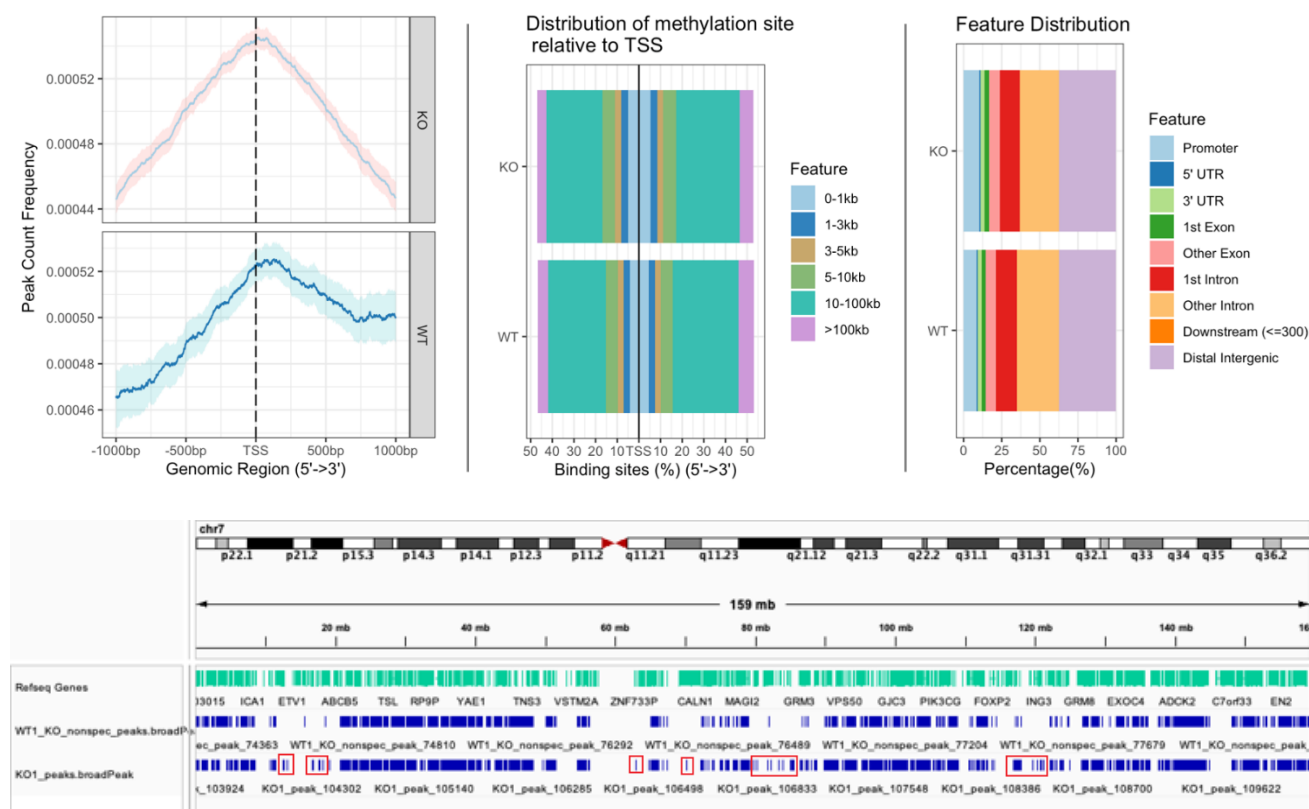


Western blot analysis of TKS4, EZH2, H3K27me3, and H3 protein levels in WT and KO cells. The blots show protein levels across different lanes: WT, WT+T, KO, and KO+T. Molecular weight markers are indicated on the left of each blot.

