

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
<i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i> |
| ☐ | ☒ 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
<i>Give P values as exact values whenever suitable.</i> |
| ☒ | ☐ 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 The absorbance measurements were performed using the Synergy HTX (BioTek) multimode plate reader with Gen5 software (version 2.09). Fly walking was measured using the Zebrafish tracking system (ViewPoint) with ZebraLab software (version 5.18.0.0). qPCR was performed on a q225 qPCR System (version 3.18.7.404) from Quantagene (Kubo Technology). Immunoblotting detection was performed using ChemiDoc MP Imaging system (Bio-Rad) with Image Lab software (version 6.1). Quantification of Dilp2 staining intensities in the brain IPCs were performed using ZEN software (version 2.3). The sucrose density gradients were fractionated using the Gradient Profiler (BioComp Instruments) with FlowCell software (version 2.40).

Data analysis Original codes for TOP mRNA, mRNA-seq, monosome-seq, and polysome-seq data analyses are publicly available at Zenodo (<https://doi.org/10.5281/zenodo.21473950>). Statistical significance was determined in GraphPad Prism (version 9.5.1). Cox proportional hazard analysis was performed using JMP Pro (version 17.1.0). Densitometric analysis of blot images was carried out using ImageJ (version 1.52a). Regular RNA-seq data analyses involved fastp (version 0.20.1), HISAT2 (version 2.2.1.0), HTSeq-count (version 0.9.1), R (version 3.2.0), and DESeq2 (version 1.20.0). Translational analyses involved fastp (version 0.23.2), Bowtie2 (version 2.3.4.1), STAR (version 2.2.1), featureCounts (version 1.6.0), R (versions 4.2.0), DESeq2 (version 1.52.0), and Cluster Profiler (version 4.10.1); TOP motif analyses additionally used ggseqlogo (version 0.2). Label-free quantification of MS data was carried out in MSFragger (version 3.4). Metabolomic data acquisition and chromatographic peak integration were performed using MultiQuant (version 3.0.3).

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 relevant datasets generated in this work are publicly available. Regular RNA-seq data have been deposited in GEO under the accession number GSE295794. Translomic data are available in GEO under the accession number GSE297586. The proteomic data have been deposited to the ProteomeXchange Consortium (<https://proteomecentral.proteomexchange.org>) via the iProX partner repository with the identifier PXD063648. Other publicly available databases/datasets used in this work are Drosophila melanogaster protein database (<https://www.uniprot.org/taxonomy/7227>), Drosophila melanogaster (BDGP6.46) reference genome (https://www.ensembl.org/Drosophila_melanogaster/), FlyAtlas 2 (<https://flyatlas.gla.ac.uk/FlyAtlas2/>), the KEGG database (<https://www.genome.jp/kegg/>), and a total of 49 CAGE-seq datasets for 7 species (complete accession numbers are provided in Supplementary Data 8), including the following datasets used for TOP mRNA prediction in Drosophila: SRR27927240, SRR27927241, SRR27927242, SRR488271, SRR488279, and SRR488280.

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	N/A
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	N/A
Recruitment	N/A
Ethics oversight	N/A

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](https://www.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 methods were used to pre-determine sample sizes. The choice of sample size was based on the consistency of measurable differences between groups, and on the common practice for the sample size required for effective quantification using adult flies. Our sample sizes for lifespan, WB, qPCR and life-history trait assays are similar to those in previous studies, e.g., Lu et al. 2021 (PMID: 37117991) and Kosakamoto et al. 2024 (PMID: 39213345). Sample sizes for fecundity, puromycin incorporation, and proteomic assays are similar to Kim et al. 2023 (PMID: 37596266). Sample sizes for polysome profiling are similar to Zid et al. 2010 (PMID: 19804760). Dilp2 level measurements used sample sizes similar to those in Sun et al. 2017 (PMID: 28102207).
Data exclusions	No data were excluded.
Replication	Experiments were repeated independently at least twice for survival assays that involved large sample sizes and for immunostainings, and at least three times for all other quantitative measurements.
Randomization	Experimental and control flies were raised in identical conditions. We matched the sex and age of flies in every experiment. Samples were allocated to groups/treatments randomly. Steps were taken to avoid batch effects and position effects.
Blinding	The investigators were not blinded to group allocations due to the fact that the genotypes of flies needed to be carefully documented, so blinding was not always possible during experimental setup. However, lifespan assays have involved additional investigators, who had no knowledge of the experiment design. qPCR, WB and deep sequencing experiments were always controlled using internal/loading controls for normalization.

