

## Author Checklist

NCOMMS-24-72394B

Please check the items below carefully and add a response in each row of the table to indicate the changes that you have made. Please also check through any additional marked-up edits we may have provided within the manuscript file.

### Abstract and editor's summary

Our guidance:	Your response:
When discussing the current work in the abstract, please use the present tense.	We have changed the tense of the abstract to present

### Author information

Our guidance:	Your response:
We ask that you consult with your coauthors to ensure that all names, affiliations, and titles are represented correctly. Note that if any authors are added or removed after this point then all authors will be requested to provide approval documentation that could potentially delay the production of your paper.	We have confirmed with co-authors that names and affiliations are correct.
Ensure affiliations are appropriately labeled and featured sequentially and in ascending order (1,2,3,... or a,b,c...). Please ensure all corresponding authors are marked with a specific symbol and include their emails. Similarly, if you have “equally contributing” or “joint supervision” authors, use a specific symbol to mark them and not a number.	We have added affiliations with an appropriate numbering system. We have marked equal contributions with a symbol and included the email address of the corresponding author.
Please ensure the author contributions section mentions each author's initials at least once with their contributions to the work. Authors with the same initials must be differentiated in the statement.	We have added an author contributions section, and each author is listed at least once.

### Article structure

Our guidance:	Your response:
We can accommodate up to 10 display items (Figures or Tables) in the main article. Each Figure and Table must fit easily within an A4 page (210 x 297 mm). Please ensure that the number and size of your Figures and Tables fulfil these requirements to avoid any delay in the acceptance of your article.	We have 8 figures all spanning two columns. We have tested them to ensure that they fit comfortably onto an A4 page.
Ensure main Figures are uploaded as separate individual files. Each figure file must contain all intended panels labelled and displayed as intended and fit entirely on a single page. Do NOT include legends within the figure files, as these must be in the main manuscript.	Each figure with labels, but no legend, is being uploaded as a pdf.

Supplementary Figures must be all contained in the Supplementary Information PDF and do NOT need to be uploaded separately.	The supplementary figures are included with legends in a separate pdf
<b>To comply with this format and optimise the presentation of data in your Article, we suggest the following changes to the display items in your paper:</b>	
<p>Please go through the formatting instructions and examples at <a href="https://www.nature.com/documents/ncomms-formatting-instructions.pdf">https://www.nature.com/documents/ncomms-formatting-instructions.pdf</a> and make sure that your submission complies with all these requirements.</p> <p>In the Supplementary Information file and the main manuscript text, supplementary items must be labelled and cited using only the following formats: Supplementary Figure 1, Supplementary Table 1, Supplementary Methods, Supplementary Note 1, Supplementary Discussion, and Supplementary References. Please note the use of "Supplementary" and that we do not use the "S" prefix.</p>	We have changed Supp. Fig. S1 to Supplementary Figure 1
<b>Please ensure your main manuscript file includes the following sections, in this order:</b> <p>Title          Author list          Affiliations          Abstract          Introduction          Results          Discussion (optional)          Results and Discussion (optional)          Methods          Data Availability          Code Availability (if relevant)          References          Acknowledgements          Author Contributions Statement          Competing Interests Statement          Tables          Figure Legends/Captions (for main text figures)</p> <p>We do not edit Supplementary Information files; they will be uploaded with the published article as they are submitted with the final version of your manuscript. Any tracked changes should be removed from the file and the file should be provided as a PDF file.          Supplementary Figures do not need to be provided separately.</p> <p>Please supply Source Data files for all data presented in graphs within the Figures.</p>	<p>We have edited the main manuscript to include these sections in the proper order</p> <p>We have created a separate Supplementary File for the Supplementary Figure legends</p> <p>All tracked changes have been removed from the supplementary information file and it has been uploaded as a pdf</p> <p>We have included Source Data files for all graphs in the main manuscript and in the supplementary figures.</p>
<p>Within the Source Data file, the relevant raw data from each figure or table (in the main manuscript and in the Supplementary Information) should be represented by a single sheet in an Excel document, or a single .txt file or other file type in a zipped folder. An example of the Source Data file is available demonstrating the correct format:</p> <p><a href="https://www.nature.com/documents/ncomms-example-source-data.xlsx">https://www.nature.com/documents/ncomms-example-source-data.xlsx</a></p> <p>The file should be labelled 'Source Data', with the title and a brief description included in your response here, and should be mentioned in all relevant figure legends using the template text below:</p> <p>'Source data are provided as a Source Data file.'</p> <p>A reference to the source data file should be added in the 'Data Availability' section, using the text "Source data are provided with this paper."</p>	<p>We have provided Source Data files as tab delimited text files labeled with the figure panel the data correspond to. Each file has a text header describing the data and the corresponding figure. We have zipped these files into a single file called Source_Data.zip</p> <p>Each figure legend now includes a statement indicating which file contains the data for the figure.</p> <p>There is a statement in the Data Availability section describing the Source Data file and how to access it</p>

