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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 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 *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	ChemBioDraw Ultra 12.0, Microsoft PowerPoint 2016, AutoCAD 2017
Data analysis	COMSOL Multiphysics (v5.2), Microsoft Excel 2016, Graphpad Prism 8, ImageJ 1.44

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 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

Data supporting the findings of this study are available within the paper and its Supplementary Information files. The source data underlying Figs. 2d-g, 3a-b, d-e, 4d, 5b, 6d, 7a, c and Supplementary Figs 4, 5, 6, 7, 15, 16, 17, 20, 23, 24, 25, 26, 27, and 28 are provided as a Source Data file. The data that support the findings of this study are available from the corresponding author on request. Source data are provided with this paper.

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	The sample size (n) of each experiment is provided in the corresponding figure captions in the main manuscript and supplementary information files. Sample size choice was based on previous studies (Refs 10, 11, and 38), not predetermined by the statistical method. Small group size of 4 animals were chosen for in vivo studies based on the observation that statistically significant differences could be observed between treatment and control groups using this group size. The Institutional Animal Care and Use Committee (IACUC) at the University of Maryland, College Park requires minimum possible number of animals be used that yield statistically significant results.
Data exclusions	No data was excluded from the analyses.
Replication	All in vitro experiments were replicated independently for at least 3 times. In vivo sample size (n) in each group is detailed in the figure legends or methods section. All attempts at replication were successful.
Randomization	In the reported in vivo experiments, mice were randomly assigned to various groups.
Blinding	All data collection and all related analyses were not performed blind. We followed standard laboratory procedures of randomization. Each experiment was designed with proper controls, and samples for comparison were collected and analyzed under the same conditions.

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
☒	☐ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

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

Antibodies

Antibodies used	The following antibodies were used in this study. They are list as antigen first, followed by supplier, catalog number and dilution as application. 1) Anti-P-selectin antibody, ThermoFisher, cat: 701257, 1 : 100 for immunofluorescence staining. 2) Anti-mouse CD31 antibody, R&D systems, AF3628, 1 : 200 for immunofluorescence staining 3) Anti-P-Glycoprotein antibody, Sigma-Aldrich, P7965, 1 : 200 for immunofluorescence staining 4) Alexa Fluor 594 labeled secondary antibody, ThermoFisher, cat: A32744, 1 : 50 for immunofluorescence staining.
Validation	All antibodies were verified by the supplier. Anti-P-selectin antibody was validated in U2OS cells using a P-selectin recombinant rabbit monoclonal antibody (Product # 701257) followed by detection using an Alexa Fluor 488-conjugated goat anti-rabbit secondary antibody. Anti-mouse CD31 antibody was validated in immersion fixed bEnd.3 mouse endothelioma cell line using Goat Anti-Mouse/ Rat CD31/PECAM-1 Antigen Affinity-purified Polyclonal Antibody (Catalog # AF3628) at 10 µg/mL for 3 hours at room temperature. Anti-P-Glycoprotein antibody was validated with literature (Ma Q J, et al. Experimental and Therapeutic Medicine 7(3), 635-639, (2014); Jansson P J, et al. The Journal of Biological Chemistry , -, (2015))

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	NCI/ADR-RES and OVCAR-8 cell lines used in this work were purchased from the American Type Culture Collection (ATCC, Manassas, VA, USA). A2780ADR cell line was purchased from the Sigma-Aldrich (St. Louis, MO, USA). Human Umbilical Vein Endothelial Cells was purchased from Lonza (Alpharetta, GA).
Authentication	Authentication of A2780ADR and Human Umbilical Vein Endothelial Cells by the vendors was confirmed prior to their purchase. A2780ADR was authenticated with STR profiling (Amelogenin: X; CSF1PO: 10,11; D13S317: 13; D16S539: 11,14; D5S818: 11,12; D7S820: 10; THO1: 6; TPOX: 8,9; vWA: 15,16). Human Umbilical Vein Endothelial Cells was authenticated with double positive of CD31 and CD105. NCI/ADR-RES and OVCAR-8 cell was authenticated with STR profiling.
Mycoplasma contamination	The cell lines were tested with Universal Mycoplasma Detection Kit (ATCC #30-1012K) and confirmed free of mycoplasma contamination
Commonly misidentified lines (See ICLAC register)	NCI/ADR-RES cell line was originally thought to be a derivative of MCF-7 and and therefore named as MCF-7/ADR. This is an important cell line to study the multidrug resistance. Therefore, this cell line is included in this study.

Animals and other organisms

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

Laboratory animals	Athymic female NU/NU nude mice (6 weeks old) were purchased from Charles River (Wilmington, MA,USA) for in vivo studies.
Wild animals	The study did not involve wild animal.
Field-collected samples	The study did not involve samples collected from field.
Ethics oversight	All animal studies were conducted by following protocols approved by the Institutional Animal Care and Use Committee (IACUC) at University of Maryland, College Park, MD. The animal protocols are compliant with all relevant ethical regulations.

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	The NCI/RES-ADR, A2780ADR, and OVCAR-8 cells were incubated in medium containing various drug formulations for 6 h. After irradiated with laser for 1 min at 0.2 W cm-2 for FSCNO-DH+L group, all the groups were washed twice with PBS, detached, and fixed with 4% paraformaldehyde for 20 min at room temperature. The fixed cells were then washed twice and analyzed using a BD (Franklin Lakes, NJ, USA) Accuri C6 flow cytometer
Instrument	BD Accuri C6 flow cytometer
Software	BD Accuri C6 Software
Cell population abundance	Population abundance was determined by diluting all tissues samples to the same volume and then collecting samples for a fixed and consistent amount of time.
Gating strategy	All cells were selected except for the debris.

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