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Corresponding author(s): Keith Al-Hasani, Assam El-Osta

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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 our <u>Editorial Policies</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	a Confirmed					
	\boxtimes	The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement				
\boxtimes		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.				
\boxtimes		A description of all covariates tested				
\boxtimes		A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons				
\boxtimes		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)				
\boxtimes		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.				
\ge		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 d, Pearson's r), indicating how they were calculated				
	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.					

Software and code

Policy information about <u>availability of computer code</u>							
Data collection	MultiNA-Microchip Electrophoresis System software, qPCR-Quantstudio 3						
Data analysis	Graphpad Prism 8						

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 Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a <u>data availability statement</u>. 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

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Field-specific reporting

Life sciences

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.

Behavioural & social sciences Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>

Life sciences study design

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

Sample size	Mouse islets isolated from 4 animals-pooled per group for 3 experimental groups (Wt, ArxKO, and PaxOE), 12 mice in total.	
Data exclusions	No data exclusions.	
Replication	3 biological replicates	
Randomization	Not relevant to this study.	
Blinding	Not relevant to 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	Methods	
n/a Involved in the study	n/a Involved in the study	
Antibodies	ChIP-seq	
Eukaryotic cell lines	Flow cytometry	
Palaeontology and archaeology	MRI-based neuroimaging	
Animals and other organisms		
Human research participants		
Clinical data		
Dual use research of concern		

Antibodies

Antibodies used	Mouse monoclonal anti-insulin (Sigma) clone K36AC10 catalogue I2018, Mouse anti-Ngn3 (Millipore) catalogue number AB5684, Rat monoclonal anti-somatostatin (Sigma) catalogue number MAB354. Lot numbers not available.
Validation	These antibodies were previously described, used and validated by our team (DOI:https://doi.org/10.1016/j.devcel.2013.05.018)

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research						
Laboratory animals	Wild-type (WT) 129/sv mice were obtained from Charles River Laboratories and from Taconic.					
Wild animals	Study did not involve wild animals.					
Field-collected samples	Study did not involve samples collected from the field.					
Ethics oversight	Animal protocols were reviewed and approved by an institutional ethics committee (Ciepal-Azur) at the University of Nice, and all colonies were maintained following European animal research guidelines. This project received approval from our local ethics committee (NCE/2011-22).					

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