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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	Cell Proliferation data was collected using Incucyte Software. Living Image 4.5 was used for in vivo imaging. ASIPro VMTM software was used for PET
Data analysis	Prism7 Software was used for statistical analysis. LivingImage4.5 was used for image quantification of in vivo modeling. ASIPro VMTM software was used for PET analysis. Incucyte was utilized for cell proliferation assays.

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

Data availability: Source data for figures 1,3 and 4 as well as Extended figures 1,3-7 are provided in the online version of the paper.

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	Sample sizes were chosen based upon previous experience with the animal models. Or following convention of the methods. No power analysis was preformed for the design of these studies.
Data exclusions	No completed data were excluded from the experiments presented in this manuscript.
Replication	Data described in this manuscript were reliably reproduced. The PET imaging in figure one was only run twice and though similar observations were made visually there was a problem with the quantification due to a failure of the CT.
Randomization	As the diet arms needed to be kept together so that the animal feed for each group could be controled, cages were randomized to treatment groups rather than individual mice. Randomization occurred before tumor implantation.
Blinding	No blinding was used in these studies. The mouse diets prevented effective blinding of the animal work. Due to the composition of the ketogenic diet blinding was not possible for our animal studies as mice on different diets are readily identified.

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

Antibodies

Antibodies used	All of the antibodies used for western blotting have been extensively used in the literature for previous studies, and validation blots are shown in the product information sheets on the Cell Signaling or Abcam Websites. pINSR CST 3024S 15 1:1000 INSR CST #3025 8 1:1000 pAKT308 CST 9275L 5 1:1000 pAKT473 CST 9271S 14 1:1000 AKT CST 4691S 20 1:1000 pERK CST 9101S 29 1:1000 ERK CST 4695S 26 1:1000 pS6 CST 2215S 14 1:1000 S6 CST 2217S 7 1:1000 Actin Abcam ab6276 gr3185620-12 1:10000 IHC staining was validated and scored by a pathologist using the antibodies at the dilutions below. Ki67 (Abcam, ab16667) 1:500; cleaved caspase-3 (Asp175; 5A1E; Cell Signaling Technology, 9664) 1:200; phospho-INSR (Tyr 1162; Thermo Fisher #AHR0271) 1:100; phospho-AKT (Ser473; Cell Signaling Technology, 8101) 1:20; and phospho-S6 ribosomal protein (Ser235/236; Cell Signaling Technology, 2211) 1:300)
Validation	All of the antibodies used for western blotting have been extensively used in the literature for previous studies, and validation blots are shown in the product information sheets on the Cell Signaling or Abcam Website. IHC staining was validated and scored by a pathologist using the antibodies listed above.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	Cell lines were acquired from ATCC, or were provided for academic use from laboratories at columbia university. Speciffically The murine KPC cell lines came from the laboratory of Kenneth Olive. The AML cell lines from the lab of Siddhartha Mukherjee. Isogenic HCT116 and DLD-1 lines were obtained from Todd Waldman at Georgetown University.
Authentication	Human Cell lines were purchased from ATCC. No authentication was possible for the murine derived lines.
Mycoplasma contamination	Cell Lines tested negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	None of the cell lines in this paper on on the ICLAC list of commonly misidentified cell lines.

Animals and other organisms

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

Laboratory animals	PDX studies were preformed in female nude (inbred) mice from Jackson Labs (Foxn1 Nu). Allograft studies were preformed using C57bl/6j mice also from Jackson Labs. Allograft studies were conducted using both male and female mice, though they were not mixed within experiments. Mice were implanted at 8-12 weeks of age (age matched per study). Typically C57 Male mice in thes cohorts weighted between 24-30 grams. While c57 female mice weighted between 22-28 grams. Nude were typically 18-24 grams at time of tumor implantation.
Wild animals	No wild animals were used in these studies.
Field-collected samples	No field collected samples were used in these studies.