

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	NIS Elements Ver 5.11.03 (Nikon) Zen Ver 3.4.91.00000 (Zeiss) Leica Application Suite X Ver 3.7.1.21655 (Leica) Leica Application Suite Ver 4.5.0 (Leica)
Data analysis	MATLAB code STRESS developed at the Campas lab (https://github.com/campaslab/STRESS) FIJI (ImageJ2) (Ver 2.3.0/1.53c to 1.53q) OrientationJ plug-in (version 2.0.5) in FIJI (ImageJ2), version 2.3.0. MATLAB (R2021b) Mathematica 12 (version 12.0.0.0) Graphpad Prism (V.8.00) Paraview (V5.10) Imaris x64 9.3.1 EpySeg version 0.1.28 Huygens Professional for Linux (22.10.0p0 64b) Cellpose version 0.6.5 Details for all code usage and analysis is available in the Methods section.

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 data supporting the findings of this study are all available within the article. Source data are provided with this study. All other data supporting the findings of this study are available from the corresponding authors.

Human research participants

Policy information about [studies involving human research participants and Sex and Gender in Research](#).

Reporting on sex and gender

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 size was chosen based on experience of the authors from previous similar studies, relevant literature (Li et al., 2016; Campas et al., 2014; Mongera et al., 2018), preliminary experiments to determine the minimum sample number required to obtain consistent results and feasibility of obtaining samples (esp. in the case of genetic mutant lines). No statistical test was used to pre-determine sample sizes.

Data exclusions

Data was excluded in the following cases -
 1. Explants that were not cut in the correct plane and thus showed an absence of incisor growth or abnormal orientation of bud and were discarded from representation and analysis.
 2. Oil droplets that were incompletely imaged or could not be imaged due to improper embedding in agarose were discarded from representation and analysis.
 3. Images that were below the quality of analysis by OrientationJ and subsequent codes were discarded from representation and analysis.
 All exclusion criteria were pre-determined before beginning the experiments.

Replication

To verify the reproducibility of the findings -
 1. All experiments were repeated with independent embryos from different batches of at least 2 independent pregnant females. Where possible, the experiments were repeated by both lead authors and the analysis was done by multiple authors and results compared.
 2. All analysis was performed on biological replicates. Representative images were from multiple experiments with similar results.
 3. Embryos were precisely weighed to ensure correct staging.
 4. The experimental procedure, reagents and equipment used were maintained throughout.
 5. All attempts at replication were successful except when one batch of the drug aphidicolin stopped working. The loss of drug activity was confirmed by testing cell proliferation and the results with the new drug batch were consistent with the original data.

Randomization

Embryos were weighed to ensure that correct staged ones were used as required for experiments. The correct staged embryos were then randomly used for planned experiments.

Blinding

The investigators were not blinded for the experiment setup and subsequent imaging since the entire process was handled by the same person and blinding would not affect the results. Data analysis for the acquired images to generate the OrientationJ maps was done without informing the investigators of the groups. For other experiments blinding would not affect the 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

Methods

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

Antibodies

Antibodies used

Primary antibodies - anti-E-Cadherin (BD Biosciences, #610181), anti-P21 (BD Biosciences, #556431), anti-BrdU (MoBu-1, Novus, #NB500-439), Click-iT EdU kit (ThermoFisher Scientific, #C10640), Alexa647-conjugated phalloidin (ThermoFisher Scientific, #A22247), anti-Yap (AbClonal, #A1002), anti-pMyoII LC (Abcam, #ab2480). Secondary antibodies - Alexa Fluor 647-conjugated anti-Mouse IgG (ThermoFisher Scientific, #A21237); Alexa Fluor 488 conjugated anti-rabbit (Thermo Fischer, #A11008); Alexa Fluor 647 conjugated anti-rabbit (Thermo Fischer, #A21244); Alexa Fluor 555 conjugated anti-mouse (Thermo Fischer, #A21422); Biotinylated Goat Anti-Mouse IgG (H+L) (Vector Laboratories, #BA-9200). The TSA Cyanine-5 kit (1:100, Akoya, #SAT705A001EA) was used for signal amplification when required.