- TKS4:** Blot showing TKS4 (~117 kDa) and GAPDH (~36 kDa) as a loading control. TKS4 is present in WT and WT+T lanes but absent in KO and KO+T lanes.
- EZH2:** Blot showing EZH2 (~85 kDa) and GAPDH (~37 kDa) as a loading control. EZH2 is present in all lanes (WT, WT+T, KO, KO+T).
- H3K27me3:** Blot showing H3K27me3 and GAPDH (~37 kDa) as a loading control. H3K27me3 is present in WT and WT+T lanes but absent in KO and KO+T lanes.
- H3:** Blot showing H3 protein levels. H3 is present in all lanes (WT, WT+T, KO, KO+T).

B



C

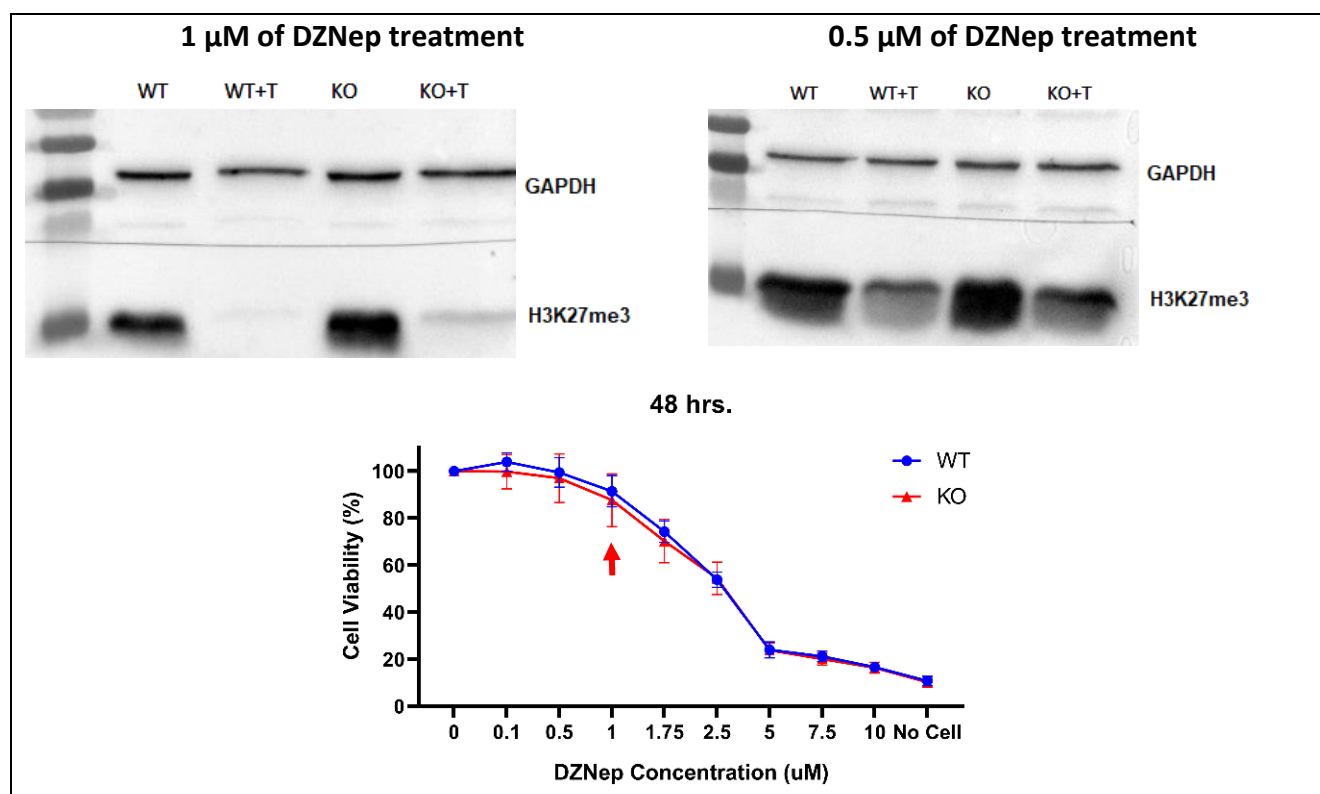
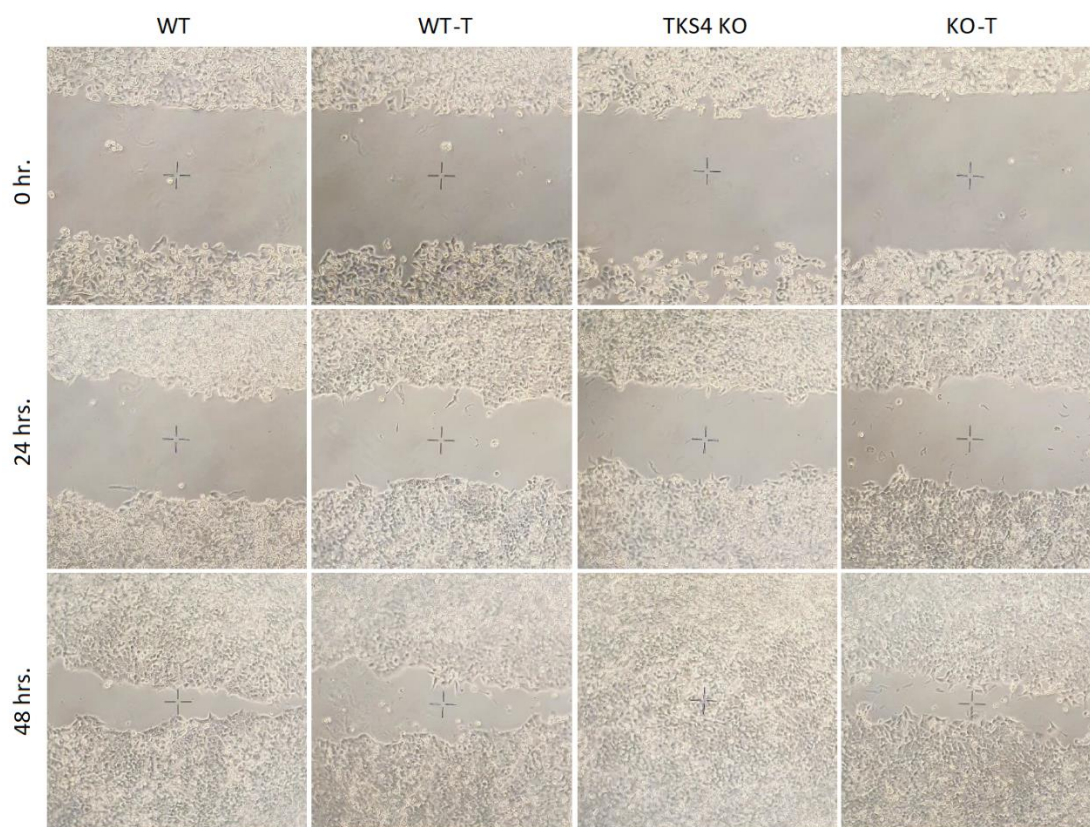


