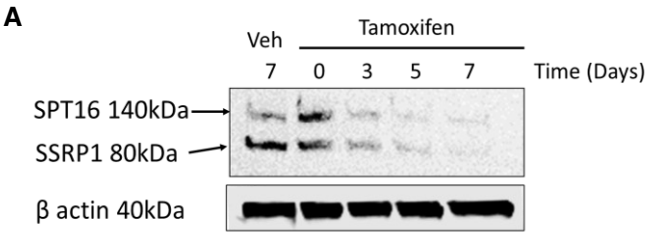
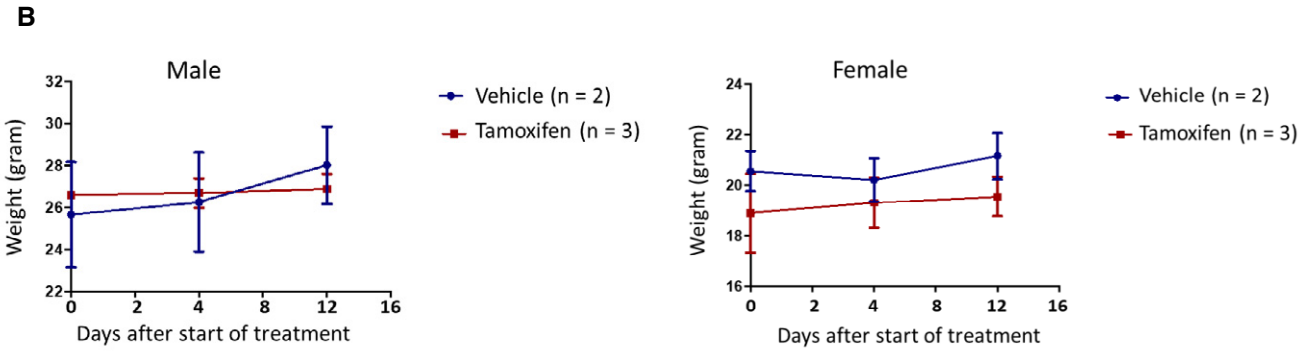
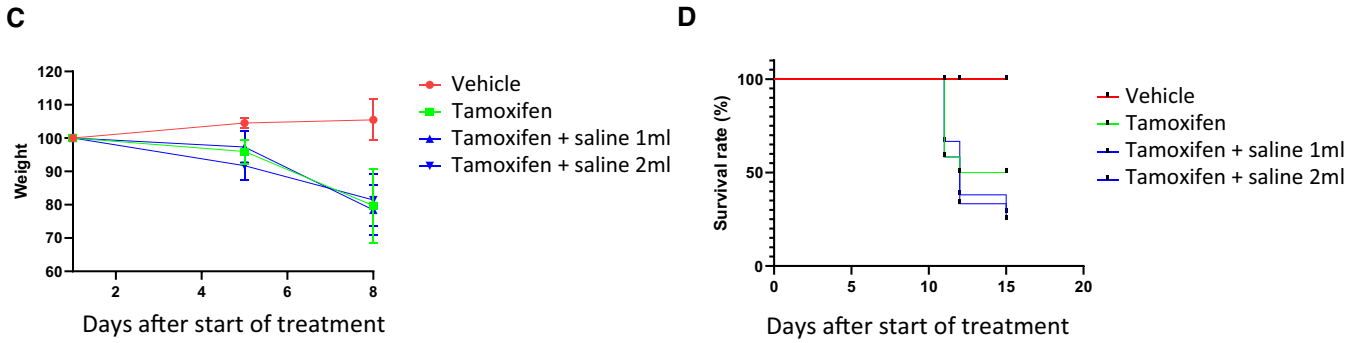
Expanded View Figures