## Main text

Our guidance:

Your response:

Please refrain from using words such as new/novel/first, when referring to the scientific findings. Please also remove exaggerated language such as 'extremely'/outstanding'	We have confirmed that we have not used exaggerated language
A full Methods section, divided into subsections and subheadings, must be provided in the main manuscript. There is no word limit to this section.	We have moved the Methods section to the main manuscript
Please ensure that gene and protein names are formatted according to community standards for the organism in question. Italicize gene symbols and functionally defined locus symbols; do not use italics for proteins.	We have checked all gene names for proper formatting
Please do not use italics, bold font, underlining or speech marks/quotations marks except in headings unless required for technical terms (in both the main text and the display items).	We have removed italics on non-technical terms. We have removed quotation marks
Please make sure that mathematical terms throughout your manuscript and Supplementary Information (including in figures, figure axes, and legends) conform strictly to the following guidelines. Equations must be supplied in editable format, and not as images. Scalar variables (e.g. x, V, $\chi$ ) must be typeset in italic, whereas multi-letter variables and functions (e.g. log) must be formatted in roman. Vectors (such as the wavevector k or the magnetic field vector B) must be typeset in bold without italics.	We have checked through the math notation to confirm alignment with guidelines.
Please use italics for species names, both in the main text and the display items.	There are two instances of a species name, and they are italicized.

## Figures and Tables

Our guidance:

Your response:

Please see the guidelines linked below for detailed instructions about how your figures should be prepared. Following these instructions will reduce the chances of delays should we need to request replacement artwork from you at a later stage.  <a href="https://www.nature.com/documents/NRJs-guide-to-preparing-final-artwork.pdf">https://www.nature.com/documents/NRJs-guide-to-preparing-final-artwork.pdf</a>	We have reviewed the figure guidelines.
Wherever statistics have been derived (e.g. error bars, box plots, statistical significance) the legend needs to provide and define the n number (i.e. the sample size used to derive statistics) as a precise value (not a range). Please define how many replicates were performed and whether they are biological (derived from different experimental units or subjects) or technical (multiple contemporary measurements from the same experimental unit or subject). Samples should be unambiguously described, including a clear definition of the unit of study. In studies using model organisms, cell lines, primary cell cultures, plants or micro-organisms, the unit of study is the smallest object that could be randomly and independently assigned to an intervention. The groups being compared, including control groups, should be clearly defined. If no control group has been used, the rationale for this should be stated. Please ensure there are enough details about sample collection to distinguish between independent data points and technical replicates- splitting a biological sample into 3 tubes or wells receiving the same treatment does not constitute independent replication.  We strongly discourage deriving statistics from technical replicates or less than 3 biological replicates, unless there is a clear scientific justification for why providing this information is important. Conflating technical and biological variability, e.g., by pooling technically replicates samples across independent experiments is strongly discouraged.	For all box plots, the n in each group is indicated either in the legend or in the figure and referred to in the legend.  No statistics have been derived from fewer than 3 biological replicates.  One of our downloaded data sets used technical replicates. This is a peripheral result, and we used an appropriate statistical test for this design (linear mixed model).
<b>Please note that this information is missing in the legend(s) of figure(s) 1C, F; 2A; 8A-D.</b>	We have added the number of individuals to Figures 1, 2, and 8.
All error bars need to be defined in the legends (e.g. SD, SEM) together with a measure of centre (e.g. mean, median). For example, the legends should state something along the lines of "Data are presented as mean values +/- SEM" as appropriate. All box plots need to be defined in the legends in terms of minima, maxima, centre, bounds of box and whiskers and percentile.  <b>Please note that the measure of centre for the error bars/error bands needs to be defined in the legend(s) of figure(s) 1F; 7B.</b>  <b>Please note that the box plots need to be defined in terms of minima, maxima,</b>	Fig 1F: centers are heritability and bands are standard error. 7B/C: centers are the mean of the rank Z normalized body weight and bands are the standard deviation. These are noted in the legend.  We have added descriptions of the features of the box plots to the legends of figures 1C, 2A, and 8A-D.

