nature portfolio

Corresponding author(s): Ang Gao, Liguo Zhang, Pu Gao

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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	SerialEM 3.8
Data analysis	MotionCor 2 1.3.2, Cryosparc v4.3.1, Chimera 1.10.1, ChimeraX 1.6.1, Phenix 1.19.1, Coot 0.9.6, Pymol2.5, ImageJ 2.14.0, Prism v8.4.3, Cell Ranger suit 6.0.1

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

The cryo-EM maps have been deposited into the Electron Microscopy Data Bank under accession numbers EMD-60808 (hSLC15A4+Fab107) and EMD-60809 (hSLC15A4+TASL+Fab235). The coordinates have been deposited at the Protein Data Bank under accession numbers 9IRB (hSLC15A4+Fab107) and 9IRC (hSLC15A4 +TASL+Fab235). All cryo-EM maps and coordinates will be released before publication.

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	N/A
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	N/A
Recruitment	N/A
Ethics oversight	N/A

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	No statistical methods were used to predetermine sample size. The data size for cryoEM was determined by the availability of the microscope time and the particle density on the grids. Sufficient cryoEM data were collected to achieve the reported resolution of map, which is sufficient for model building.
Data exclusions	No data were excluded.
Replication	Each experiment was repeated at least three times in independent experiments.
Randomization	No group allocation was needed for functional experiments in this study.
Blinding	Investigators were not blinded to group allocation, because no grouping was needed for this study.

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

Antibodies

Antibodies used	Flow cytometry (anti-human antibodies) HLA-DR (APC-Cy7); Biolegend, Cat#307618, Clone:L243

CD14 (PerCP-Cy5.5); Biolegend, Cat#325622, Clone: HCD14

Flow cytometry (anti-mouse antibodies)
CD3e (APC-eFluor™ 780); Invitrogen, Cat#47-0031-82, Clone: 145-2C11
B220 (PerCP-Cy5.5); Biolegend, Cat#103236, Clone:RA3-6B2
CD19 (PE-Cy7); Biolegend, Cat#115519, Clone:6D5
GL7 (Alexa Fluor™ 488); Invitrogen, Cat#53-5902-82, Clone:GL-7
CD38 (BV421); Biolegend, Cat#102732, Clone:90

Flow cytometry (secondary antibodies)
PE anti-DYKDDDDK Tag, Biolegend, Cat# 637310, Clone:L5
PE goat anti mouse IgG; Biolegend, Cat# 405307, Clone: Poly4053
PE mouse anti Myc; Cell Signaling, Cat:3739S, Clone: 9B11

Fc Blockade
Human Fc receptor Binding Inhibitor Antibody; Invitrogen, Cat#14-9161-73; Polyclonal Antibody
TruStain FcX™ (anti-mouse CD16/32) Antibody; Biolegend, Cat#101320; Clone:93

Co-immunoprecipitation and Western blot
Anti-MYC Nanobody Agarose Beads; AlpaLifeBio, Cat# KTSM1306
FLAG M2 monoclonal antibody affinity gel; Sigma-Aldrich; Cat# A2220, Clone: M2
C-Myc-Tag Rabbit Polyclonal Antibody; huaxingbio; Cat# HX1821, Polyclonal Antibody
Flag-Tag Rabbit Polyclonal Antibody; huaxingbio; Cat# HX1819, Polyclonal Antibody
Goat anti-rabbit IgG HRP conjugated; ZSGB-BIO; Cat# ZB-2301, Polyclonal Antibody

The following antibodies were produced in the author's lab:
Monoclonal antibodies against human SLC15A4 (Clone 107 and 235) were expressed in HEK 293F cells.
Mouse anti Myc antibody (Clone 9B11) was purified from ascites.

Validation

The binding of purified antibodies to human SLC15A4 or Myc tag were confirmed by Western blot or FACS.

The binding of Fab fragment used in Cryo-EM reconstructions was shown by the co-migration of the Fab and the transporter on the size-exclusion column.

Other antibodies used in this study were bought from commercial vendors and were validated by the manufacturers or relevant literature was cited on their websites (see vendor websites listed above).

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	HEK293-T cells , HEK293-F cells and THP-1 cells were present in the lab at the time this study began. Sf9 cells were purchased from Thermo Fisher Scientific.
Authentication	No further authentications were performed for this study.
Mycoplasma contamination	No mycoplasma contamination tests were performed for this study.
Commonly misidentified lines (See ICLAC register)	None.

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals	Female BALB/c mice were obtained from SPF (Beijing) Biotechnology (aged 4 to 6 weeks).
Wild animals	N/A
Reporting on sex	N/A
Field-collected samples	N/A
Ethics oversight	The animal work was approved by Institute of Biophysics, Chinese Academy of Sciences.

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

Flow Cytometry

Plots

Confirm that:

☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☒ All plots are contour plots with outliers or pseudocolor plots.

☒ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	The cells were harvested, washed with 0.5% BSA-2mM EDTA-PBS and used for further downstream analysis.
Instrument	Multicolor flow cytometry was performed on the following machines: BD FACSAria™ III Cell Sorter, BD FACS LSRFortessa, Thermo Fisher Scientific Attune™ NxT Flow Cytometer.
Software	Data was analyzed using FlowJo 10.8.1.
Cell population abundance	Purity was greater than 95% after post sort analysis by flow cytometry.
Gating strategy	Preliminary FSC/SSC gating was used to gate on total population and single cells. Specific cell population were gate based on the specific antibody staining as described in each experiment.

☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.