Editorial Policy Checklist

This form is used to ensure compliance with Nature Research editorial policies related to research ethics and reproducibility. For further information, please see our Authors & Referees site. All relevant questions on the form must be answered.

Competing interests

Policy information about competing interests

Competing interests declaration

In the interest of transparency and to help readers form their own judgements of potential bias, Nature Research journals require authors to declare any competing financial and/or non-financial interest in relation to the work described in the submitted manuscript.

☐ We declare that none of the authors have competing financial or non-financial interests as defined by Nature Research.
☒ We declare that one or more of the authors have a competing interest as defined by Nature Research.

10x Genomics was involved in producing this work. I.T.F., J.G.A., L.J.A., K.A.P., E.J.M., J.M.T., D.P.R., N.S., and T.S.M. are employees of 10x Genomics. The Regents of the University of California with T.M.N., J.S.W., and B.A. as inventors have filed patent applications related to CRISPRi/a screening, Perturb-seq, and GI mapping. J.S.W. consults for and holds equity in KSQ Therapeutics, Maze Therapeutics, and Tenaya Therapeutics, is a venture partner at 5AM Ventures, and is a member of the Amgen Scientific Advisory Board. J.M.R. and T.M.N. consult for Maze Therapeutics. B.A. is a member of a ThinkLab Advisory Board for and holds equity in Celsius Therapeutics.

Authorship

Policy information about authorship

Prior to submission all listed authors must agree to all manuscript contents, the author list and its order and the author contribution statements. Any changes to the author list after submission must be approved by all authors.

☒ We have read the Nature Research Authorship Policy and confirm that this manuscript complies.

Data availability

Policy information about availability of data

Data availability statement

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

☒ We have provided a full data availability statement in the manuscript.

Mandated accession codes (where applicable)

Confirm that all relevant data are deposited into a public repository and that accession codes are provided.

☐ All relevant accession codes are provided  ☒ Accession codes will be available before publication  ☐ No data with mandated deposition

Code availability

Policy information about availability of computer code

Code availability statement

For all studies using custom code or mathematical algorithm that is deemed central to the conclusions, the Methods section must include a statement under the heading "Code availability" describing how readers can access the code, including any access restrictions.

☒ We have provided a full code availability statement in the manuscript
Data presentation

For all data presented in a plot, chart or other visual representation confirm that:

- Confirmed
- n/a

- Individual data points are shown when possible, and always for \( n \leq 10 \)
- The format shows data distribution clearly (e.g. dot plots, box-and-whisker plots)
- Box-plot elements are defined (e.g. center line, median; box limits, upper and lower quartiles; whiskers, 1.5x interquartile range; points, outliers)
- Clearly defined error bars are present and what they represent (SD, SE, CI) is noted

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Policy information about image integrity

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Additional policy considerations

Some types of research require additional policy disclosures. Please indicate whether each of these apply to your study. If you are not certain, please read the appropriate section before selecting a response.

| Does not apply | Involved in the study |
|----------------|-----------------------|
| ☑ Macromolecular structural data |
| ☑ Unique biological materials |
| ☑ Research animals and/or animal-derived materials that require ethical approval |
| ☑ Human embryos, gametes and/or stem cells |
| ☑ Human research participants |
| ☑ Clinical data |

Biological materials

Policy information about availability of materials

Obtaining biological materials

- Gel beads described in our manuscript are available as part of the Chromium Single Cell 3’ Reagent Kits v3 with Feature Barcoding technology from 10x Genomics.

- We have described these restrictions in the manuscript.

- We have described how to obtain all materials in the manuscript.

I certify that all the above information is complete and correct.

Typed signature: Jonathan S. Weissman, Britt Adamson

Date: Feb 17, 2020