Figure S1. (a) Western blotting images of TKS4, Ezh2, H3K27me3 and Mono-Methyl Lysine. **(b)** ChIP-seq data analysis. Top panel indicates the increased number of peaks in KO cells compared to WT, especially in the promoter regions. Lower: Red rectangles indicate peaks only present in the KO samples. **(c)** Top: Western blotting picture of H3K27me3 testing two different concentrations of DZNep. Bottom: Viability of cells in response to different concentration of DZNep used.

A



B

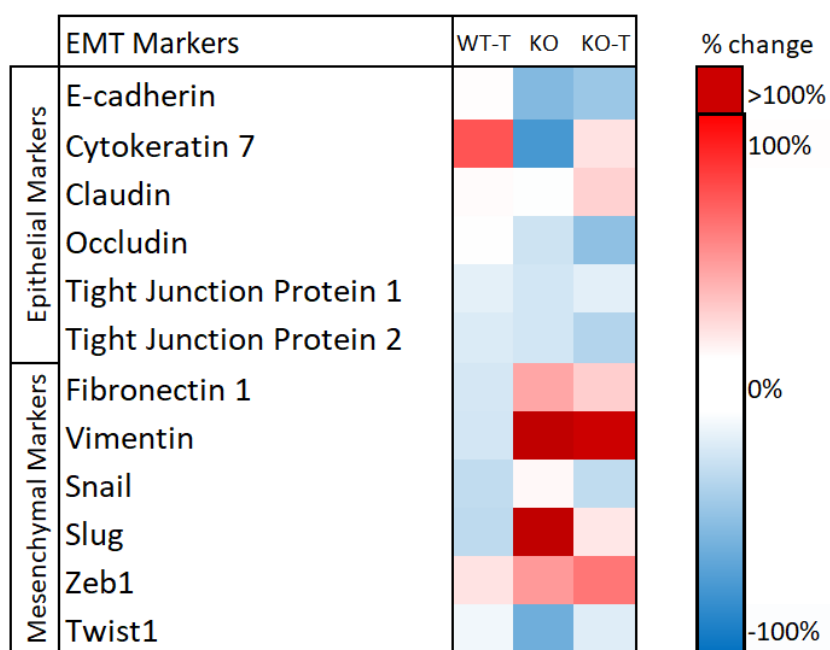
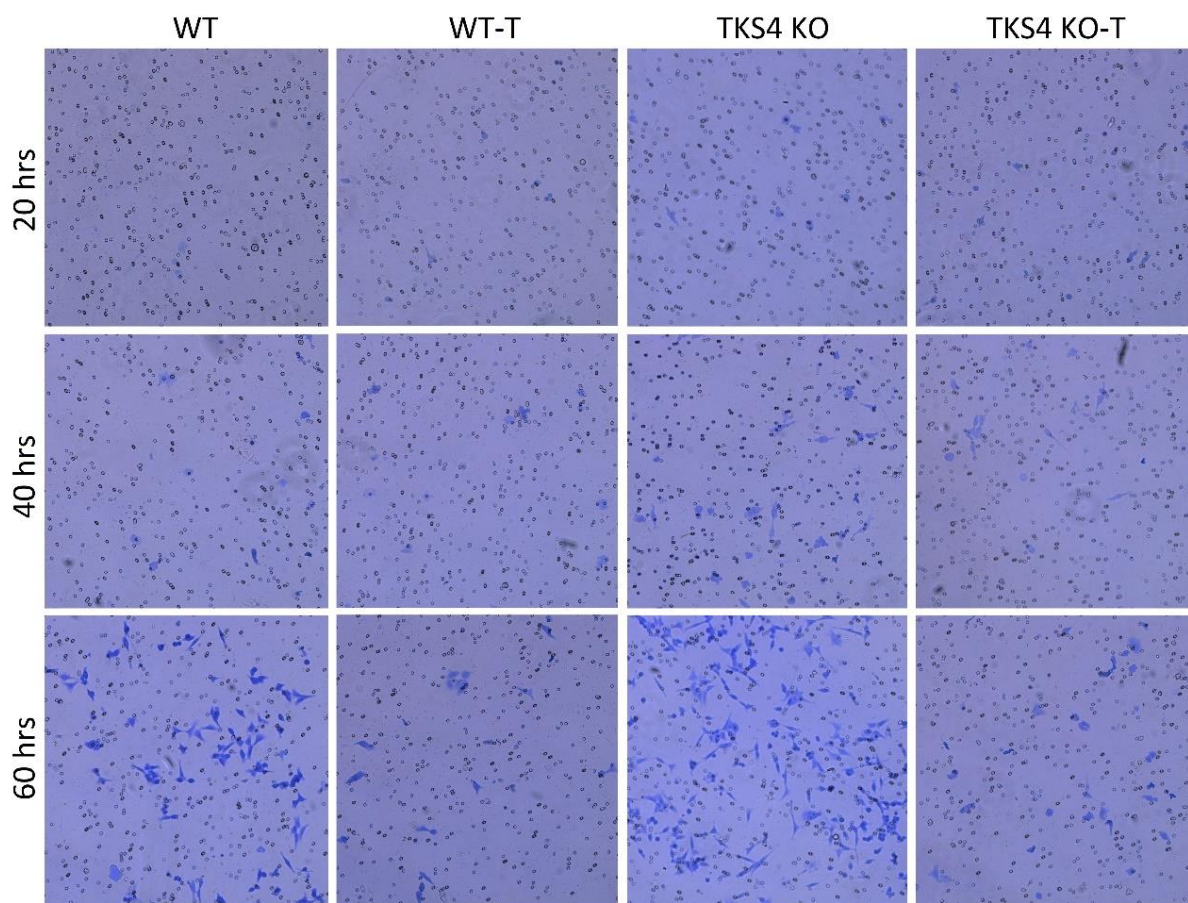


