

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 (<i>n</i>) 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 <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☒	☐ 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
☒	☐ 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 <i>d</i> , Pearson's <i>r</i>), 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	Mouse livers and zebrafish larvae and adults were imaged using a SteREO Discovery V2.0 microscope equipped with AxioVision Rel 4.8.2 software (Carl Zeiss). Antibody-stained samples, live larvae, and liver sections were imaged using ZEN 2010 software equipped on LSM880/LSM780 confocal microscope (Carl Zeiss). All figures, labels, arrows, scale bars, and outlines were drawn using Adobe Photoshop 2021.
Data analysis	Unpaired two-tailed Student's t-test was used for statistical analysis by GraphPad Prism 8; P < 0.05 was considered statistically significant. Quantitative data were shown as means ± s.e.m.

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](#)

N/A

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	Sample sizes chosen was based on recognised zebrafish and mouse standards in the field and previously published literature (e.g. PMID: 28459441, 37311876, 29720662, and 28395729). We have described the exact sample size for each experiment in the manuscript. No statistical methods were used to predetermine the sample size. Briefly, more than ten pairs of fish were used to set one specific cross for each experiment. For a cross between sox9b homozygous parents, more than 5 larvae were used for analyses in each treatment. For mice experiment, more than 5 mice were selected in each experiment.
Data exclusions	No data were excluded from analyses.
Replication	All experiments were verified with at least 3 biological replicates and/or independent experiments. The exact number of repetitions for all experiments is illustrated in the legend, and our attempts at repetition were successful.
Randomization	All experiments comparing treatment groups were carried out using randomly assigned siblings.
Blinding	Phenotyping preceded genotyping in mutant analyses, hence analysis was genotype blinded. In the other experiments. As different transgenic zebrafish embryos, larvae, juveniles, adults, and mice were used in the experiments, researchers were not blinded to group assignment during data collection and/or analysis.

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	Primary antibodies including: EpCAM (1:500, BD Biosciences, #552370), CK19 (1:1000, Abcam, AB133496), aSMA (1:500, Thermofisher, # PA5-18292), ALDH1A2 (1:500, Abcam, AB75674), GFP (1:500, Abcam #ab6658; Santa Cruz #sc9996; Invitrogen #A11122; Invitrogen, Cat#A11122), SGP (1:500, #PC-.064, Kamiya Biomedical Company), Anxa4 (1:1000, Abcam #Ab71286), Tomato (1:500, Biorbyt #aorb182397), Anti-mCherry (1:500, Arigo biolaboratories #ARG55723), Anti-PCNA (1:500, Sigma #SAB2701819), Anti-Dig AP (1:2000, Roche #11093274910), Anti-Dig POD (1:1000, Roche #11207733910). Secondary antibodies used in the study included Donkey anti-goat IgG Alexa fluor 647-conjugated (1:1000, Invitrogen), Donkey anti-goat IgG Alexa fluor 568-conjugated (1:1000, Invitrogen), Donkey anti-goat IgG Alexa fluor 488-conjugated (1:1000, Invitrogen), donkey anti-mouse IgG Alexa fluor 488-conjugated (1:1000, Invitrogen), donkey anti-mouse IgG Alexa fluor 647-conjugated (1:1000, Invitrogen), donkey anti-mouse IgG Alexa fluor 568-conjugated (1:1000, Invitrogen), donkey anti-Rat IgG Alexa fluor 568-conjugated (1:1000, Invitrogen), donkey anti-rabbit IgG Alexa fluor 647-conjugated (1:1000, Invitrogen), goat anti-rabbit IgG Alexa fluor 568-conjugated (1:1000, Invitrogen), donkey anti-rabbit IgG Alexa fluor 488-conjugated (1:1000, Invitrogen), goat anti-rabbit IgG Alexa fluor 405-conjugated (1:1000, Invitrogen).
Validation	For anti-GFP, anti-Anxa4, anti-PCNA, anti-Tomato, anti-mCherry, anti-Dig AP, anti-Dig POD, and secondary antibodies were validated in references (He et al., 2019, 2020, 2022, 2023); For anti-CK19, anti-aSMA, and anti-ALDH1A2 see references (Ota et al., 2021; Raven et al., 2017) in this paper, anti-EpCAM was validated in reference (Serrena Singh et al., 2023) in this paper, anti-ALDH1A2 was validated in reference (Sugimoto et al., 2012), anti-SGP was validated in zebrafish in reference (Choi et al., 2014).

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	All animals are housed in temperature- and light-controlled facilities and are maintained in accordance with the Guide for Care and Use of Laboratory Animal and the Animal Welfare Act at Southwest University. The Alb:Cre (Wang et al., 2020), Krt19:DreER (NO. T056046, Gempharmatech), and DeaLT-IR (He et al., 2017), and wild-type astrains were on a C57BL/6J background. Both 3-8 months adult male and female mice were used. The transgenic or mutant zebrafish lines Tg(Tp1:Tomato) (Zhang et al., 2021), Tg(Krt18:Tomato), Tg(cldn15lb:GFP-NTR), Tg(cldn15lb:mCherry-NTR), Tg(anxa4:CreER), Tg(anxa4:GFP), Tg(aSMA:CreER), Tg(hsp70l:DnRAR-2a-venus), Tg(hsp70l:cyp26a1-mCherry), Tg(βactin:loxP-STOP-loxP-DsRed) (Bertrand et al., 2010), Tg(βactin:loxP-DsRed-loxP-GFP) (Kikuchi et al., 2010), and sox9b mutant (Delous et al., 2012) were AB background. All the strains are used as stable, germline transgenic lines in this study. Both adult male and female zebrafish (3-8 months) and larvae were randomly selected for experiments.
Wild animals	The study did not involve wild animals.
Reporting on sex	For zebrafish, in the larvae stage, the sex of zebrafish larvae was unknown. In adult stage, both male or female fish were selected randomly for this experiment. The male and female mice were randomly selected for this experiment.
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	Experiments were performed with the approval of the Institutional Animal Care and Use Committee (IACUC) at Southwest University (Protocol number: IACUC-20190115-05 and IACUC-20231228-02).

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

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A