
Supplementary information

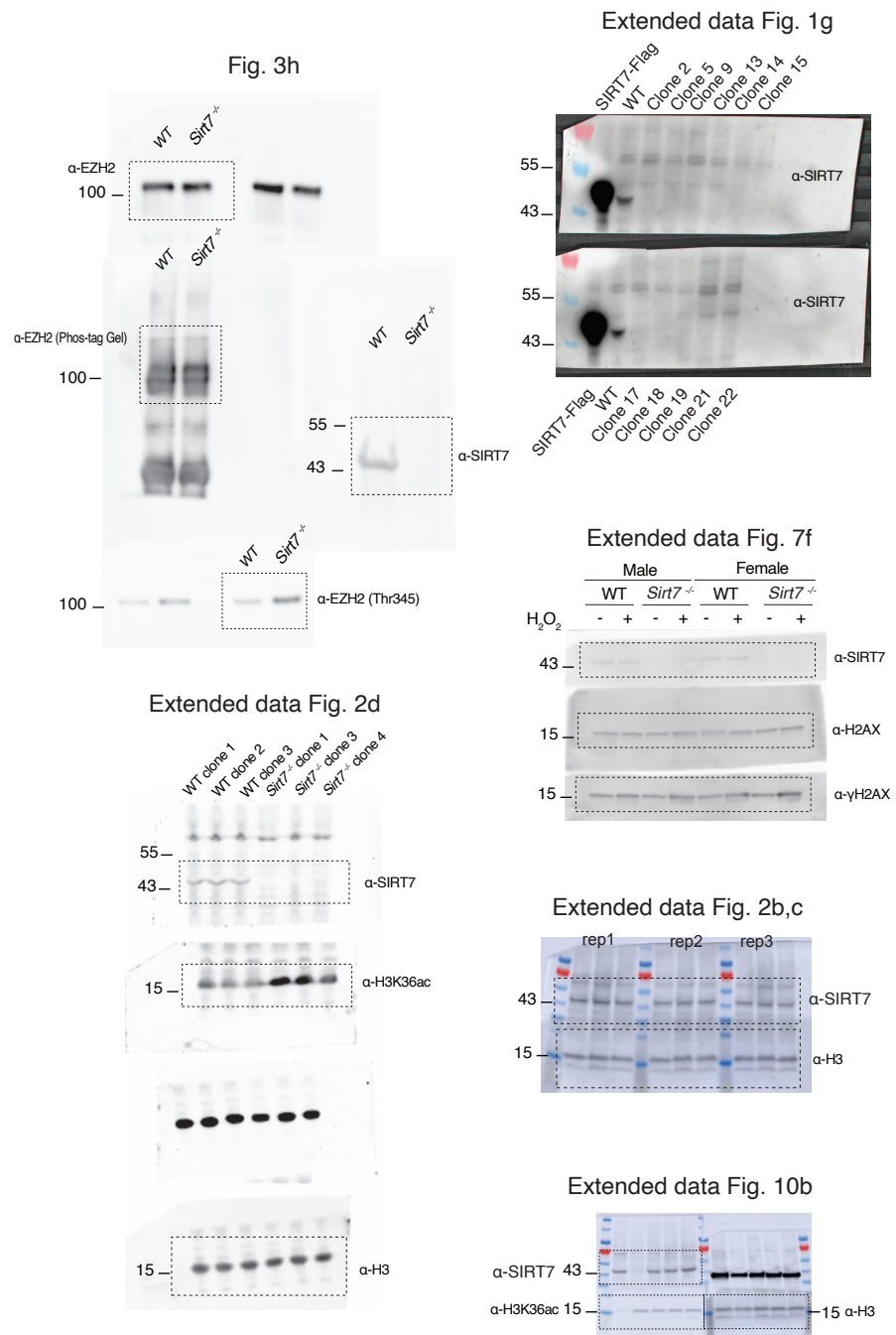
SIRT7 regulates dosage compensation and safeguards the female X chromosome

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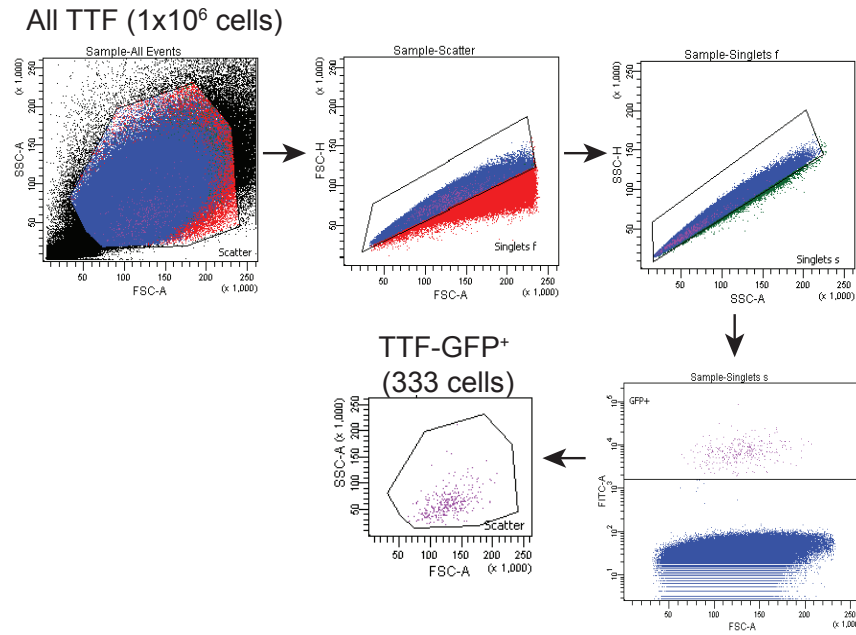
Supplementary Information

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Supplementary Figure 1: Raw blots



Supplementary Figure 2: FACS



Supplementary Figure 2. Gating strategy for detection and isolation of GFP-positive (GFP⁺) TTF cells nucleofected with Alt-R CRISPR-Cas9 system, corresponding to the experiments described in materials and methods section; CRISPR-cas9 gene editing (Alt-R CRISPR-Cas9 system).

