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Reporting Summary

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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	LABVIEW 2012 for data collection and COMSOL 4.3 for simulations.
Data analysis	MATLAB R 2014B for all SNACS analysis and statistical tests, Igor Pro 8 for AFM data analysis, OriginPro 8 SR0 for plotting and statistical tests, Image J 1.47v for image display, DeltaVision software SoftWorx for image deconvolution.

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 that support the findings of this study are available from the authors on reasonable request.

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	No statistical tests were used to determine the sample size. The sample size (n) for single-cell traces (Fig. 3 and Fig. 4) refers to the number of cells independently monitored. The sample size for population measurements (Fig. 2, Fig. 3b, and Fig. 4d) reflects the number of cells measured within 20-30 minutes with a throughput, typically around 1,000-1,500 cells/hour.
Data exclusions	Single-cell traces: no data exclusions. Population comparisons - Asymmetric peaks (differences between left node deviation and right node deviation is bigger than 3 times the standard deviation of the instrument noise OR anti-node peaks with different height that is bigger than 3 times the standard deviation of the instrument noise) were excluded. This data exclusion criteria mostly results in exclusion of particles with buoyant mass lower than that of live cells (e.g. cell debris, which would bias the data) or cell clumps. All data exclusion criteria are also detailed in the Methods section.
Replication	All attempts at replication were successful. All single-cell SNACS traces were obtained on separate days. All single-cell SNACS traces were repeated at least five times in independent experiments. The population SNACS measurements were repeated at least in three independent experiments, always yielding comparable results.
Randomization	We did not use any pre-selection criteria on which cells to measure SNACS (stiffness measurement). A population of cells was loaded in to the SMR device and the first cell to go through was trapped for single cell monitoring experiments. For population measurements the order of drug treatments/measurements was randomized.
Blinding	Drug treatments and the consequent measurements were carried out by a single researcher, so no blinding was applicable. For image analysis, separate researchers carried out the imaging and image analysis. The researcher carrying out the image analysis was not aware of our experimental hypothesis.

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)	L1210 and BaF3 cell lines were obtained from ATCC. S-Hela cell line was kindly provided by Dr. Kevin Elias (Brigham and Women's Hospital, Department of Obstetrics and Gynecology, Boston, MA 02115).
Authentication	L1210 and BaF3 cell lines were authenticated by ATCC. S-Hela was not authenticated.
Mycoplasma contamination	L1210 and BaF3: tested for mycoplasma regularly. No contaminations have been found. S-Hela: not tested.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.