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# *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), life science research (see the BioSharing Information Resource), or the ARRIVE guidelines for reporting work involving animal research. Where applicable, authors should refer to any relevant reporting standards documents in this form.

If you have any questions, please consult our Journal Policies and/or contact us: editorial@elifesciences.org.

**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:

| |
|---|
| Formal power analyses were not performed; sample sizes were determined based on our own experience with the methodologies. |

**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:

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| Information for all experiments is specified in the relevant subsections of "Materials and Methods." See "Additional data files" section for discussion of high-throughput sequencing data. |

**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.

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:

| |
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| This information is provided in the relevant figure legends and the "Statistics" subsection of "Materials and Methods." |

(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

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:

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| Information about group allocation is specified in the figure legends and in the "Materials and Methods" section. For the qPCR and NanoString analyses, samples were processed in random order, then unblinded for graphing and statistical analysis. |

**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:

Due to IRB restrictions and privacy considerations, the human high-throughput sequencing data (RNA-seq and scRNA-seq) generated in this study cannot be made accessible in a public repository, but is being deposited in dbGaP (accession phs002438.v1.p1) for controlled access by qualified researchers (from not-for-profit organizations, for FSHD-related research, with local IRB approval). We do however provide processed versions of this data – an R Seurat object that includes read counts for each gene in each cell (deposited at Zenodo; doi:xx.xxxx/zenodo.xxxxx), and a table of pseudobulk counts for each gene in each sample (Supplementary file 3) – along with the R code for the figures and analyses that use this processed data (Figures 3 and 3; Supplementary files 1 and 2). Tables of the NanoString and qPCR data shown in Figures 1, Figure 1-figure supplement 1 and 2, 4, Figure 4-figure supplement 1, 5, Figure 5-figure supplement 1, 6, Figure 6-figure supplement 1 and 2, 7, 8, 9, 10 are also provided as source data files. Uncropped Western blots for Fig 9F are also included as source data files.