nature portfolio

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Reporting Summary

Nature Portfolio 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 Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	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.*
☐	☒	A description of all covariates tested
☐	☒	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. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	No software is used to collect the data
Data analysis	PLINKE v1.90b6.26 were used to manage and QC the genotype of OneK1K. We used sctransform (v0.3.2) algorithm implemented in Seurat (v4.1.1) in R-4.0.5 to remove the technical confounders such as sequencing depth and batch effects. All cells were classified into 14 different cell types by a semi-supervised method, scPred (v1.9.2). The glmGamPoi R package (v1.8.0) was used to estimate the within-individual dispersion of gene expression. TensorQTL (v1.0.7) in Python 3.7.12 was used to run the main eQTL/veQTL/deQTL mapping analysis, as well as interaction analysis. FUMA platform (v1.5.3) was used to perform functional annotation for the deQTLs and gene enrichment for the dGenes. The phateR (v1.0.7) was used to calculate the pseudotime of each cell and visualise the trajectory. The analysis code will be available prior to acceptance on [https://github.com/powellgenomicslab/sc-veQTL] and [https://doi.org/10.5281/zenodo.20746908].

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 Portfolio 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 description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

All data analysed in the study is available on the Gene Expression Omnibus (GSE196830) and also the HCA data science platform [https://cellxgene.cziscience.com/collections/dde06e0f-ab3b-46be-96a2-a8082383c4a1]. The genotype, covariates, pseudobulk matrcies, eQTL/veQTL/deQTL summary statistics, and updated Seurat object of the raw and normalized single-cell gene expression matrix used in this study are available in the Zenodo platform [https://doi.org/10.5281/zenodo.18910121].

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	The self-reported sex was collected for this cohort, and there are 58% females and 42% males. Only biological sex was considered in the statistical analysis.
Reporting on race, ethnicity, or other socially relevant groupings	Most of the OneK1K participants identified themselves with a Northern European ancestry. The ancestry information was further analysed based on genotype information and adjusted in the statistical analyses.
Population characteristics	The OneK1K participants have the age from 19 to 97. The SNP data was assessed using Illumina Infinium Global Screening Array.
Recruitment	The participants were ascertained from patients or their relatives attending the Royal Hobart Hospital, Hobart Eye Surgeons as well as individuals residing in the retirement villages within Hobart, Australia. We acknowledge that this cohort has a higher prevalence of eye disease than the average population in Australia.
Ethics oversight	The OneK1K cohort was approved by the Tasmania Health and Medical Human Research Ethics Committee (H0012902)

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	The sample size is determined based on the published OneK1K dataset, which is 982 individuals.
Data exclusions	We removed two individuals (one due to a low number of cells and the other due to extremely imbalanced cell composition) and ended up with 980 individuals for the main analyses.
Replication	The replication analysis was performed on a published dataset from Perez et al. and we conducted sc-deQTL mapping for the individuals of East Asian (EAS) ancestry (97 individuals including 75 healthy controls and 22 lupus patients)
Randomization	NA. We did not use any study design that required randonmization.
Blinding	NA. We did not use any study design that required blinding.

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.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Plants

Seed stocks

Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.

Novel plant genotypes

Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.

Authentication

Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.