***eLife’s* transparent reporting form**

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**Sample-size estimation**

* You should state whether an appropriate sample size was computed when the study was being designed
* You should state the statistical method of sample size computation and any required assumptions
* If no explicit power analysis was used, you should describe how you decided what sample (replicate) size (number) to use

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn’t apply to your submission:

This information does not apply, as this paper described the analysis of large numbers of single-cell transcriptomes (~30,000 in total) and main statistical tests performed (e.g. differential gene expression between cell populations) are therefore on inherently large sample sizes.

**Replicates**

* You should report how often each experiment was performed
* You should include a definition of biological versus technical replication
* The data obtained should be provided and sufficient information should be provided to indicate the number of independent biological and/or technical replicates
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* Criteria for exclusion/inclusion of data should be clearly stated
* High-throughput sequence data should be uploaded before submission, with a private link for reviewers provided (these are available from both GEO and ArrayExpress)

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The experiments and number of single-cell transcriptomes following quality control filtering for each experiment is detailed in the Results section. Specific quality control metrics for filtering of data is either described in Materials and Methods or contained in the R code used for filtering in Source Code File 1. Sequencing data has been deposited in ArrayExpress with reviewer login codes shown under section Data Availability.

**Statistical reporting**

* Statistical analysis methods should be described and justified
* Raw data should be presented in figures whenever informative to do so (typically when N per group is less than 10)
* For each experiment, you should identify the statistical tests used, exact values of N, definitions of center, methods of multiple test correction, and dispersion and precision measures (e.g., mean, median, SD, SEM, confidence intervals; and, for the major substantive results, a measure of effect size (e.g., Pearson's r, Cohen's d)
* Report exact p-values wherever possible alongside the summary statistics and 95% confidence intervals. These should be reported for all key questions and not only when the p-value is less than 0.05.

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Descriptions of statistical analyses used in this paper can be found in Materials and Methods. Results from differential gene expression testing and Gene Ontology over-representation testing is available in Supplementary Files 1 and 3 – 10.

(For large datasets, or papers with a very large number of statistical tests, you may upload a single table file with tests, Ns, etc., with reference to sections in the manuscript.)

**Group allocation**

* Indicate how samples were allocated into experimental groups (in the case of clinical studies, please specify allocation to treatment method); if randomization was used, please also state if restricted randomization was applied
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Experimental group allocation information can be found in Materials and Methods.

**Additional data files (“source data”)**

* We encourage you to upload relevant additional data files, such as numerical data that are represented as a graph in a figure, or as a summary table
* Where provided, these should be in the most useful format, and they can be uploaded as “Source data” files linked to a main figure or table
* Include model definition files including the full list of parameters used
* Include code used for data analysis (e.g., R, MatLab)
* Avoid stating that data files are “available upon request”

Please indicate the figures or tables for which source data files have been provided:

Source data is provided for Figure 1—figure supplement 6D,E, Figure 1—figure supplement 7B,C, Figure 4—figure supplement 2E and Figure 6I. R code for quality control filtering and clustering of single-cell RNA-seq data generated for this study can be found in Source Code File 1. R code for new computational approaches developed during this study (Differential Proportion Analysis and ligand-receptor network analysis) can also be found in Source Code File 1.