***eLife’s* transparent reporting form**

We encourage authors to provide detailed information *within their submission* to facilitate the interpretation and replication of experiments. Authors can upload supporting documentation to indicate the use of appropriate reporting guidelines for health-related research (see [EQUATOR Network](http://www.equator-network.org/%20)), life science research (see the [BioSharing Information Resource](https://biosharing.org/" \t "_blank)), or the [ARRIVE guidelines](http://www.plosbiology.org/article/info:doi/10.1371/journal.pbio.1000412) for reporting work involving animal research. Where applicable, authors should refer to any relevant reporting standards documents in this form.

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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:

Sample size and power analysis information is detailed in the *Study Rigor* section of methods. The sample sizes and statistical tests performed for each figure are added in its respective figure legend.

**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)

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:

In vivo studies for the experimental groups were performed in two independent cohorts, wherever possible. Further details available in the *Study Rigor* section of methods. A definition of biological vs. technical replicates and inclusion-exclusion criteria is explained in the *Study Rigor* section. When mean values were calculated from technical replicates, it is reported in the methods subsection for the experiment:

*Immunofluorescence Staining and Imaging*

*Immunofluorescence Staining, Imaging, and Analysis for Muscle Fiber Types*

*Intramuscular vs. Intermuscular Adipose Tissue Quantification*

*Masson’s Trichrome Staining and Analysis*

*Circulating Klotho and FGF23 quantification*

*Exercise-induced injury*

We state how we handled outliers in the figure legend, wherever applicable.

GEO reference number has been provided in the main text, as well as the *Data Availability* section with a private link for reviewers to access.

**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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The information is reported in *Statistical Analysis* section of the methods. All figure legends have sample size and statistical analysis method in their description. P-values have been reported in the figure legend wherever applicable.

(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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Group allocation, randomization, and blinding descriptions are described in the *Study Rigor* section of the methods.

**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
* Where provided, these should be in the most useful format, and they can be uploaded as “Source data” files linked to a main figure or table
* Include model definition files including the full list of parameters used
* Include code used for data analysis (e.g., R, MATLAB)
* Avoid stating that data files are “available upon request”

Please indicate the figures or tables for which source data files have been provided:

Python code used for network analysis is uploaded on GitHub, and the link has been provided in the *Methods*, as well as the *Key Resources Table* in the manuscript. Raw data for all figures are available in the accompanying source data file. This is stated in the *Study Rigor* section of the methods.