies must dis	sclose on these points even when the disclosure is negative.			
Sample size	Describe how sample size was determined, detailing any statistical methods used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient.			
Data exclusions	Describe any data exclusions. If no data were excluded from the analyses, state so OR if data were excluded, describe the exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.			
Replication	Describe the measures taken to verify the reproducibility of the experimental findings. If all attempts at replication were successful, confirm this OR if there are any findings that were not replicated or cannot be reproduced, note this and describe why.			
Randomization	Describe how samples/organisms/participants were allocated into experimental groups. If allocation was not random, describe how covariates			

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Describe whether the investigators were blinded to group allocation during data collection and/or analysis. If blinding was not possible,

Ma	terials & experimental systems	Met	hods
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×	Antibodies	x	ChIP-seq
x	☐ Eukaryotic cell lines	x	Flow cytometry
x	Palaeontology and archaeology	x	MRI-based neuroimaging
x	Animals and other organisms		
x	Human research participants		
x	☐ Clinical data		
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Blinding