<b>centre, bounds of box and whiskers and percentile in the legend(s) of figure(s) 1C; 2A; 8A-D.</b>	
The figure legends must indicate the statistical test used. Where appropriate, please indicate in the figure legends whether the statistical tests were one-sided or two-sided and whether adjustments were made for multiple comparisons. For null hypothesis testing, please indicate the test statistic (e.g. F, t, r) with confidence intervals, effect sizes, degrees of freedom and P values noted. Please provide the test results (e.g. P values) as exact values whenever possible and with confidence intervals noted.	We have added text to figure legends with statistics to indicate the statistical test used, the test statistic, confidence intervals, degrees of freedom and p values. We have also indicated whether corrections for multiple testing were used.
<b>Please indicate the statistical test used for data analysis and where appropriate, please specify whether it was one-sided or two-sided and whether adjustments were made for multiple comparisons, in the legend(s) of figure(s) 1C-E; 4E; 8D.</b>	
<b>Please note that the information on whether the statistical test used was one-sided or two-sided, where appropriate, is missing in the legend(s) of figure(s) 2B-C; 4E; 5A-C.</b>	
Shadings or symbols in graphs must be defined in some fashion. We prefer that you use a key within the image; do not include colored symbols in the legend/caption.	There are no colored symbols in any figure legends
Any abbreviations, symbols or colours present in your figures must be defined in the associated legends.	We have verified that all symbols and colors are defined in the legends
Please provide main figures as individual files (one file per figure) without embedded legends. Legends should be provided at the end of the main manuscript text only. The figure files should only contain the parts of the figure that should be reproduced in the final paper. Please do not include labels such as 'Figure 1' that you do not wish to appear in the HTML/PDF version.	We have provided individual files corresponding to each figure as it should be printed.

## Data and Code

Our guidance:

Your response:

Nature journals strongly support public availability of data and code. Please deposit the data and code used in your paper into a public data repository, or alternatively, present the data as Supplementary Information. If data can only be shared on request, please explain why in your Data Availability Statement, and also in the correspondence with your editor.	All data have been deposited in public repositories. Source data for figures are supplied in the file Source_Data.zip. Access to all data is described in the Data Availability section
Please note that for some data types, deposition in a public repository is mandatory. Any restrictions on sharing of these data types must be clearly indicated in the statement and discussed with the editor. More information on our data deposition policies and available repositories can be found here: <a href="https://www.nature.com/nature-research/editorial-policies/reporting-standards#availability-of-data">https://www.nature.com/nature-research/editorial-policies/reporting-standards#availability-of-data</a>	
All published manuscripts reporting original research in Nature Portfolio journals must include a data availability statement, within the Methods and under the heading 'Data Availability'.  The data availability statement must make the conditions of access to the "minimum dataset" that are necessary to interpret, verify and extend the research in the article, transparent to readers. We ask that you don't use phrases like 'available on reasonable request' but instead specify any restrictions to accessing your data as described below.	All data have been made freely available and access is described in the Data Availability section
This minimum dataset may be provided through deposition in public community/discipline-specific repositories, custom proprietary repositories or general repositories like Figshare, Zenodo and Dryad. Providing large datasets in supplementary information is strongly discouraged and the preferred approach is to make data available in repositories. Please see <a href="https://www.springernature.com/gp/authors/research-data-policy/recommended-repositories">https://www.springernature.com/gp/authors/research-data-policy/recommended-repositories</a> for a list of recommended repositories.  If DOIs are provided, we also strongly encourage including these in the Reference list	We have added citations in the reference list for all DOIs

