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☐ Initial submission ☐ Revised version ☒ Final submission

Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form is intended for publication with all accepted life science papers and provides structure for consistency and transparency in reporting. Every life science submission will use this form; some list items might not apply to an individual manuscript, but all fields must be completed for clarity.

For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

Experimental design

1. Sample size

Describe how sample size was determined.

Unpaired T-test (two-tailed) and one-way Anova followed by Tuky's test were used to determine the significance. Sample sizes in this manuscript were similar to previous papers (Chavez, A. et al., Nature Methods, 2016. Konermann S. et al., Nature, 2015).

2. Data exclusions

Describe any data exclusions.

In methods. Poor transfected/infected mice were excluded.

3. Replication

Describe whether the experimental findings were reliably reproduced.

All attempts at replication were successful.

4. Randomization

Describe how samples/organisms/participants were allocated into experimental groups.

Randomization was used in all experiments.

5. Blinding

Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

To compare the fluorescence intensity of different activators, BFP-positive cells were selected and analyzed randomly per group(Figure 1), blindness was not used in other experiments. However, all samples were collected and all data were analyzed in an unbiased manner.

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
☐	☒ A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ A statement indicating how many times each experiment was replicated
☐	☒ The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
☐	☒ A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☐	☒ The test results (e.g. *P* values) given as exact values whenever possible and with confidence intervals noted
☐	☒ A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
☐	☒ Clearly defined error bars

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.	Custom algorithms or software was not used in this study. Fluorescence intensity: Zen (zeiss) Flow cytometry: FlowJo RNA-seq: Illumina Genome Analyzer, Trimmomatic (v0.36), Hisat2 (v2.0.0), Stringtie (v2.0) Western Blot: Image J Electrophysiology: Clampex 10 Statistics: SPSS 17.0

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* guidance for providing algorithms and software for publication provides further information on this topic.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.	The SPH transgenic mice will be donated to the jackson laboratory (https://www.jax.org/) and Shanghai Model Organism Center Inc., Shanghai, China (http://www.shmo.com.cn/). Other materials are available upon reasonable request.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	rabbit monoclonal antibody to HA-tag (Brain, 1:1000, #3724, CST, ref. 45), rabbit polyclonal NeuN antibody (Brain, 1:500, #ABN78, Millipore, ref. 46), mouse monoclonal DsRed2 Antibody (Liver, 1:1000, #sc-101526, Santa cruz), mouse monoclonal GS antibody (liver, 1:500, Millipore, ref. 47), rabbit polyclonal antibody to GAPDH (1:2000, #10494-1-AP, Proteintech, ref. 48), rabbit polyclonal CYP2E1antibody (liver, 1:1000, #ab28146, Genetex, ref. 49), rabbit polyclonal antibody to mCherry (liver, 1:2000, #GTX128508, Genetex, ref. 50), mouse monoclonal antibody to ASCL1 (liver, 1:2000, Liver, #556604, BD biosciences, ref. 51), rabbit polyclonal to DKK1 (brain, 1:2000, #ab61034, Abcam) and rabbit polyclonal antibody to HBB (brain, 1:2000, # AP11557b, Abgent, ref. 52, anti-digoxygenin antibody (1:2000, #11093274910, Roche, ref. 54).

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.	Cell bank, Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences
b. Describe the method of cell line authentication used.	Cell lines were authenticated by the supplier.
c. Report whether the cell lines were tested for mycoplasma contamination.	Cell lines were tested for mycoplasma contamination.
d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.	None of the cell lines used was listed in the database of ICLAC.

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study.

Cre-dependent SPH transgenic mice were generated with piggyBac transposon system in F1 zygotes. Three chimeric male founders were selected to cross with wild type C57BL/6 mice. SPH;GFAP-Cre double-transgenic mice were generated by crossing SPH transgenic mice with GFAP-Cre (JAX stock #004600, forward primer: 5'-GCCTGCATTACCGGTCGATGC-3' and reverse primer: 5'-CAGGGTGTTATAAGCAATCCCC -3') transgenic mice. Mice aged 1-3 months were typically used for experiments. Mice were housed at constant temperature with a 12 h/12 h dark/light cycle (lights on at 9 a.m.) and 1-6 mice were kept per cage. All experiements were approved by the institutional animal care and use committee of Chinese Academy of Sciences. Mice of either sex were used and randomly assigend to different groups for all experiments.

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.

No human participants.

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Flow Cytometry Reporting Summary

Form fields will expand as needed. Please do not leave fields blank.

Data presentation

For all flow cytometry data, confirm that:

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

☒ 2. 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).

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

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

Methodological details

5. Describe the sample preparation.	Cell were digested by trypsin (0.05%), contrifuged at 1000 rpm and filtered with a 35μm nylon mesh. (Supplementary Figure 2b)
6. Identify the instrument used for data collection.	MoFlo XDP (Beckman)
7. Describe the software used to collect and analyze the flow cytometry data.	Collect: Summit Software version 5.2 Analyze: FlowJo
8. Describe the abundance of the relevant cell populations within post-sort fractions.	20000 cells were sorted per group. Positive and negative boundaries were determined by control cells that were not transfected with any plasmids.
9. Describe the gating strategy used.	Positive and negative boundaries were determined by control cells that were not transfected with any plasmids.

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