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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 Authors & Referees and the Editorial Policy Checklist.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	No software was used
Data analysis	RNA-seq data were analyzed using samtools, pysam version 0.15.1, R version 3.5.1, ggplot2 version 3.1.0 and DESeq version 1.34.0, python version 2.7.15, perl version 5.22.2, STAR version 2.5.3a, STAR version 2.6.0c. STAR aligner, Dobin, A. et al. STAR: ultrafast universal RNA-seq aligner. Bioinformatics 29, 15–21 (2013). SAMtools version, Li, H. et al. The Sequence Alignment/Map format and SAMtools. Bioinformatics 25, 2078–2079 (2009). DESeq, Love MI. et al. Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2. Genome Biol. 15(12):550 (2014). Amplicon sequencing was analyzed using CRISPResso version 1.0.13. CRISPResso, Pinello, L. et al. Analyzing CRISPR genome-editing experiments with CRISPResso. Nat. Biotechnol. 34, 695–697 (2016). GraphPad Prism version 7.01 was used for plotting figures. CellQuest Pro version 4.0.1 was used to analyze FACS data.

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 upon request. 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

Accession codes will be available before publication. A full code availability statement is included in the manuscript.

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

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

Sample size	At least 3 independent samples per tested condition were evaluated.
Data exclusions	No data was excluded.
Replication	3 or more independent biological replicates were evaluated for both in vitro studies in cultured cells, and in vivo studies using mice. Findings were consistent in all replicates.
Randomization	Mice were randomly assigned into groups prior to injection.
Blinding	No blinding was carried out.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☒	☐ Unique biological materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☒	☐ Human research participants

Methods

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

Antibodies

Antibodies used	The antibodies used in this study include: Rabbit anti-dystrophin (Immunofluorescence and western blot 1:200), abcam 15277, Lot no. GR 305946-5 Rabbit anti-nNOS (Immunofluorescence 1:100), Immunostar 24431, Lot no. 401001 Rabbit anti-Ornithine Carbamoyltransferase (Western blot 1:800), abcam 203859, Lot no. GR 278002-5 Rabbit anti-GAPDH (Western blot 1:4000), Cell Signaling 2118S, Lot no. 10 Mouse anti-ADAR2 (Western blot 1:150), Santa Cruz Biotechnology 73409, Lot no. K0917 Donkey anti-rabbit AlexaFluor 546 (Immunofluorescence 1:400), ThermoFisher A10040, Lot no. 1833519 Anti-rabbit IgG HRP-linked (Western blot 1:20,000), Cell Signaling 7074S, Lot no. 26 Anti-mouse IgG HRP-linked (Western blot 1:20,000), Cell Signaling 7076P2, Lot no. 32
Validation	Antibodies were validated and optimized by immunostaining and/or western blots carried out on tissue samples harvested from positive and negative control mice, simultaneously, as per the manufacturers instructions. The antibodies against dystrophin,

nNOS, OTC and GAPDH were validated for the mouse proteins. The antibody against ADAR2 was validated for the human protein.
References:
1. Nelson, C. E. et al. In vivo genome editing improves muscle function in a mouse model of Duchenne muscular dystrophy. Science (80-.). 351, (2016).
2. Tabebordbar, M. et al. In vivo gene editing in dystrophic mouse muscle and muscle stem cells. Science (80-.). 351, 407–411 (2016).

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	HEK293T, HEK293FT, HeLa (ATCC)
Authentication	STR, by vendor
Mycoplasma contamination	Tested by vendor, no mycoplasma contamination
Commonly misidentified lines (See ICLAC register)	HEK293T cells were used for cell culture experiments, and AAV production per established procedures.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	Laboratory mice used in this study were obtained from the Jackson Laboratory C57BL/10ScSn-Dmdmdx/J, strain 001801, male and female, 6-10 weeks B6EiC3Sn a/A-Otcspf-ash/J, strain 001811, male, 10-16 weeks
Wild animals	Study did not involve wild animals.
Field-collected samples	Study did not involve samples collected from the field.

Flow Cytometry

Plots

Confirm that:

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

☒ 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).

☐ All plots are contour plots with outliers or pseudocolor plots.

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

Methodology

Sample preparation	The HEK293T cell line was used for all flow cytometry experiments. Flow cytometry was carried out on the transfected cells 48 or 72 hours post transfection to quantify GFP expression. No antibodies were used for flow cytometry.
Instrument	FACScan (Becton Dickinson)
Software	CellQuest Pro (Becton Dickinson)
Cell population abundance	n/a
Gating strategy	Un-transfected control cells were used to define non-fluorescent cells (with a gating boundary defined at a fluorescence intensity of 10^1).

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