Figure legends of Supplementary Videos 1-4

Supplementary Video 1. 3D Hi-C models of Xa A/B compartments in WT (left) and *Sirt7*^{-/-} (right) TTF, with A compartments in red and B compartments in blue.

Supplementary Video 2. 3D Hi-C models of Xa H3K36ac enrichment in WT (left) and *Sirt7*^{-/-} (right) TTF. White indicates no enrichment, and increasing H3K36ac enrichment is shown from light to dark green.

Supplementary Video 3. 3D Hi-C models of Xi A/B compartments in WT (left) and *Sirt7*^{-/-} (right) TTF, with A compartments in red and B compartments in blue.

Supplementary Video 4. 3D Hi-C models of Xi H3K36ac enrichment in WT (left) and *Sirt7*^{-/-} (right) TTF. White indicates no enrichment, and increasing H3K36ac enrichment is shown from light to dark green.

Figure legends of Supplementary Tables 1-17

Supplementary Table 1. Absolute numbers and percentages of causes of death by age and sex. Counts and proportions of *Sirt7*^{-/-} females and males in each age class (1–5, 6–10, 11–15, 16–20, and 21–25 months) are shown for megaesophagus, conjunctivitis, bacterial enterocolitis, poor body condition, cataract, hydronephrosis/possible endometriosis, and tumor.

Supplementary Table 2. Differential gene expression in mESCs at days 0 and 7. DESeq2 results for all detected genes, including chromosomal location, gene identifier, normalized mean expression, log₂ fold change (*Sirt7*^{-/-} vs. WT), and adjusted P values for mus, cas and comp alleles.

Supplementary Table 3. Allele-specific differential expression of X-linked genes in *Sirt7*^{-/-} vs. WT mESCs. Gene list from day 7 mESCs reporting log₂ fold change (*Sirt7*^{-/-} vs. WT), allele (mus or cas) and quantile group for genes included in the cumulative distribution function (CDF) analyses.

Supplementary Table 4. Vector-based integration of transcriptional and H3K36ac changes in *Sirt7*^{-/-} (KO) vs. WT from day 7 mESCs. For each DEG, RNA-seq and H3K36ac values, ΔH3K36ac (dX), ΔRNA (dY), vector angle, magnitude, significance, and angle group are shown.

Supplementary Table 5. H3K36ac hyperacetylated peaks on Xa and autosomes (cas) in *Sirt7*^{-/-} mESCs at day 7. GREAT output listing H3K36ac ChIP-seq peaks (genomic coordinates, nearest gene, and distance to TSS) used to identify enriched phenotypes (failure of heart looping, abnormal bone morphology, and hearing loss). Association rule: Basal+extension (5 kb upstream, 1 kb downstream, 1 Mb maximum extension; curated regulatory domains included).

Supplementary Table 6. H3K36ac hyperacetylated peaks on Xi and autosomes (mus) in *Sirt7*^{-/-} mESCs at day 7. GREAT output listing H3K36ac ChIP-seq peaks (genomic coordinates, nearest gene, and distance to TSS). Association rule: Basal+extension (5 kb upstream, 1 kb downstream, 1 Mb maximum extension; curated regulatory domains included).

Supplementary Table 7. H3K36ac hyperacetylated peaks on Xa (cas) in *Sirt7*^{-/-} mESCs at day 7. GREAT output listing H3K36ac ChIP-seq peaks (genomic coordinates, nearest gene, and distance to TSS) used to identify enriched phenotypes (failure of heart looping, abnormal bone morphology, and hearing loss). Association rule: Basal+extension (5 kb upstream, 1 kb downstream, 1 Mb maximum extension; curated regulatory domains included).

Supplementary Table 8. H3K27me3 enrichment at autosomal and X-linked genes in *Sirt7*^{-/-} vs. WT, grouped as Up-DEGs, Down-DEGs, or unchanged on autosomes and the X chromosome.

Supplementary Table 9. RT-qPCR analysis of Xist expression in *Sirt7*^{-/-} and WT TTF and primary MEFs.

Supplementary Table 10. List of Xi-linked genes gaining PC1 status and H3K27me3 in *Sirt7*^{-/-} TTF.

Supplementary Table 11. Metaphase spread quantifications of chromosome fusions in WT and *Sirt7*^{-/-} TTF.

Supplementary Table 12. Differential gene expression by DESeq2 analysis in *Sirt7*^{-/-} vs. WT female MEF.

Supplementary Table 13. Differential gene expression by DESeq2 analysis in *Sirt7*^{-/-} vs. WT male MEF.

Supplementary Table 14. Differential gene expression by DESeq2 analysis in *Sirt7*^{-/-} vs. WT, *Sirt7*^{-/-} vs. WT, rescue vs. WT, *Sirt7*^{H187Y} vs. WT TTFs.

Supplementary Table 15. Illumina TruSeq adapter and PCR primer sequences used for Hi-C libraries. Universal and indexed TruSeq adapter oligonucleotides and the PCR primers used for library amplification are listed with their 5'→3' sequences.

Supplementary Table 16. ENCODE quality metrics for SIRT7 ChIP-seq in MEF and TTF cells.

Supplementary Table 17. Oligonucleotide sequences used for qPCR.