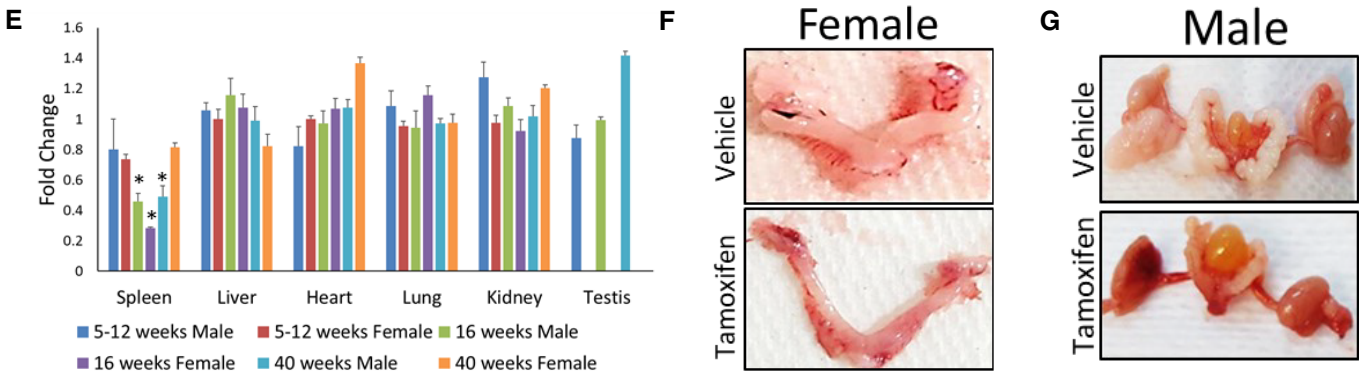


Figure EV1.

◀ **Figure EV1. Effect of tamoxifen administration on mice with wild type or floxed *Ssrp1* alleles.**

A Kinetic of FACT protein subunit loss in spleen of *Ssrp1*$^{fl/fl}$; *CreER*$^{T2+/+}$ mice upon tamoxifen administration. Western blotting of total protein extracts of spleen collected from mice at indicated time points. Veh is vehicle.

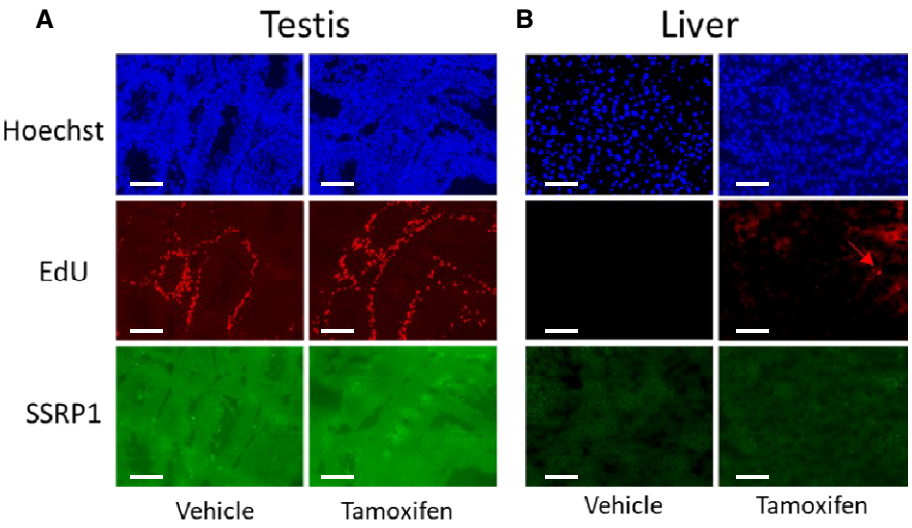
B Kinetic of weight changes of *Ssrp1*$^{+/+}$; *CreER*$^{T2+/+}$ mice upon tamoxifen administration. Mean ± SD for tamoxifen treated mice and mean ± range for vehicle treated mice.

C Effect of rehydration on weight of *Ssrp1*$^{+/+}$; *CreER*$^{T2+/+}$ mice treated with vehicle or tamoxifen. Kinetic of weight loss in control and tamoxifen treated animals either provided with subcutaneous saline injection (1 or 2 ml/day) or not. Mean ± SD, $n = 3$.

D Effect of rehydration on survival of *Ssrp1*$^{+/+}$; *CreER*$^{T2+/+}$ mice treated with vehicle or tamoxifen. Kaplan-Mayer curves of control and tamoxifen treated groups either provided with subcutaneous saline injection (1 or 2 ml/day) or not. $n = 3$.

E Changes in organ weight in *Ssrp1*$^{fl/fl}$; *CreER*$^{T2+/+}$ mice treated with tamoxifen versus vehicle treated animals. Mean ± SD. *P-value < 0.05. $n = 5$.

F, G Representative photographs of female (F) and male (G) reproductive organs excised from vehicle and tamoxifen treated mice.