<p>(authors, title, publisher (repository name), identifier, year).</p> <p>The Data Availability Statement should also reference any source data published alongside the paper.</p> <p>For clinical datasets or third party data, please ensure that the Data Availability statement adheres to our policy (<a href="https://www.nature.com/nature-research/editorial-policies/reporting-standards#availability-of-data">https://www.nature.com/nature-research/editorial-policies/reporting-standards#availability-of-data</a>)</p> <p>If data are unavailable, please indicate the exact reasons why data cannot be made available in a suitable public repository or upon request, including any conditions related to ethical approval, consent from study subjects, commercial or legal restrictions, etc.</p> <p>For data that are available under restricted access, the Data Availability statement must specify</p> <ul style="list-style-type: none"> <li>- the reasons for access restrictions</li> <li>- what the restrictions are</li> <li>- how one can get access to the data</li> <li>- who to contact to request access</li> <li>- any restrictions on who the data can be made available to or for which purpose</li> <li>- the expected timeframe for response to access requests</li> <li>- for how long the data will be available once access has been granted.</li> </ul>	<p>The Data Availability Statement references the Source Data file</p> <p>There are no clinical data sets associated with this manuscript</p> <p>No data are unavailable</p> <p>There are no restrictions on data access</p>
<p>Please use the following template to provide all the information stated above:</p> <p>The XX data generated in this study have been deposited in the YY database under accession code ZZ [add hyperlink here]. The XX data are available under restricted access for {insert reason}, access can be obtained by {explain how}. The raw XX data are protected and are not available due to data privacy laws. The processed XX data are available at YY. The XX data generated in this study are provided in the Supplementary Information/Source Data file. The XX data used in this study are available in the YY database under accession code ZZ [Add hyperlink here].</p>	<p>We have ensured that all information relevant in the template is included in the Data Availability section</p>
<p>Please be sure to include the final version of your reporting summary in your submission as a supplementary information file. The reporting summary will be published alongside the paper. Please note that this form is a dynamic 'smart pdf' and must therefore be downloaded and completed in Adobe Reader, instead of opening it in a web browser</p>	<p>We have provided a reporting summary with our submission</p>
<p>Please ensure that all DNA sequencing or RNA-seq data is deposited in an approved, publicly accessible repository listed here (<a href="https://www.nature.com/nature-research/editorial-policies/reporting-standards#availability-of-data">https://www.nature.com/nature-research/editorial-policies/reporting-standards#availability-of-data</a>), and that relevant accession codes are stated in the data availability statement.</p>	<p>Gene expression and RNA-Seq have been deposited in the Gene Expression Omnibus and the Sequence Read Archive. The accession codes are stated.</p>
<p>Please ensure that all accession codes used in this study (new ones as well as previously published ones) are listed in the Data Availability statement, together with their corresponding hyperlink. Use precisely the following formats to ensure that the links are permanent:</p> <p>CODE [hyperlink] (description if necessary)</p> <p>Use full DOI hyperlinks [<a href="http://doi.org/xxxxx">http://doi.org/xxxxx</a>] whenever possible.</p> <p>Example for the GEO entries:</p> <p>GSE151664 [<a href="https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE151664">https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE151664</a>] (CRAC datasets of Get4-HTP and the wild type yeast control)</p>	<p>We have added hyperlinks for all accession numbers</p>

## Methods

Our guidance:

The Methods must include a "Statistics & Reproducibility" section with general information on study design, how the statistical analyses of the data were conducted and general information on the reproducibility of experiments. Please include statements on how sample sizes were chosen, on whether any data were excluded (including why), whether randomization and blinding was used. If statements are negative please include the

Your response:

We have added a Statistics and Reproducibility section at the beginning of the Materials and Methods section.