Figure S2. (a) Migration assay images at 0, 24, and 48 hours. Images of the untreated samples are adapted from our previous publication [35]. (b) Expression of EMT markers based on RNA-seq data in different conditions of cells compared to WT.

A



B

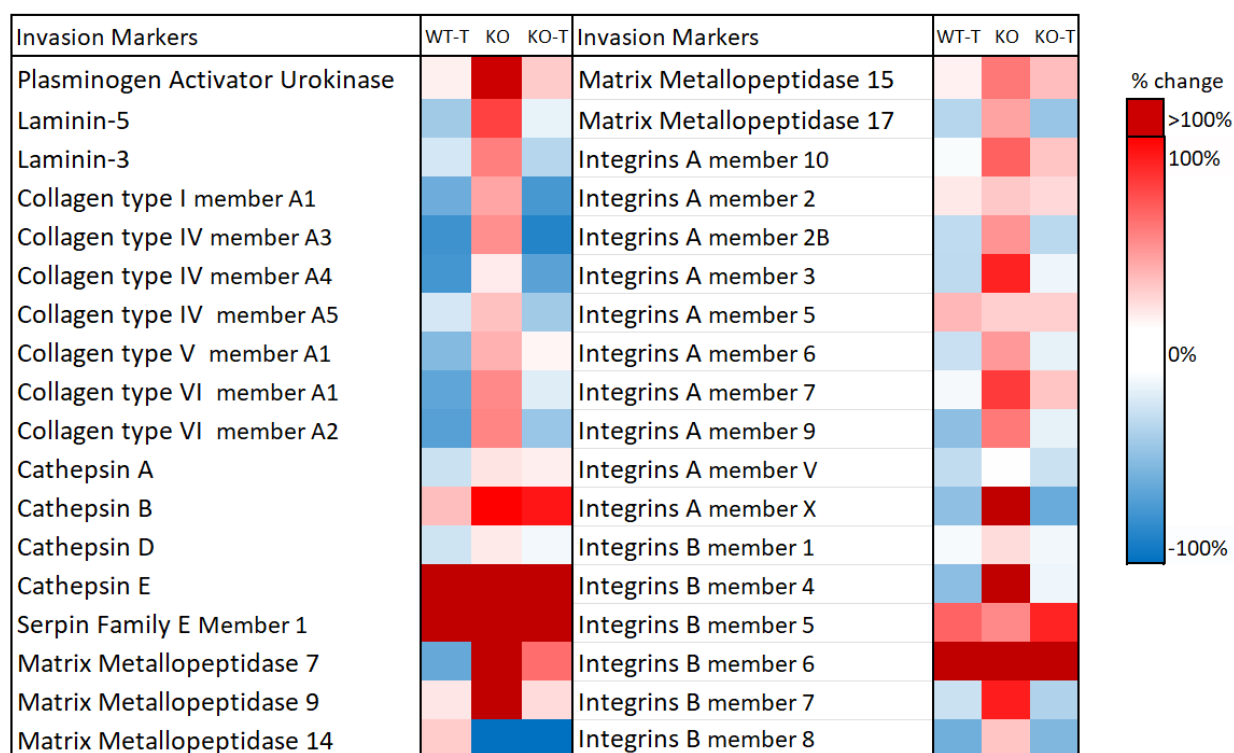


Figure S3. (a) Invasion Assay images at 20, 40, and 60 hours. Images