# natureresearch

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# **Reporting Summary**

Nature Research 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 Research policies, see <u>Authors & Referees</u> and the <u>Editorial Policy Checklist</u>.

#### 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
	$\square$ 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 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. <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> .
$\boxtimes$	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
$\boxtimes$	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
$\boxtimes$	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	NA	
Data analysis	NA	

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/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

All data generated or analysed during this study are included in this published article (and its supplemental information files)

# 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

# Life sciences study design

Sample size	The samples were randomly chosen avoiding subjects affected by other concomitant diseasese. Considering the complexity of the analysis and the differences between affected and not affected subjects we reguarded the number to be sufficient.
Data exclusions	No data were excluded
Replication	All data were reproducible
Randomization	Samples have been randomly selected and accurately represent their respective populations.
Blinding	All fluorescence data were observed by 2 researchers, blindly.

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

## 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

Animals and other organisms

Human research participants

terials & experimental systems		Methods		
Involved in the study	n/a	Involved in the study		
Antibodies	$\boxtimes$	ChIP-seq		
Eukaryotic cell lines	$\boxtimes$	Flow cytometry		
Palaeontology	$\boxtimes$	MRI-based neuroimaging		

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 $\boxtimes$ 

Clinical data

n/a

 $\boxtimes$ 

 $\boxtimes$ 

 $\boxtimes$ 

Antibodies used	For all the antibodies name, clone and manifacturer is described
Validation	All the antibodies have a reference

#### Eukaryotic cell lines

Policy information about <u>cell lines</u>	<u> </u>
Cell line source(s)	Skin explants or duodenal biopsies were immediately placed in Dulbecco's Modified Eagle's Medium (DMEM) (GIBCO, San Giuliano Milanese, Italy) supplemented with 20% foetal bovine serum (FBS) (GIBCO, San Giuliano Milanese, Italy), 100 units/ ml penicillin-streptomycin (GIBCO, San Giuliano Milanese, Italy), and 1 mM glutamine (GIBCO, San Giuliano Milanese, Italy) and incubated for 24 hours. Subsequently, each skin or duodenal explant was divided into about approximately 50 small fragments, plated on T 25 flasks and incubated in the presence of 95% oxygen and 5% CO2 at 37°C to allow adhesion and the subsequent release of fibroblasts. Seven-ten days later, the fibroblasts began to emerge from the fragments. When the fibroblasts reached confluence, the cells were harvested with trypsin and immediately frozen. In all experiments, the fibroblasts were used between the 2nd and 4th passage.
Authentication	Authentication was done by vimentine staining and fluorescence microscope observation. All the fibroblasts were positive for this marker
Mycoplasma contamination	All the cell used in the study were tested for micoplasma contamination by Hoechst staining and fluorescence microscope observation
Commonly misidentified lines (See <u>ICLAC</u> register)	ΝΑ

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### Clinical data

Policy information about <u>clinical studies</u>

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	NA. Our study is not a clinical trial
Study protocol	NA
Data collection	NA
Outcomes	NA