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**Sample-size estimation**

* You should state whether an appropriate sample size was computed when the study was being designed
* You should state the statistical method of sample size computation and any required assumptions
* If no explicit power analysis was used, you should describe how you decided what sample (replicate) size (number) to use

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn’t apply to your submission:

No statistical method of sample size computation was used since there was no reasonable way to estimate the anticipated effect size. Rather, sample sizes were estimated based on similar experiments previously performed in the published papers. The sample sizes for the experiments are given in the figures or figure legends.

**Replicates**

* You should report how often each experiment was performed
* You should include a definition of biological versus technical replication
* The data obtained should be provided and sufficient information should be provided to indicate the number of independent biological and/or technical replicates
* If you encountered any outliers, you should describe how these were handled
* Criteria for exclusion/inclusion of data should be clearly stated
* High-throughput sequence data should be uploaded before submission, with a private link for reviewers provided (these are available from both GEO and ArrayExpress)

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Biological replicates are replicates on independent biological samples versus technical replicates that use the same starting samples. All experiments in this study were repeated using biological replicates. These information are mentioned in the ‘Materials and Methods’ section. The number of replicates is given in each figure legends. In the experiments using animals, data were excluded when the investigator noted a technical error had obviously affected the results (Figure 7A-B and D-E). Criteria for exclusion/inclusion of RNA-seq data are stated in the ‘Materials and Methods’ section.

**Statistical reporting**

* Statistical analysis methods should be described and justified
* Raw data should be presented in figures whenever informative to do so (typically when N per group is less than 10)
* For each experiment, you should identify the statistical tests used, exact values of N, definitions of center, methods of multiple test correction, and dispersion and precision measures (e.g., mean, median, SD, SEM, confidence intervals; and, for the major substantive results, a measure of effect size (e.g., Pearson's r, Cohen's d)
* Report exact p-values wherever possible alongside the summary statistics and 95% confidence intervals. These should be reported for all key questions and not only when the p-value is less than 0.05.

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Information for statistical analysis can be found in the ‘Materials and Methods’ section, figures, and figure legends. Raw data, exact p-values, and 95% confidence intervals are presented in the figures, figure legends, or separate source data files.

(For large datasets, or papers with a very large number of statistical tests, you may upload a single table file with tests, Ns, etc., with reference to sections in the manuscript.)

**Group allocation**

* Indicate how samples were allocated into experimental groups (in the case of clinical studies, please specify allocation to treatment method); if randomization was used, please also state if restricted randomization was applied
* Indicate if masking was used during group allocation, data collection and/or data analysis

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Not applicable.

**Additional data files (“source data”)**

* We encourage you to upload relevant additional data files, such as numerical data that are represented as a graph in a figure, or as a summary table
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* Include model definition files including the full list of parameters used
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Please indicate the figures or tables for which source data files have been provided:

Figure 1-source data 1; Excel file containing quantitative data for Figure 1.

Figure 2-source data 1; Excel file containing quantitative data for Figure 2.

Figure 3-source data 1; Excel file containing quantitative data for Figure 3.

Figure 4-source data 1; Excel file containing quantitative data for Figure 4.

Figure 5-source data 1; Excel file containing quantitative data for Figure 5.

Figure 6-source data 1; Excel file containing quantitative data for Figure 6.

Figure 7-source data 1; Excel file containing quantitative data for Figure 7.

Figure 7-source data 2; Excel file containing quantitative data for Figure 7.

Figure 2-figure supplement 1-source data 1; Excel file containing quantitative data for Figure 2-figure supplement 1.

Figure 2-figure supplement 2-source data 1; Excel file containing quantitative data for Figure 2-figure supplement 2.

Figure 2-figure supplement 3-source data 1; Excel file containing quantitative data for Figure 2-figure supplement 3.

Figure 3-figure supplement 1-source data 1; Excel file containing quantitative data for Figure 3-figure supplement 1.

Figure 3-figure supplement 2-source data 1; Excel file containing quantitative data for Figure 3-figure supplement 2.

Figure 4-figure supplement 1-source data 1; Excel file containing quantitative data for Figure 4-figure supplement 1.

Figure 6-figure supplement 1-source data 1; Excel file containing quantitative data for Figure 6-figure supplement 1.

Figure 7-figure supplement 1-source data 1; Excel file containing quantitative data for Figure 7-figure supplement 1.

Supplementary file 1 Table 1-source data 1; Excel file containing all 57 pancreatic ductal adenocarcinoma patients information.

Supplementary file 1 Table 2-source data 1; Excel file containing detailed description of mass spectrometry data.