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Corresponding author(s): Antonella Bongiovanni

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Reporting Summary

Nature Portfolio 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 Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the 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
☐	☒ A statement on 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 statistical parameters 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

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	LAS X Leica software,
Data analysis	GraphPad software, NanoSight Software NTA 3.1 Build 3.1.46, macromedia Firework software, ImageJ 1.52t

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 and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio 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 description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

All data supporting the findings of this study are available within the paper and its Supplementary Information. All raw data evaluated and used in Figures 1-8 and Supplementary Figures 1-10 are available in the file Supplementary 1_RawData available and Supplementary 2_RawData on figshare repository (https://figshare.com/s/3359ba02cdeea1d9d881); the uncropped and unedited gel images supporting Figure 1f is also available in supplementary Figure 11. Further

information and requests for resources and reagents should be directed to and will be fulfilled by the lead contact, Antonella Bongiovanni (antonella.bongiovanni@cnr.it).

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	The Sex and Gender Equity in Research was ensured following the SAGER guidelines. Specifically, blood samples for the basotest tests were obtained from randomly selected volunteers. In this study, we enrolled 1 man and 2 women. The ethical committee authorization number was disclosed in the supplementary section. Additionally, the volunteers signed an informed consent. The THP-1 human cell line used for the antioxidant studies are commercially available immortalized cells derived from the peripheral blood of a 1 year old male with acute monocytic leukaemia (ATCC # TIB-202).
Reporting on race, ethnicity, or other socially relevant groupings	No data or analyses were conducted based on race and/or ethnicity
Population characteristics	Blood samples for the basotest tests were obtained from randomly selected volunteers. In this study, we enrolled 1 man and 2 women.
Recruitment	Randomly selected volunteers
Ethics oversight	The volunteers participating in the ex vivo assays were formally informed that their data would be treated confidentially and used exclusively for scientific publication with no reference to donors.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is 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/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	No statistical method was used to predetermine cell and C.elegans sample sizes, but our sample sizes were similar to those reported in previous publications. Sample size was determined to be adequate based on the magnitude and consistency of measurable differences between groups. For studies in mouse models, sample sizes was set using G*Power software, v 3.1.9.2 (Faul, F., et al., (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior Research Methods, 39, 175-191). For our studies, using 70% power and 90% confidence, 25-50% practical difference and 20% coefficient of variation, a number of 4-6 gender-balanced, adult animals per group (untreated vs. treated groups) was sufficient.
Data exclusions	No data were excluded
Replication	To verify the reproducibility of our findings, experiments were performed using at least two biological replicates, unless clearly stated otherwise in the figure legends. All attempts at replication were successful.
Randomization	For the in vivo experiments, mice were randomly allocated to experimental groups. For the remaining studies, randomization for different experimental groups was not relevant as they were performed on uniform biological material, i.e. cell lines procured from commercial sources. C.elegans animals have been divided by simple randomisation, since all animals originate from one plate with thousands of animals that are isogenic and clonal siblings from self-fertilizing homozygous hermaphrodite.
Blinding	Blinding was not relevant to this study because no bias could be made by the subject or the tester in the experiments performed. For instance, we performed a blind quantification when the pgst-4::GFP expression in C.elegans animals was evaluated by ImageJ software, that provides unbiased data analysis.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☐	☒ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used

All antibodies used in this study are detailed in material and methods and Supplementary informations sections. More specifically:

H+ATPase - Plasma Membrane H+ATPase (Rabbit antibody). Agrisera AS07 (https://www.agrisera.com/cgi-bin/ibutik/SkapaFaktura.pl?SkrivPDF=J&funk=visa_artikel&artgrp=43&Friendly_Grupp=&Friendly=hatpase-plasma-membrane-hatpase&Sprak=EN&skrivpdf=j&artnr=AS07%20260);

Alix (clone 3A9): sc-53538. (Santa Cruz https://datasheets.scbt.com/sc-53538.pdf);

beta-actin (clone 10-B3): Sigma Aldrich (https://www.sigmaaldrich.com/IT/en/product/sigma/a0480);

CD63 clone MX- 49.129.5: Santa Cruz (https://be.vwr.com/store/product/fr/20388913/anti-cd63-mouse-monoclonal-antibody-hrp-clone-mx-49-129-5);

LAMP1 clone 1D4B, Sigma-Aldrich (https://www.sigmaaldrich.com/IT/it/product/mm/mabc39);

Calnexin clone NB100-1965, Novus Biologicals

Validation

All antibodies are commercially available and were commercially validated (see website links).

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

1–7 HB2, a normal mammary epithelial (ECACC #10081201) - https://www.culturecollections.org.uk/products/celllines/generalcell/detail.jsp?refId=10081201&collection=ecacc_gc#:~:text=1%2D7HB2%20is%20a%20clonal,using%20the%20SV40%20T%20antigen.

MDA-MB 231, an epithelial human breast (ECACC #92020424) - https://www.culturecollections.org.uk/products/celllines/generalcell/detail.jsp?refId=92020424&collection=ecacc_gc

THP-1 human monocytic leukemia cell lines (ECACC 88081201) - https://www.culturecollections.org.uk/products/celllines/generalcell/detail.jsp?refId=88081201&collection=ecacc_gc

Authentication

These commercially available cell lines were used at low passage number after purchasing at ECACC. None of the cell lines used were authenticated

Mycoplasma contamination

Cell lines used were monthly tested for mycoplasma contamination

Commonly misidentified lines
(See ICLAC register)

No misidentified lines were used

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals

6-weeks old wild type BALB/c and athymic nude mice, male and female, were purchased from Janvier Labs (France). Mice were housed in specific pathogen-free conditions with food and water were provided ad libitum. Housing conditions entailed a 12:12 light:dark cycle, room temperature at 20±2°C°, and 70% relative humidity. Mice were acclimatized for one week and were regularly handled by personnel for gentling and habituating to the procedures. On the day of the experiment, male and female animals were randomly allocated into 3 different treatment groups. C.elegans invertebrate animals were obtained from CGC stock center or from two laboratories and maintained as previously reported (Brenner et al, 1974).

Wild animals

No wild animals were used

Reporting on sex	For the biocompatibility study, groups contained 2 male and 2 female BALB/c mice (n1=4); for the biodistribution study, groups consisted of 3 male and 3 female athymic nude mice (n2=6). Each group received a different treatment. The results were presented as mean ± standard deviation (SD). Multiple comparisons between the groups were performed using GraphPad software. C.elegans self-fertilizing hermaphrodites were used in all experiments.
Field-collected samples	The study did not involve field collected samples
Ethics oversight	Animals were used in accordance with Cellvax approved standard operation procedures and with all national or local guidelines and regulations, and in compliance with the Federation of European Laboratory Animal Science Association (FELASA) guidelines. All experiments with C.elegans invertebrate animals comply with ARRIVE guidelines and the U.K. Animals (Scientific Procedures) Act, 1986 and associated guidelines and with EU Directive 2010/63/EU for animal experiments.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Plants

Seed stocks	The study did not involve seed stocks
Novel plant genotypes	The study did not involve novel plant
Authentication	The study did not involve plant