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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	https://github.com/mgolkaram/Nature-Neuroscience-2018-miRNA-mRNA-paper , protocol 100-6667 at http://www.fluidigm.com/
Data analysis	https://github.com/mgolkaram/Nature-Neuroscience-2018-miRNA-mRNA-paper , Geneious® bioinformatics platform (version 9.1.8), http://www.novocraft.com/). Fluidigm Real-Time PCR Analysis Software (v.3.0.2), miRdeep2, DESeq2, R version 3.3.1 (2016-06-21)

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

The data used in this study are available as part of the publicly available Gene Expression Omnibus database under the accession number GSE107468.

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	We generated data based on the availability of primary tissue samples. In total we processed 9 primary tissue samples for AGO2-clip, and used saturation analysis to determine that this number was effective in recovering the majority of targeted genes.
Data exclusions	For single cell qPCR we excluded any assay that did not give positive value after 30 cycles of amplification in at last two single cells. We removed cells with positive signal from at least 5 assays.
Replication	We used strict measures to highlight high confidence AGO2 binding clusters in the mRNA. Firstly, we used multiple biological replicates for each age-range of specimens and curated the dataset to the list of target sites detected in at least two biological specimens. For all other experiments that were carried out, all attempts at replication were successful.
Randomization	Samples were randomized due to the random collection of primary tissue specimens and were processed in random order. Sc-qPCR data was generated and processed in random order.
Blinding	Sample collection was performed by researchers at UCSF, the samples were processed for AGO2-CLIP at UCSB without cross-referencing with sample metadata. For single cell qPCR,m data was processed in parallel and only analyzed together following a melting curve analysis.miR2115 overexpression analysis and brdU analysis experiment was performed by blinding the experimental conditions for brdu/sox2 quantification

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

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	HEK293 cells were obtained from a commercial source.
Authentication	This cell line was never authenticated
Mycoplasma contamination	We have not tested this line for mycoplasma contamination
Commonly misidentified lines (See ICLAC register)	We used the HEK293 cell line and there was no particular reason for chosing it, other than that it is commonly used in the lab for luciferase experiments.

Animals and other organisms

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

Laboratory animals	We have pregnant dams Swiss-Webster in this experiment, but only analyzed embryonic animals. We never test embryos for sex. therefore we expect approximately even representation of males and females. We used three pregnant dams in this

	experiments. Because Simonsen does not inform us about the age of these animals, we do not know what ages they are. The embryos used in the analysis were at E15.5 stage of development. However, we did not confirm the age by Theiler criteria, and the age is only based on the plug check information provided by Simonsen.
Wild animals	this study did not involve wild animals
Field-collected samples	this study did not involve field-collected animals