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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.

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
☐	☒ The exact sample size (*n*) 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. *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

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	ASTRA6.1 (GPC); Dynamics7.5.0.17 (DLS); Bruker TopSpin 4.0 (NMR); Bruker OPUS (FTIR); Bruker Daltonics (MALDI-TOF-MS); Living Image 4.5 (IVIS); Chem Station (HPLC); Tecan i-Control (in vitro viability); BD FACS Diva (flow cytometry); JASCO Spectra Manager (CD); RDKit 2019.03, OpenMM 7.3.1 (SHAKE and Particle Mesh Ewald were used as implemented), LigParGen (http://zarbi.chem.yale.edu/ligpargen/, accessed on 7th July 2019) Orca 4.1.1, and OpenBabel 2.4.1 (molecular dynamic simulations); HOOMD-Blue v2.9.4 (coarse-grain simulations).
Data analysis	OriginPro 8 and GraphPad Prism 8 for data analysis and plotting; MestReNova v12.0.4 for NMR analysis; Dynamics 7.5.0.17 for DLS; Living Image 4.5 for IVIS, BD FACS Diva for flow cytometry. VMD 1.9.3, MDTraj 1.9.5, MSMBuilder 3.8.0 (BACE was used as implemented), PyEMMA 2.5.9, PyMOL 2.4, and ProteinCSM 1.0.1 for molecular dynamic simulations.

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 supporting the findings of this study are available within the Article and its Supplementary Information and can also be obtained from the corresponding author upon reasonable request.

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

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

Life sciences study design

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

Sample size	For in vitro experiments, 3 and 4 independent biological experiments were conducted for viability studies and cell uptake studies, respectively, affording statistically significant means and standard deviations; For in vivo experiments, groups of 3 mice were used for each condition for pharmacokinetics and biodistribution studies, affording statistically significant means and standard deviations.
Data exclusions	There were no data exclusions.
Replication	We have not attempted to replicate our in vitro and in vivo experiments beyond the data presented here.
Randomization	Cells and mice were randomly grouped for each experimental condition.
Blinding	Investigators were blinded for in vitro and in vivo studies.

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

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

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)	HUVEC from Lonza, HeLa and MCF-7 from the MIT Koch Institute High Throughput Screening Core
Authentication	Cell lines were used as received from commercial source (Lonza) or from the MIT Koch Institute High Throughput Screening Core. All cell lines stored in this facility were authenticated by STR profiling prior to deposition.
Mycoplasma contamination	All cell lines were tested for mycoplasma infection.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified lines were used.

Animals and other organisms

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

Laboratory animals	BALB/c mice, female, 8-12 weeks old, from Taconic Biosciences
Wild animals	No wild animals were involved in this work.
Field-collected samples	No field-collected samples were involved in this work.
Ethics oversight	In vivo experiments were reviewed and approved by the MIT Committee for Animal Care (CAC).

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

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	Cells were incubated with polymers for the indicated periods of time, washed, suspended, and analyzed by flow cytometry.
Instrument	BD Biosciences FACS LSR II HTS
Software	BD FACS Diva
Cell population abundance	Single cell types were used for these experiments.
Gating strategy	Gating were performed to eliminate signal from cellular debris.

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