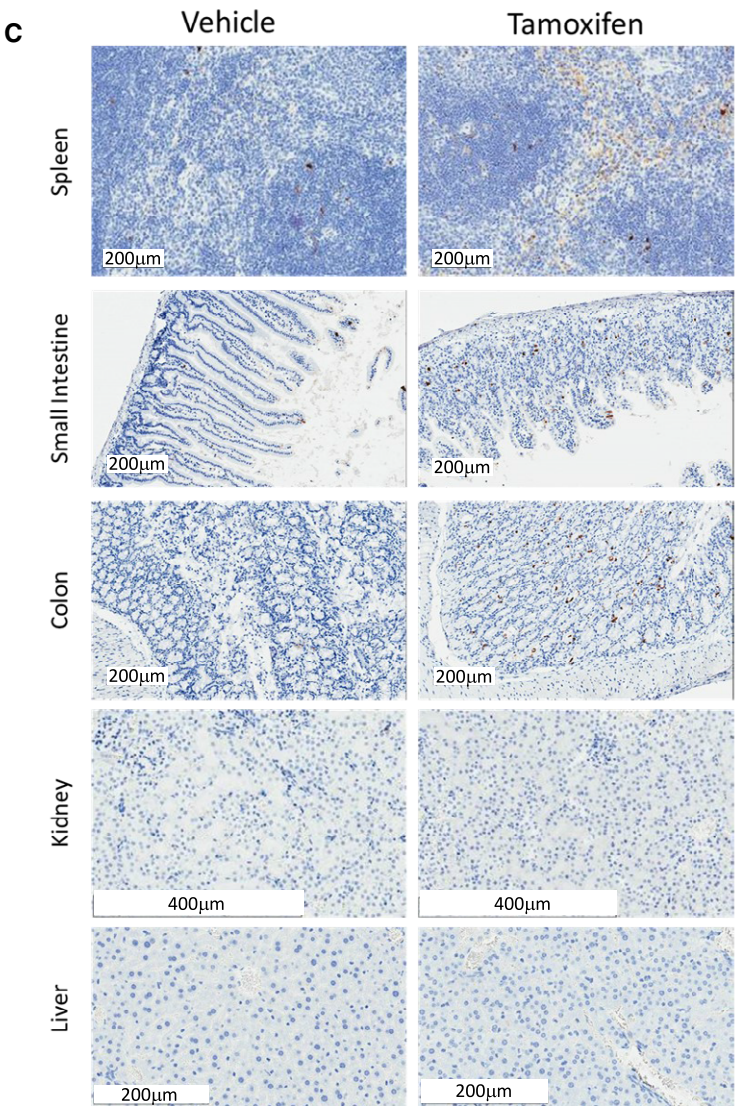


Figure EV2. Effect of FACT loss on DNA replication and apoptosis in mouse organs.

A, B Effect of tamoxifen administration to *Ssrp1*$^{fl/fl}$; *CreER*$^{T2+/+}$ mice on replication in testis (A) and liver (B). EdU was given to mice 3 days after stop of tamoxifen treatment for 1 h followed by organ isolation and staining for total DNA (Hoechst), EdU and SSRP1. Red arrow indicates EdU positive nucleus in liver. Scale bars – 100 μm.

C Staining of sections of several organs of in *Ssrp1*$^{fl/fl}$; *CreER*$^{T2+/+}$ mice for cleaved caspase 3, 3 days after stop of treatment with tamoxifen or vehicle.

Figure EV3. Analyses of scRNA sequencing of bone marrow and intestine of in *Ssrp1*$^{fl/fl}$; *CreER*$^{T2+/+}$ mice next day after stop of treatment with vehicle or tamoxifen.

A Comparison of the numbers of sequenced cells, mean reads per cell and mean identified genes between samples.

B Dot plots showing the number of features (nFeature_RNA, the number of genes detected in each cell), RNA molecules (nCount_RNA, the total number of molecules detected within a cell) and proportion of reads corresponding to mitochondrial RNA (percent.mt) in each sample.

C Overlapped UMAP plots of bone marrow and intestinal samples color coded according to the treatment type.

D, E UMAP plots of bone marrow (D) and intestine (E) color-coded based on the expression of markers of cell cycle.