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

rabbit anti-Dilp2, gift from Jan Veenstra;
 rabbit anti-Lsp2, this study;
 rabbit anti-p-RpS6, this study;
 mouse anti-RpS6, CST #2317;
 rabbit anti-p-eIF2a, CST #3398;
 rabbit anti-eIF2a, Abcam #ab26197;
 rabbit anti-p-Akt, CST #9271;
 rabbit anti-Akt, CST #9272;
 rabbit anti-p-4E-BP1 (Thr37/46), CST #2855;
 rabbit anti-non-phospho-4E-BP1 (Thr46), CST #4923;
 mouse anti-GFP, Proteintech #66002;
 rabbit anti-RpS15A, ABclonal #A10241;
 rabbit anti-RpL30, ABclonal #A13690;
 rabbit anti-RpL40, Abcam #ab109227;
 rabbit anti-HA, CST #3724;
 rabbit anti-Actin, ABclonal #AC026;
 mouse anti-Tubulin, DSHB #4A1;
 mouse anti-Puromycin, Kerafast #Kf-Ab02366-1.1;
 HRP goat anti-rabbit IgG, Abbkine #A21020;
 HRP goat anti-mouse IgG, Abbkine #A21010;
 goat anti-rabbit IgG (H+L) Alexa Fluor 488, Invitrogen #A11008.

Validation

Dilp2 antibody has been used in many studies including Brown et al. 2020 (PMID: 32160200); Lsp2 antibody was generated in this study and validated using flies mutant for/overexpressing Lsp2; p-RpS6 antibody was produced following the same procedure as and used in Romero-Pozuelo et al. 2017 (PMID: 28829945). The mouse anti-GFP antibody (Proteintech #66002) and the rabbit anti-HA antibody (CST #3724) are tag antibodies and therefore are not species-specific. The mouse anti-Puromycin antibody (Kerafast #Kf-Ab02366-1.1) was previously used in WB to detect global protein synthesis in *Drosophila* (PMID: 37596266). The rabbit anti-RpS15A (ABclonal #A10241), and anti-RpL30 (ABclonal #A13690) antibodies have not been previously used for WB of *Drosophila* tissues, but we found that they reproducibly detect proteins of correct sizes expected for the respective *Drosophila* RPs.

All commercially available antibodies have additional validation references on the manufacturer's website, besides the following validations in *Drosophila*.

The mouse anti-RpS6 antibody (CST #2317) was validated for WB (PMID: 41423448).
 The rabbit anti-p-eIF2a antibody (CST #3398) was validated for WB (PMID: 35879463).
 The rabbit anti-eIF2a antibody (Abcam #ab26197) was validated for WB (PMID: 35879463).
 The rabbit anti-p-Akt antibody (CST #9271) was validated for WB (PMID: 38252824).
 The rabbit anti-Akt antibody (CST #9272) was validated for WB (PMID: 20074526).
 The rabbit anti-p-4E-BP1 (Thr37/46) antibody (CST #2855) was validated for WB (PMID: 26252766).
 The rabbit anti-non-phospho-4E-BP1 (Thr46) antibody (CST #4923) was validated for WB (PMID: 26252766).
 The rabbit anti-RpL40 antibody (Abcam #ab109227) was validated for WB (PMID: 34283226).
 The rabbit anti-Actin antibody (ABclonal #AC026) was validated for WB (PMID: 41821096).
 The mouse anti-Tubulin antibody (DSHB #4A1) was validated for WB (PMID: 38262414).

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

Drosophila melanogaster was used as our experimental organism. The strain, genotype, sex, and age information are described in

Laboratory animals	Methods and also in relevant figure legends. Essentially, 3–5-day-old mated females (unless otherwise noted) were subjected to further treatments clearly specified in figure legends, except for the assays for flies at the early-adult stage (Extended Data Figs. 6k(left),7f-h,9a(left)) where 2–3-day-old females were used and the assays for males (see below).
Wild animals	This study did not involve any wild animals.
Reporting on sex	The sex of flies used was described in the Methods and also in the relevant figures or figure legends. Females were used for all the experiments, except data shown in Figs. 2b,2d and Extended Data Figs. 1f(right panel),3f(right panel),4a(right panel) where males were used.
Field-collected samples	This study did not involve any field-collected samples.
Ethics oversight	No ethical approval was required.

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

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A