of the untreated samples are adapted from our previous publication [35]. **(b)** Expression levels of invasion markers based on RNA-seq data in different conditions of cells compared to WT.

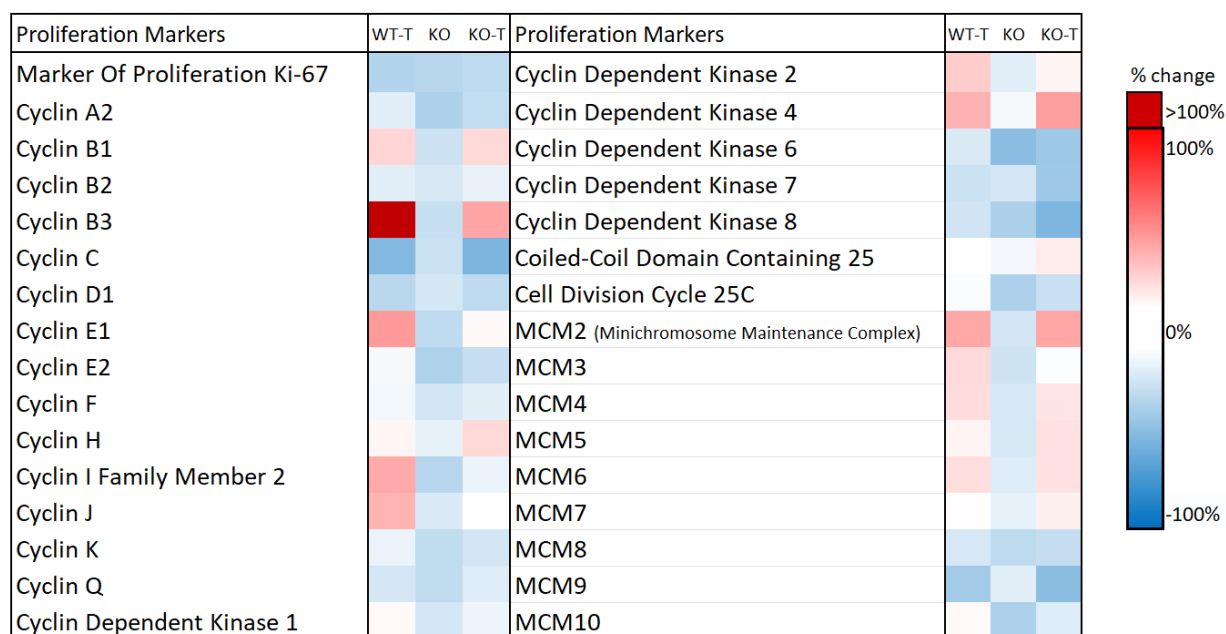


Figure S4. Expression of proliferation markers based on RNA-seq data in different condition of cells compared to WT.