Validation

Antibodies were purchased from pre-validated, reputable, commercial sources. Validation data is available on the manufacturer's websites listed below -
 anti-E-cadherin (<https://www.bdbiosciences.com/en-us/products/reagents/microscopy-imaging-reagents/immunofluorescence-reagents/purified-mouse-anti-e-cadherin.610181>)
 anti-P21 (<https://www.bdbiosciences.com/en-au/products/reagents/microscopy-imaging-reagents/immunofluorescence-reagents/purified-mouse-anti-p21.556431>)
 anti-BrdU (https://www.novusbio.com/products/bromodeoxyuridine-brdu-antibody-mobu-1_nb500-439)
 Click-iT EdU kit (<https://www.thermoFisher.com/order/catalog/product/C10640>)
 Alexa647-conjugated phalloidin (<https://www.thermoFisher.com/order/catalog/product/A22287>)
 anti-Yap (<https://abclonal.com/catalog-antibodies/YAP1RabbitAb/A1002>; This antibody was also validated on mouse intestinal organoids)
 anti-pMyo II LC (<https://www.abcam.com/products/primary-antibodies/myosin-light-chain-phospho-s20-antibody-ab2480.html>)
 Alexa647-conjugated anti-Mouse IgG (<https://www.thermoFisher.com/antibody/product/Goat-anti-Mouse-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-21237>)
 Alexa Fluor 488 conjugated anti-rabbit (<https://www.thermoFisher.com/antibody/product/Goat-anti-Rabbit-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-11008>)
 Alexa Fluor 647 conjugated anti-rabbit (<https://www.thermoFisher.com/antibody/product/Goat-anti-Rabbit-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-21244>)
 Alexa Fluor 555 conjugated anti-mouse (<https://www.thermoFisher.com/antibody/product/Goat-anti-Mouse-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-21422>)
 Biotin-conjugated Goat Anti-Mouse IgG (<https://vectorlabs.com/products/antibodies/biotinylated-goat-anti-mouse-igg>)
 TSA Cyanine-5 (https://my.akoyabio.com/ccrz_ProductDetails?sku=SAT705A001EA&cclcl=en_US)

The specific staining pattern in experimental controls for all antibodies was matched to previously published data using other antibodies to further confirm results.

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

Strains used - K14Cre; R26mT/mG; R26-pCAG-nuc-3x mKate2; Ctnna1cKO; K14CreER; Piezo1/2fl/fl and C57BL/6J. The R26mT/mG females were crossed to K14Cre males to obtain the dual labeled K14Cre;R26mT/mG/mTmG line which has been used for most experiments. At the time of acquisition, the mouse strains were on B6 backgrounds but they were subsequently maintained on mixed backgrounds. For all lines, 2 – 5 month old females were mated to plug, and pregnant females were euthanized at E12.5 and E13.5 to collect eGFP+ embryos. The embryos were staged for growth/age according to their molecular weight and divided into the following groups - 0.10 gm (E11.5 - initiating bud stage), 0.11 gm (E12 - pre-EK stage), 0.12 gm (E12.5 - pre-EK stage), 0.13–0.14 gm (E13.5 - EK formation stage), 0.15–0.16 gm (E14.5 - post-EK stage) and 0.17–0.18 gm (E15.5 - post-EK stage).

Wild animals

The study did not involve wild animals.

Reporting on sex	Since the study involved the use of E11.5 - E15.5 embryos or live tissue from these embryos, segregation based on sex was not possible. Correctly staged embryos were randomly assigned to experimental groups. Information based on sex has not been collected and was not used for the analysis.
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	All experiments involving mice were approved by the Institutional Animal Care and Use Committee of the University of California, San Francisco (protocol #AN180876-03C) and the University of California, Los Angeles (protocol #ARC-2019-013).

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