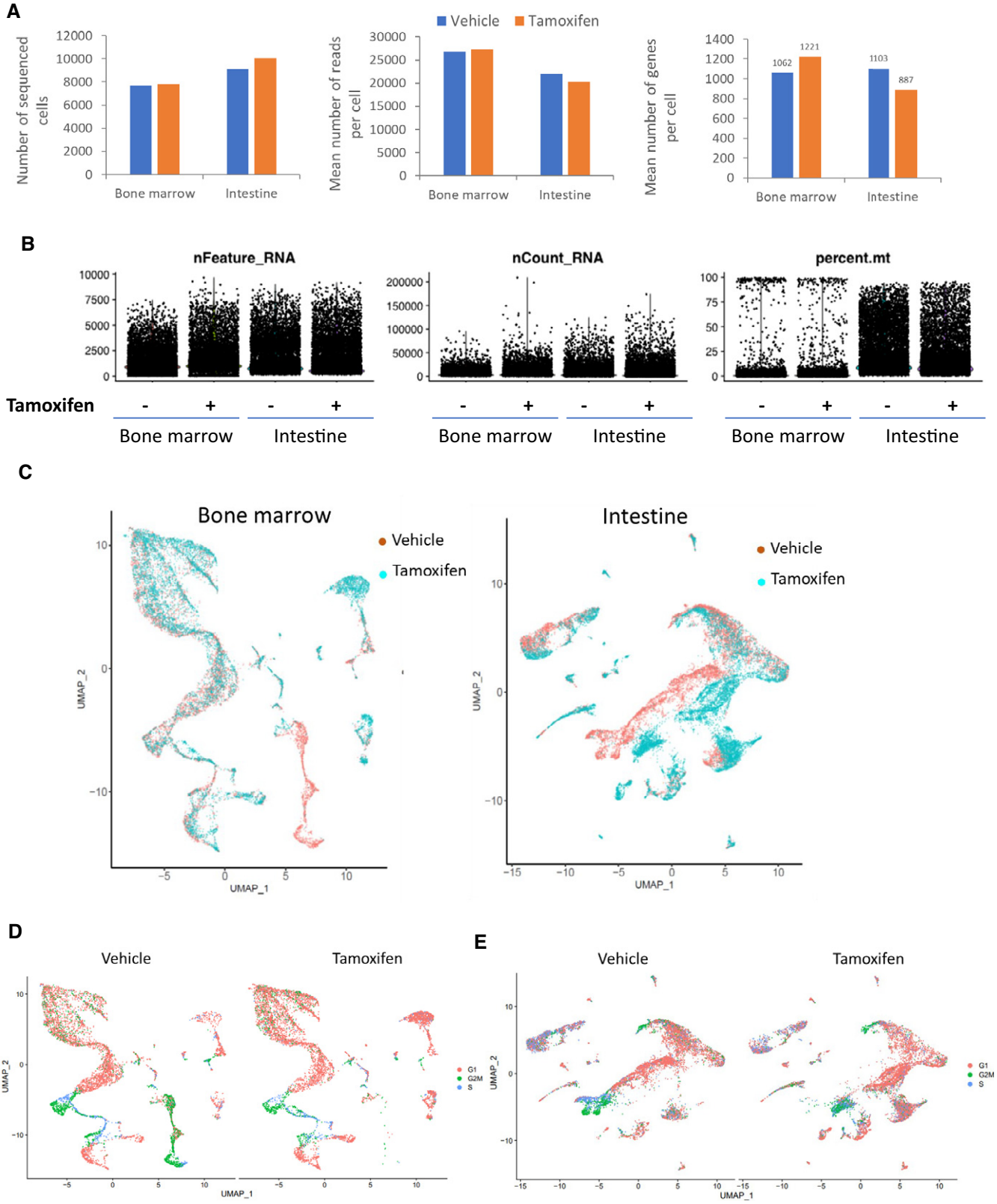

A
Number of sequenced cells
12000
10000
8000
6000
4000
2000
0
Bone marrow
Intestine
Vehicle
Tamoxifen
Mean number of reads per cell
30000
25000
20000
15000
10000
5000
0
Bone marrow
Intestine
Mean number of genes per cell
1400
1200
1000
800
600
400
200
0
1062
1221
1103
887
Bone marrow
Intestine
B
nFeature_RNA
10000
7500
5000
2500
0
nCount_RNA
200000
150000
100000
50000
0
percent.mt
100
75
50
25
0
Tamoxifen
- + - +
Bone marrow
Intestine
C
Bone marrow
Vehicle
Tamoxifen
UMAP_2
UMAP_1
Intestine
Vehicle
Tamoxifen
UMAP_2
UMAP_1
D
Vehicle
Tamoxifen
UMAP_2
UMAP_1
G1
G2M
S
E
Vehicle
Tamoxifen
UMAP_2
UMAP_1
G1
G2M
S

Figure EV3.