following statements: "No statistical method was used to predetermine sample size. "No data were excluded from the analyses"; "The experiments were not randomized"; "The Investigators were not blinded to allocation during experiments and outcome assessment".	
<p>For animal studies, indicate the species, strain (including substrain), sex, number and age of animals in every experiment. In the Reporting Summary and Methods, confirm that the study received ethical approval, naming the organization that approved the study and indicating the protocol number where applicable. Alternatively, explain why ethical approval was not required.</p> <p>The Reporting Summary and Methods should also include whether sex was considered in the study design and analysis and if not clarify why.</p> <p>Data should be reported disaggregated for sex where this information has been collected; disaggregated numbers for individual experiments must be provided in the source data as appropriate whereas overall numbers may be provided in the methods section and Nature Portfolio Reporting Summary.</p> <p>For more information please see <a href="https://www.nature.com/articles/s41467-022-30398-1">https://www.nature.com/articles/s41467-022-30398-1</a></p>	<p>We have verified that all this information is included in the manuscript</p> <p>We have reported numbers of males and females</p>
Please include your Methods section in the main manuscript file rather than as a separate document.	We have moved the Methods to the main manuscript file
Sufficient details of the experiments must be provided in the Methods section such that they could be reproduced without reference to published papers. Use of the term "as described previously" is not encouraged.	We reference previous publications, but also describe methods thoroughly enough here for reproduction
Sequences of oligonucleotides (e.g. primers, RNAi, Crispr), or company names and catalog numbers if reagents are commercial, should be provided in the Methods. If this information is lengthy, it may be provided in Excel format, as separate Supplementary Data, mentioning the file in the Methods.	We have confirmed that all catalog information is provided
Centrifugation speeds must be reported in x g.	We have changed RPM to g
<p>Please ensure that all accession codes used in this study (new ones AND previously published ones) are listed in the Data Availability statement, together with their corresponding hyperlink. Use precisely the following format to ensure that the links are permanent:</p> <p>CODE [hyperlink] (description if necessary)</p> <p>Use full DOI hyperlinks [<a href="http://doi.org/xxxxx">http://doi.org/xxxxx</a>] whenever possible.</p> <p>For example:</p> <p>5XRN [<a href="http://doi.org/10.2210/pdb5XRN/pdb">http://doi.org/10.2210/pdb5XRN/pdb</a>]</p> <p>1483958 [<a href="https://doi.org/10.5517/ccdc.csd.cc1lt5m6">https://doi.org/10.5517/ccdc.csd.cc1lt5m6</a>]</p> <p>SRP109982 [<a href="https://www.ncbi.nlm.nih.gov/sra/?term=SRP109982">https://www.ncbi.nlm.nih.gov/sra/?term=SRP109982</a>]</p> <p>GSE101099 [<a href="https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE101099">https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE101099</a>]</p> <p>NQLW00000000 [<a href="https://www.ncbi.nlm.nih.gov/assembly/GCA_002312845.1/">https://www.ncbi.nlm.nih.gov/assembly/GCA_002312845.1/</a>]</p> <p>PXD016640 [<a href="http://proteomecentral.proteomexchange.org/cgi/GetDataset?ID=PXD016640">http://proteomecentral.proteomexchange.org/cgi/GetDataset?ID=PXD016640</a>]</p> <p>EMD-10857 [<a href="https://www.ebi.ac.uk/pdbe/entry/emdb/EMD-10857">https://www.ebi.ac.uk/pdbe/entry/emdb/EMD-10857</a>]</p> <p>BMRB 28095 [<a href="https://dx.doi.org/10.13018/BMRB28095">https://dx.doi.org/10.13018/BMRB28095</a>]</p>	We have verified that all data used in the manuscript are listed in the Data Availability statement with hyperlinks

## End matter

Our guidance:

Your response:

Please supply an "Author Contributions" section after the "Acknowledgements" section that refers to all authors. For more information on the Author Contributions statement, please refer to our authorship policy( <a href="https://www.nature.com/nature-research/editorial-policies/authorship">https://www.nature.com/nature-research/editorial-policies/authorship</a> ), and to the following Nature Editorial: <a href="https://www.nature.com/articles/4581078a">https://www.nature.com/articles/4581078a</a> .	We have added an author contribution statement after the acknowledgements.
Please thoroughly review our policy on Competing Interests ( <a href="http://www.nature.com/authors/policies/competing.html">http://www.nature.com/authors/policies/competing.html</a> ) and include a detailed statement in your final manuscript file, and in our manuscript tracking system. Please ensure the	We have added a competing interests statement

