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☐ Initial submission    ☐ Revised version    ☒ Final submission

# 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. | For mouse experiments, no statistical methods were used to predetermine sample size.

2. **Data exclusions**

   Describe any data exclusions. | No data were excluded.

3. **Replication**

   Describe whether the experimental findings were reliably reproduced. | All experiments were performed in two or three biological replicates, and independently reproduced as indicated in figure legends.

4. **Randomization**

   Describe how samples/organisms/participants were allocated into experimental groups. | For mouse experiments, the mice were not randomized.

5. **Blinding**

   Describe whether the investigators were blinded to group allocation during data collection and/or analysis. | For mouse experiments, the investigators performing tumour volume measurements were blinded.

   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 <u>exact sample size</u> (*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 <u>central tendency</u> (e.g. median, mean) and <u>variation</u> (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.

> Statistical analyses for all experiments were performed using GraphPad Prism 7.0a, except RNA-seq analysis which was performed using TopHat v2.0.6, CuffDiff v2.0.2, and pathway analysis with Ingenuity Pathway Analysis software as described in the Methods section.

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 materials used are commercially available except CRISPR-modified cell lines which are all available upon request.

### 9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).

> anti-GPX4 (rabbit) polyclonal Ab (Abcam, ab41787) and anti-β-Actin (mouse) mAb (Sigma, A5441) were validated in human cells by the manufacturers.

### 10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.

> BT474 (ATCC), PC9 (Sigma-Aldrich), Kuramochi (JCRB), A375 (ATCC) and MCF10A (ATCC).

b. Describe the method of cell line authentication used.

> STR fingerprint analysis

c. Report whether the cell lines were tested for mycoplasma contamination.

> All lines were tested and found to be negative for mycoplasma with MycoAlert (Lonza).

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.

> None are listed in this database.

## ▶ 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.

> Athymic female mice aged 10-12 weeks of average body weight 24 grams were used for the experiment in ED Fig 3h, and male mice aged of average body weight 25 grams were used in the experiment in Fig 4d/ED Fig 3g.

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.

> Not applicable.