

Reporting Summary

Nature Portfolio 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 Portfolio policies, see our [Editorial Policies](#) 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
<i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i> |
| ☒ | ☐ | 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
<i>Give P values as exact values whenever suitable.</i> |
| ☒ | ☐ | 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 No software was used for data collection.

Data analysis FlowJo (v 10.0.7) was used for flow cytometry analysis. Proteomics data were processed using Raw data, which were processed using DIA-NN (v 1.9.2), followed by downstream analysis in R (v 4.5.2). Molecular docking was performed using Molecular Operating Environment (v 1.15). Image data were processed using FIJI. Spectrum data and statistical analysis were processed using Graphpad (v 10.6.1)

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 Portfolio [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 description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

The experimental data and the simulation results that support the findings of this study are available within the paper and its Supplementary Information.

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender This research does not involve human participants, their data, or biological material.

Reporting on race, ethnicity, or other socially relevant groupings This research does not involve human participants, their data, or biological material.

Population characteristics This research does not involve human participants, their data, or biological material.

Recruitment This research does not involve human participants, their data, or biological material.

Ethics oversight This research does not involve human participants, their data, or biological material.

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

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](https://www.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	No calculations were done to predetermine the sample size except to have a minimum of $n = 3$ for statistics. This sample size balances precision with resources, but where the expected effect size is smaller or variability of the system is high (e.g. in the case of certain animal experiments), larger sample sizes were used to increase the statistical power of the experiment.
Data exclusions	No data were excluded from the analyses.
Replication	All studies were conducted with a minimum of three replicates. Experiments supporting the main conclusions were repeated using multiple technical and biological replicates and were cross-validated using orthogonal approaches. For example, nano-biomolecular condensate internalization was demonstrated by electron microscopy, fluorescence microscopy, chemical inhibition, and flow cytometry. Key experiments were performed across multiple KRAS mutant types (SW480, HT29, and H441), different cell types (tumor cells and neuroblastoma), and inhibitor panels (lysosomal and proteasomal inhibitors targeting distinct steps within each pathway. The Methods section is described in detail to maximize reproducibility for readers.
Randomization	Mice were randomly assigned to experimental groups for all experiments.
Blinding	Sample preparation was typically performed by multiple researchers blinded to the experimental conditions. For example, tissue processing and immunohistochemical staining were conducted by staff at the Mouse Histology & Phenotyping Laboratory, who were blinded to experimental group assignments. Sample preparation for transmission electron microscopy was performed by personnel at the Northwestern University Atomic and Nanoscale Characterization Experimental Center, also blinded to experimental details. Proteomic analyses were carried out by staff at the Northwestern Proteomics Center of Excellence under blinded conditions. In vitro experiments involving flow cytometry, ICP-MS, and image analysis were not blinded. Flow cytometry and ICP-MS are quantitative analytical techniques whose measurements are not influenced by operator bias. Image analysis was based on predefined biological features and computational metrics rather than subjective interpretation.

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 and archaeology
- ☐ ☒ Animals and other organisms
- ☒ ☐ Clinical data
- ☒ ☐ Dual use research of concern
- ☒ ☐ Plants

Methods

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

Antibodies

Antibodies used

Antibodies used for staining, imaging, and biochemical assays:

AF555 Anti-RAS Abcam (ab308603)
 AF555 rabbit IgG, Abcam (ab208569)
 APC Anti-RAS Abcam (ab310809)
 AF 488 Anti-Alpha-synuclein Abcam (ab195025)
 Anti-Actin CST (4970S)
 Anti-KRAS CST (33197)
 Anti- α -Synuclein CST (4179S)
 Anti-RAS (G12V mutant) CST (51813)
 Anti-phospho-MEK 1/2 CST (9154)
 Anti-MEK 1/2 CST (9122)
 Anti-phospho-AKT CST (4060S)
 Anti-AKT CST (9272S)
 Anti-Rab5 CST (3547)
 Anti cRaf Santa Cruz (sc-133)
 Anti-IgG (Fc specific) Invitrogen (31125)
 Goat anti-rabbit IgG, HRP Invitrogen (31460)
 Goat anti-mouse IgG, HRP Invitrogen (31430)
 Anti-Ki-67 CST (12202)
 Anti-RAS CST (91054)
 Anti-p53 CST (2527)

Therapeutic antibody cargoes used in this study:

Anti-RAS Abcam (ab52939)
 Rabbit IgG Abcam (ab172730)
 AF488 anti-RAS Abcam(ab308532)
 Anti-RAS (G12V mutant) Abcam (ab313698)
 Anti- α -synuclein Abcam (ab212184)

Validation

All antibodies were validated by the respective manufacturers for their intended applications.

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)

SW480, HT29, H441, SK-N-SH cells cell lines were purchased from ATCC; LentiX HEK 293T cells were purchased from TaKaRa

Authentication

Purchased directly from ATCC

Mycoplasma contamination

Tested by ATCC.

Commonly misidentified lines
(See [ICLAC](#) register)

No commonly misidentified cell lines were used in this study.

Animals and other research organisms

Policy information about [studies involving animals; ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

Laboratory animals

CD1 athymic nude mice (Charles River Laboratory Crl:CD1-Foxn1nu) were purchased at 6-8 weeks old.

Wild animals

The study did not involve wild animals.

Reporting on sex	Sex was reported in the methods section.
Field-collected samples	The study did not involve samples collected from the field
Ethics oversight	All animal experiments and procedures were conducted in compliance with the guidelines approved by the Institutional Animal Care and Use Committee (IACUC) of Northwestern University. The approved animal study protocol number is IS00021267. Female athymic nude mice, aged 6–8 weeks, were obtained from Jackson Laboratories (USA). Animals were housed at Northwestern University's animal facility, which was maintained under controlled environmental conditions, including a 12-hour light/dark cycle (lights on at 07:00 and off at 19:00), a constant temperature of 22°C, and regulated humidity. Upon arrival the animals were allowed to acclimate to the facility environment 1 week before start of the experiment.

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

Plants

Seed stocks	Not applicable.
Novel plant genotypes	Not applicable.
Authentication	Not applicable.

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	For flow cytometry analysis, cells were dissociated using trypsin–EDTA, quenched with complete culture medium, and washed twice with phosphate-buffered saline (PBS). Cells were resuspended in PBS at a density of 1×10^6 cells mL ⁻¹ and passed through a 40-µm cell strainer to remove aggregates. Where indicated, cells were incubated with fluorescently labeled antibodies or isotype controls according to the manufacturer's instructions, followed by PBS washes prior to acquisition. Flow cytometry data were collected using standard forward- and side-scatter gating to exclude debris and doublets. Detailed materials information can be found in the methods section.
Instrument	BD FACSymphony S6 SORP system
Software	FlowJo v.10.0.7
Cell population abundance	At least 20,000 cells were collected for all flow cytometry experiments
Gating strategy	For flow cytometry analysis of cultured cells, dead cells and debris were gated out using an FSC-A vs SSC-A plot. Next, singlets were gated in as cells aligned on the major slope of an FSC-A vs FSC-H plot. Nano-biomolecular condensates' uptake was quantified using the geometric mean fluorescence intensity of this non-debris, singlet population.

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