<p>statements are identical in both. Be specific about how each point stated relates to the research, list applicable author initials, and/or patent numbers. If there are no competing interests, a negative statement ("The authors declare no competing interests") must be included.</p>	<p>No authors have any competing statements. This is now indicated.</p>
<p>Nature Portfolio defines Competing Interest (CI) as financial and non-financial interests (including but not limited to funding, employment, stocks, shares, patents, personal or professional relationships with individuals or institutions, and unpaid membership advocacy) that could be perceived to directly undermine the objectivity, integrity, and value of a publication, or could be seen as having an influence on the judgments and actions of authors with regard to objective data presentation, analysis, and interpretation.</p> <p>Please thoroughly review our policy on Competing Interests and include a detailed statement both in your final manuscript file and in our manuscript tracking system. Please ensure the statements are identical in both. Be specific about how each point stated relates to the research and list applicable author initials, and/or patent numbers.</p> <p>If there are no competing interests, a negative statement must be included.</p> <p><a href="https://www.nature.com/nature-research/editorial-policies/competing-interests">https://www.nature.com/nature-research/editorial-policies/competing-interests</a></p>	<p>We have included a negative statement relating to competing interests</p>
<p>Please confirm that all relevant funding awarded to each author is described in the Acknowledgements section. List each grant number, followed by the initials of the author who received it.</p>	<p>All relevant grants have been reported with grant numbers where relevant.</p>

## Additional Revisions

Our Guidance:	Your Response:
<p>For any Supplementary Figures, please check and confirm that:</p> <ul style="list-style-type: none"> <li>* If data is presented as bar charts, individual data points are shown using overlaid dot plots.</li> <li>* The n number (i.e. the sample size used to derive statistics) is provided and defined as a precise value (not a range), using the wording "n=X samples/cells/independent experiments" etc. where applicable.</li> <li>* Any chart axis, error bars, scale bars, molecular weight markers, symbols and colour scales are defined.</li> <li>* Any statistical tests used for data analysis are specified and exact p-values are provided either on the figures themselves, in the legend or in the Source Data file.</li> <li>* Wherever representative data such as blots or micrographs are shown, the legend indicates how many times the experiment was repeated with similar results.</li> <li>* Full uncropped scans of any cropped gel/blot images are provided as an additional Supplementary Figure or in the Source Data file.</li> </ul>	<p>There are no bar charts representing multiple data points</p> <p>No statistical tests were performed in the supplementary figures</p> <p>All axes, bars, and colors are defined</p> <p>There are no blots or micrographs</p>

## Preparing your manuscript files

Our guidance:	Your response:
<p>Unless otherwise stated please limit individual file sizes to approximately 30MB. We strongly encourage the use of repositories for large datasets or source data due to size considerations.</p>	<p>The required source data file is ~566 Mb. We have added it to Figshare</p>
<p>Please supply a brief (maximum 250 characters, including spaces) summary of the main findings of the paper to be used on our website and in our e-alerts. The summary should be written in the third person in language suitable for a broad audience. The summary may be edited by the editors prior to publication. Please provide this summary in your cover letter.</p>	<p>We have supplied a 250-character summary in our cover letter.</p>
<p>Large datasets exceeding an A4 page size should be supplied as Supplementary Data files to allow reuse, not Supplementary Tables.</p>	<p>All tables larger than a sheet of paper have been supplied as data files</p>
<p>Please supply the main manuscript file in either Microsoft Word or LaTeX format</p>	<p>We have supplied the manuscript in LaTeX format</p>