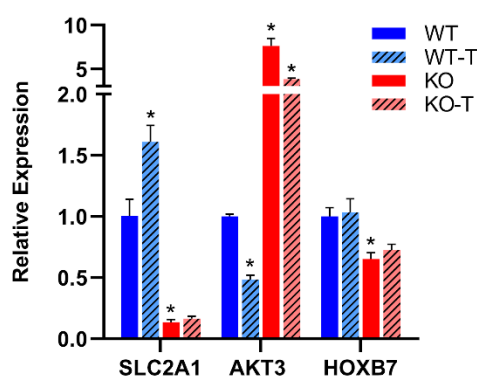


Figure S5. Quantitative analysis of selected mRNAs to validate RNA-seq data

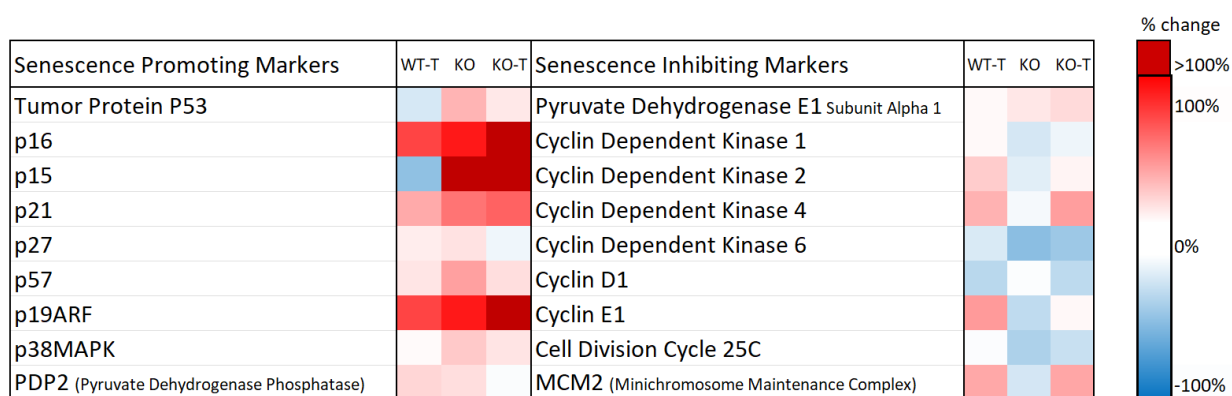
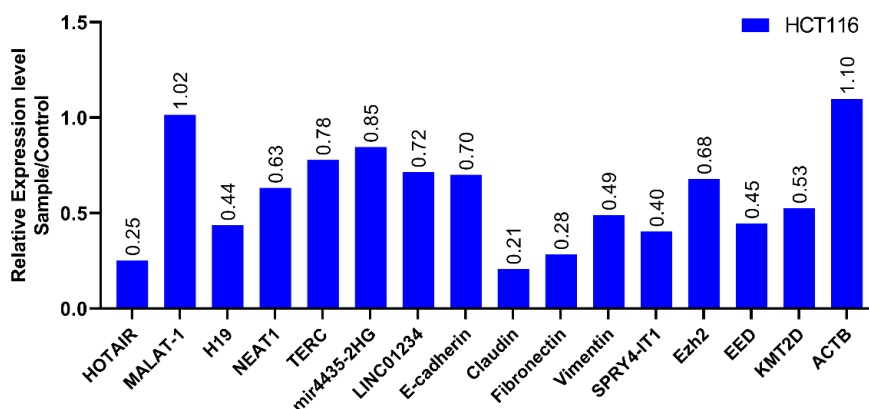


Figure S6. Senescence promoting and inhibiting markers based on RNA-seq data in different conditions of cells compared to WT.