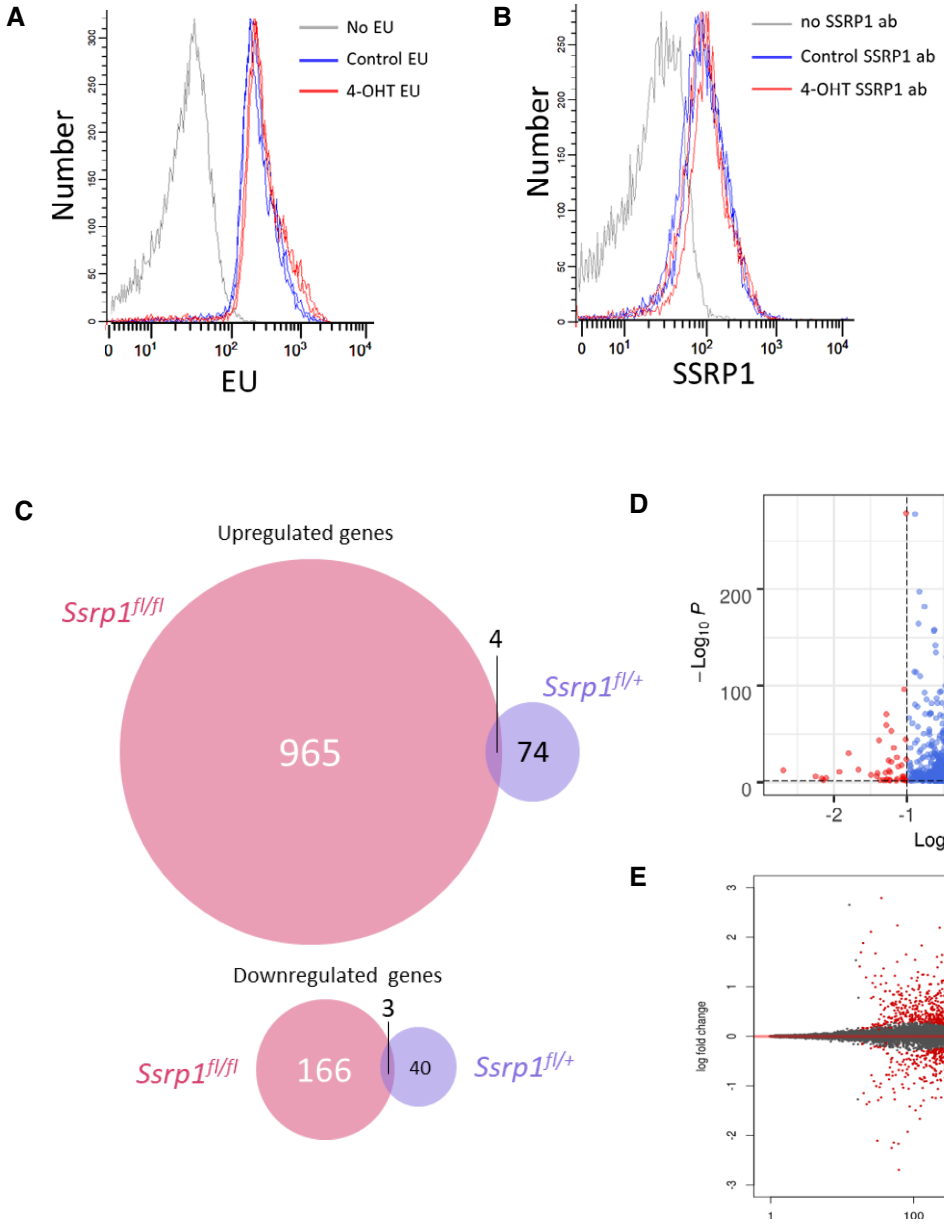


Figure EV4. Comparison of changes in transcription in MSC of two genotypes treated with vehicle of 4-OHT for 5 days and then split and analyzed 24 h after.

A, B EU incorporation assay (30 min) (A) and staining with SSRP1 antibody (B) of *Ssrp1*$^{fl/+}$; *CreER*$^{T2+/+}$ MSC. Two replicates are shown.

C–E Data of RNA-seq experiment with two replicates of MSC. C. Venn diagrams showing number of up- and downregulated genes in homo- and heterozygous cells. D. Volcano plot of gene expression changes in heterozygous cells upon 4-OHT treatment. E. MA plot of gene expression changes in heterozygous cells upon 4-OHT treatment.