<p>Please provide figures as individual vector files with editable text. Acceptable file types for figures are .ai, .eps, .pdf, .ppt or Chem Draw for fully editable vector-based art. For detailed guidance on figure preparation, see <a href="https://www.nature.com/documents/aj-artworkguidelines.pdf">https://www.nature.com/documents/aj-artworkguidelines.pdf</a></p>	<p>All figures are supplied as vector files with editable text.</p>
<p>Please note that all Supplementary Information must be provided as a single separate PDF file, not within the manuscript file.</p> <p>All Supplementary Information items (e.g. Supplementary Figures, Supplementary Tables, Supplementary Methods, Supplementary Notes, Supplementary Discussion, Supplementary References) must be included in one PDF document. Please refer to our formatting guide when preparing your supplementary information file:  <a href="https://www.nature.com/documents/ncomms-formatting-instructions.pdf">https://www.nature.com/documents/ncomms-formatting-instructions.pdf</a></p>	<p>The Supplementary information is provided as a single pdf</p>
<p>All Supplementary Information files (e.g. Supplementary Data, Supplementary Software, etc.) must be cited in the main text.</p> <p>Every Supplementary Figure must be accompanied by a legend of up to 350 words, referring to all panels, and a brief title that summarises the whole figure.</p>	<p>We have verified that all supplementary information is cited in the main text</p>
<p>Only Supplementary Movie, Audio, Data and Software files should be submitted separately from the Supplementary Information.</p>	
<p>The use or adaptation of previously published images is strongly discouraged. If this is unavoidable, please request the necessary rights documentation to re-use such material from the relevant copyright holders and return this to us when you submit your revised manuscript. Please check whether your manuscript or Supplementary Information contain third-party images, such as figures from the literature, stock photos, clip art or commercial satellite and map data.</p>	<p>Not reproducing published images, putting in images in accordance with documentation of Pathview</p>
<p>If any elements of your submitted work have been created with BioRender you will need to ensure you have obtained a publication license from BioRender, adhering to the user requirements as outlined within the license. The reference for BioRender created graphics should be present in the accompanying legend of the display material it is present in.</p>	<p>Biorender was not used</p>
<p>A copy of the publication license should be uploaded to our system as a related manuscript file upon resubmission.</p>	
<p>For more information please see the BioRender knowledge article here:  <a href="https://help.biorender.com/hc/en-gb/articles/21283116932765-CC-BY-publishing-and-reader-permissions">https://help.biorender.com/hc/en-gb/articles/21283116932765-CC-BY-publishing-and-reader-permissions</a></p>	
<p>For more information on what constitutes ownership by a third party, please contact our Editorial Assistant at <a href="mailto:naturecommunications@nature.com">naturecommunications@nature.com</a></p>	
<p>Please check in particular:</p>	
<p><b>Please note that suspected third party content is present in figure Supplementary fig 6.</b></p>	<p>Figure 6 was generated entirely with the R package pathview</p>

## Forms to complete

Our guidance:

Your response:

<p><b>Editorial Policy Checklist</b></p>	
<p>Please update and upload a final version of the Editorial Policy Checklist with your revised manuscript files. A blank Editorial Policy Checklist can be found via the link below. Note that this form is a dynamic 'smart pdf' and must be downloaded and completed in Adobe Reader.</p> <p>Please update your current checklist or download from:</p>	<p>We have uploaded an updated version of the Editorial Policy Checklist</p>

<https://www.nature.com/documents/nr-editorial-policy-checklist.pdf>

**Reporting Summary**

Please revise the Reporting Summary according to the requests below. After making the requested changes, please be sure to include the final version of your Reporting Summary in your submission as a supplementary information file. Please note that this form is a dynamic 'smart pdf' and must therefore be downloaded and completed in Adobe Reader, instead of opening it in a web browser.

Please update your current checklist or download from:

<https://www.nature.com/documents/nr-reporting-summary.pdf>

We have updated and uploaded the reporting summary

## Reporting Summary

Our guidance:

Your response:

General Instructions	
Please mention the last updated date in 'Last updated by author(s):' section.	We have added the date to this section
Software	
Please ensure all the data collection/data analysis software/tools/algorithms/packages used in the study are clearly mentioned in the manuscript and are also listed in the reporting summary (with version numbers).	All tools are listed with version numbers
Code	
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