A



B

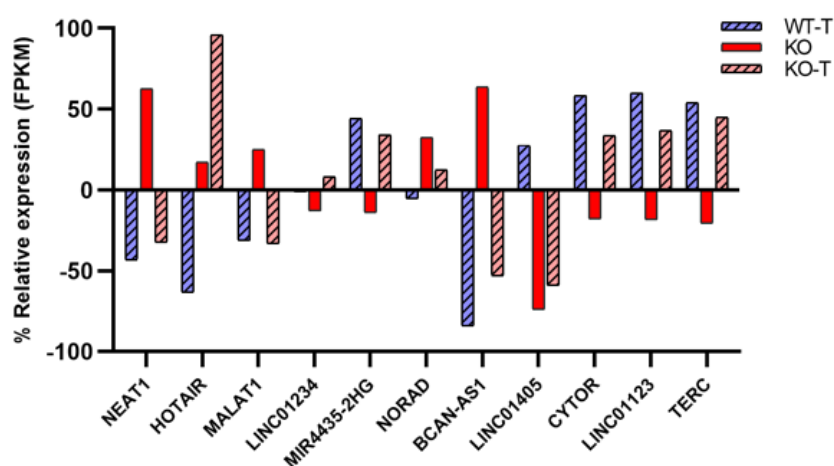


Figure S7. (a) Expression levels of different lncRNAs compared to GAPDH control based on the Ct (Cq) of qPCR. (b) Relative expression levels of selected lncRNAs based on transcriptomic analysis in different conditions of cells compared to WT (WT=0 line).

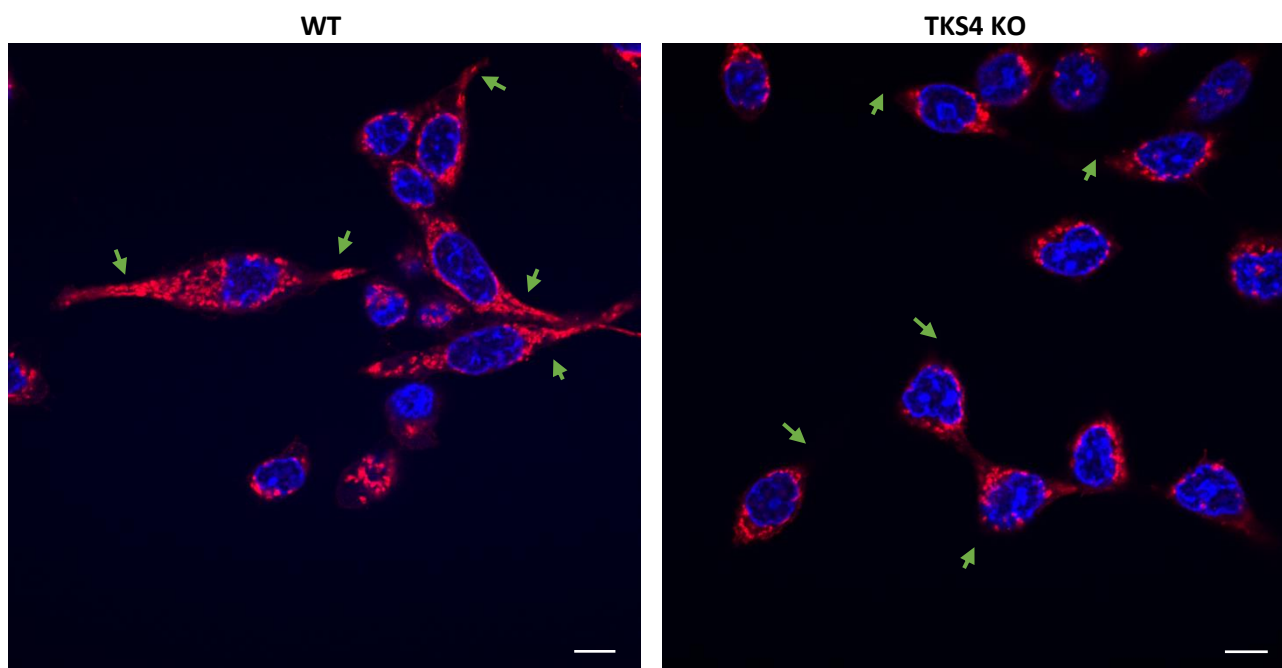


Figure S8. ICC images show the localization changes of MMP14 in TKS4 KO cells compared to WT cells. Blue: DAPI, red: MMP14. Differences in MMP14 localization indicated by green arrows. Scale bar: 20 μ m.