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Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form is intended for publication with all accepted life science papers and provides structure for consistency and transparency in reporting. Every life science submission will use this form; some list items might not apply to an individual manuscript, but all fields must be completed for clarity.

For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

Experimental design

1. Sample size

Describe how sample size was determined.

No sample size calculation was performed for animal studies. The number of animals assigned per condition was selected to provide sufficient statistical power to discern significant differences. This was based on prior experience with the model and based on several published manuscripts using these models.
In human studies, sample size was determined to detect a statistically significant difference in survival between patients in highest and lowest quantiles of plasma branched chain amino acids and body composition measurements by CT imaging.

2. Data exclusions

Describe any data exclusions.

Statistical outliers were calculated using Grubb's outlier test (Prism) and excluded from final analysis.
No patient data was excluded from the analysis.

3. Replication

Describe whether the experimental findings were reliably reproduced.

All attempts at replication were successful.

4. Randomization

Describe how samples/organisms/participants were allocated into experimental groups.

For diet studies in PDAC mice (Figure 3j-k, Figure S3e-i), PDAC mice were weighted and randomly assigned either a control diet or a diet supplemented with pancreatic enzymes. Animals were weighted to ensure similar starting body weights in both groups. For caloric restriction studies (Figure S3a-d), C57Bl/6J mice were injected with PDAC-derived cells to develop subcutaneous tumors. After tumors were palpable, tumor volume and mouse body weight were measured to ensure both groups of mice (control and calorically restricted) had similar starting tumor volume and body weight.
The study involving pancreatic cancer patients was observational, and therefore no randomization was performed. Experimental groups were defined by quantiles of plasma BCAAs and body composition measurements by CT imaging.

5. Blinding

Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

Animals were numbered and experiments conducted in a blinded manner. After data collection, genotypes were revealed and animals assigned to groups for analysis. For subcutaneous and orthotopic allograft tumor implantation, blinding of experiments was not feasible.
For the human studies, all collected data including exposure variables (plasma BCAAs and body composition measurements by CT imaging) were obtained with blinding to outcome data (patient survival).

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
☐	☒ A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ A statement indicating how many times each experiment was replicated
☐	☒ The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
☐	☒ A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☐	☒ The test results (e.g. *P* values) given as exact values whenever possible and with confidence intervals noted
☐	☒ A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
☐	☒ Clearly defined error bars

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.	GraphPad Prism, Excel, ImageJ, SAS

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* guidance for providing algorithms and software for publication provides further information on this topic.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.	All unique materials used are available from the authors.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	Antibodies recognizing pHSL (Ser563) (#4139) and total HSL (#4107) were purchased from Cell Signaling Technologies. pHSL had been validated in preliminary experiments where adipose tissue explants were treated with isoproterenol to induce lipolysis.

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.	Murine PDAC cell lines were isolated from tumor-bearing C57Bl/6J KP-/-C (Kras G12D; P53 fl/fl; Pdx1-cre) mice. Pancreatic stellate cells were isolated from wild-type C57Bl/6J mice. All cell lines utilized were mycoplasma free.
b. Describe the method of cell line authentication used.	Cell lines used were not authenticated.
c. Report whether the cell lines were tested for mycoplasma contamination.	All cell lines were tested and tested negative for Mycoplasma contamination.
d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.	No commonly misidentified cell lines were used in these studies.

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study.

All animals (Mus Musculus) used in this study were fully back-crossed to the C57Bl/6J background. Unless otherwise stated (Figure 1A-C), all animals were male. All experimental groups included age-matched litter-mate controls and animals were co-housed (unless otherwise stated, Figure S3a-d,f,h). For end-stage tissue weights in KP-/-C studies, animals were approximately 10-12 weeks of age (Figure 1A-C). For "early KP-/-C" studies, animals were 6 weeks of age (Fig 1a-c). For KC studies, animals were 15 weeks of age (Figure 1k-l, Figure S1m). For orthotopic and subcutaneous implantation studies (Figure 2a-f, Figure s3a-d), 10-12 week old male C57Bl/6J (Jackson mice, 000664) were utilized.

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.

This study included 782 pancreatic cancer patients who received care at five U.S. cancer centers: Dana-Farber/Brigham and Women's Cancer Center, Massachusetts General Hospital, Mayo Clinic, Stanford University, and University of North Carolina-Chapel Hill. Detailed demographic and clinical characteristics of those patients are shown in Supplementary Table 1.