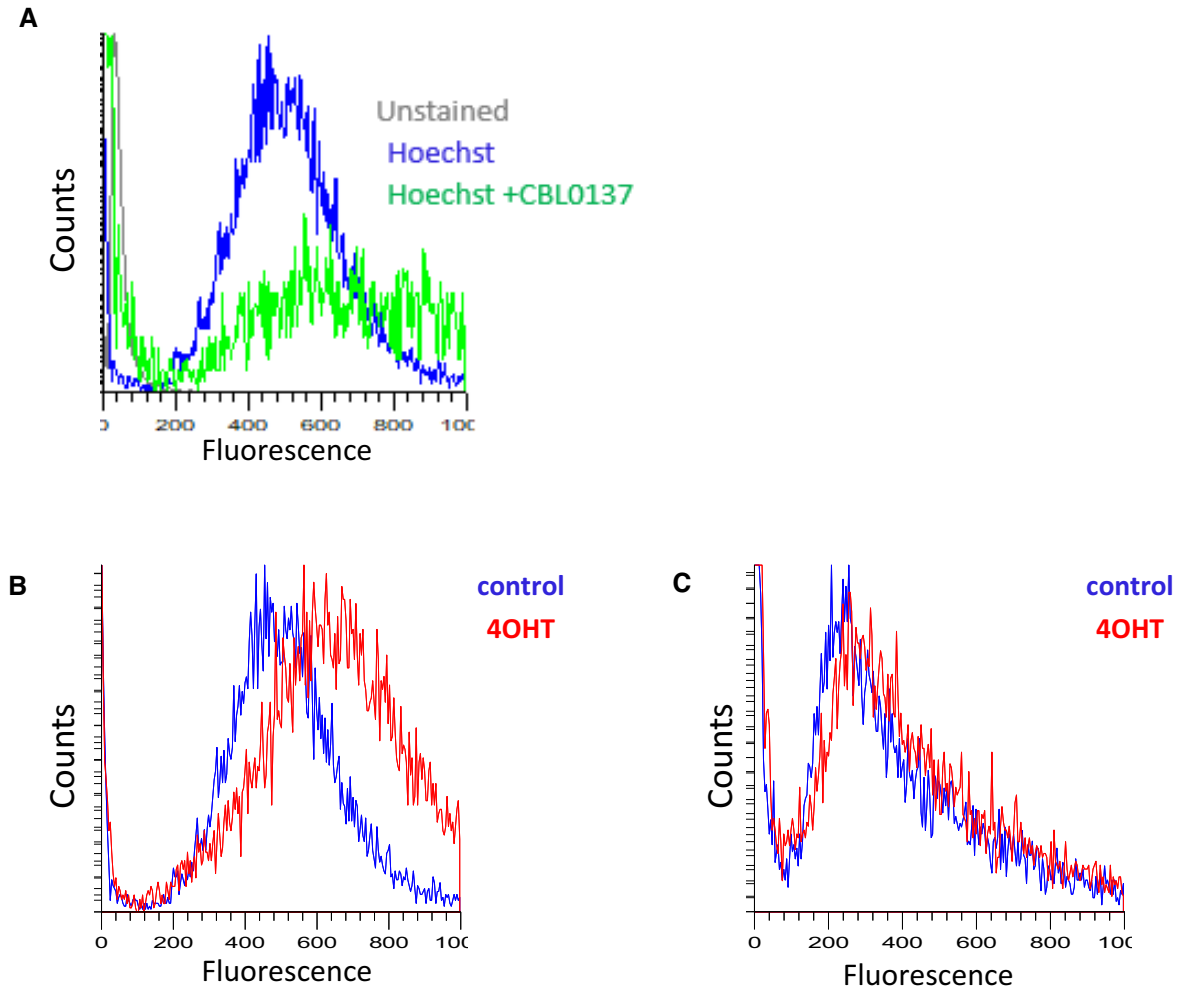


Figure EV5. Assessment of general chromatin accessibility by staining DNA in live cells with Hoechst 33342. Histograms of fluorescent intensity of MSC stained with 3 μM of Hoechst 33342 for 15 min.

A After incubation with CBL0137 (1 μM) for 30 min. This plot also includes overlap of histogram of negative control (cells unstained with Hoechst).
B *Ssrp1*$^{fl/fl}$; *CreER*$^{T2+/+}$ cells untreated or treated with 4OHT.
C *Ssrp1*$^{fl/+}$; *CreER*$^{T2+/-}$ cells untreated or treated with 4OHT.