Total RNA of triplet replicates of five conditions (control, TFEB-WT 3h dox + 21h chase, TFEB-WT 24h chase, TFEB-K3R 3h dox + 21h chase, TFEB-K3R 24h chase) was harvested using XXXX extraction kit according to manufacturer’s instructions. A mean of 22,284,091 single-end, 83 nt Illumina reads were generated. Sequencing reads containing adapters and bases with a score of less than Q20 were trimmed using the tool TrimGalore (http://www.bioinformatics.babraham.ac.uk/projects/trim\_galore/). The trimmed high-quality reads were then aligned to the human reference assembly hg38 using STAR [PMID: 23104886]. Based on the mapping file, the tools RseQC [PMID: 22743226] and Preseq [PMID: 23435259] report several quality metrics such as alignment statistics and library complexity. FeatureCounts [PMID: 24227677] was employed to obtain the number of uniquely mapped reads to each gene. The high reproducibility between the biological replicates was confirmed by the Principal component analysis (PCA) plot. Normalization and differential expression analyses were carried out with DESeq2 [PMID: 25516281]. Significantly differentially expressed genes (DEGs) were defined with fold change ≥ 4 and adjusted P-value ≤ 0.05. The volcano plots for each comparison and clustering analysis of all DEGs from comparisons were graphed and performed in R with the ggplot2 and pheatmap packages, respectively.

Publicly available datasets were analyzed in this study. The data are stored in the European Nucleotide Archive (ENA) with accession number as follows: Study PRJEB51651 (https://www.ebi.ac.uk/ena/data/view/PRJEB51651), ENA accession numbers: ERR9285751-ERR9285765.