

Figure S1. STC1 depletion attenuates MSC senescence. (A) *Stc1* expression level in MSCs isolated from young and aged mice. n=3. (B and C) SA- $\beta$ -Gal staining and quantitation of SA- $\beta$ -Gal-positive MSCs after knockdown of STC1. Scale bar, 100  $\mu$ m. n=3. (D) Western blot assay for p16 and p21 protein expression in STC1-depleted MSCs. n=3. (E) Cell counting kit 8 assay for STC1-depleted MSCs. n=3. \*\*\*P<0.001. STC1, stanniocalcin-1; Scr, scrambled; MSCs, mesenchymal stromal cells; SA- $\beta$ -Gal, senescence associate  $\beta$ -galactosidase.

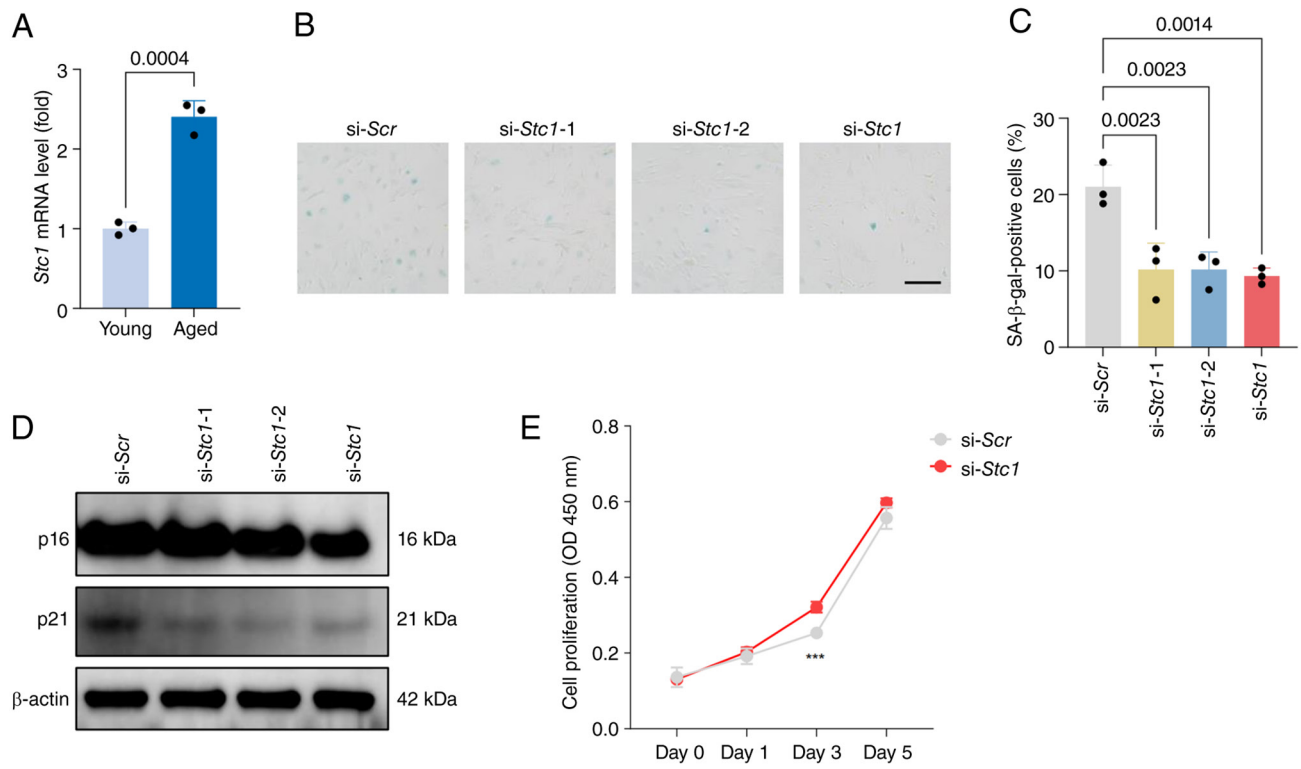


Figure S2. Knockdown of STC1 does not affect chondrogenic differentiation of MSCs. (A) *Stc1* mRNA level after 3 and 7 days of chondrogenic induction, compared with undifferentiated MSCs. n=3. (B and C) Alcian blue staining and quantitative glycosaminoglycans of MSCs underwent chondrogenic induction after knockdown of STC1. Black scale bar, 5 mm. White scale bar, 400  $\mu$ m. n=3. (D and E) mRNA expression of chondrogenic marker genes (D) *Sox9* and (E) *Col2a1* in MSCs underwent chondrogenic induction after knockdown of STC1. n=3. STC1, stanniocalcin-1; Scr, scrambled; MSCs, mesenchymal stromal cells.

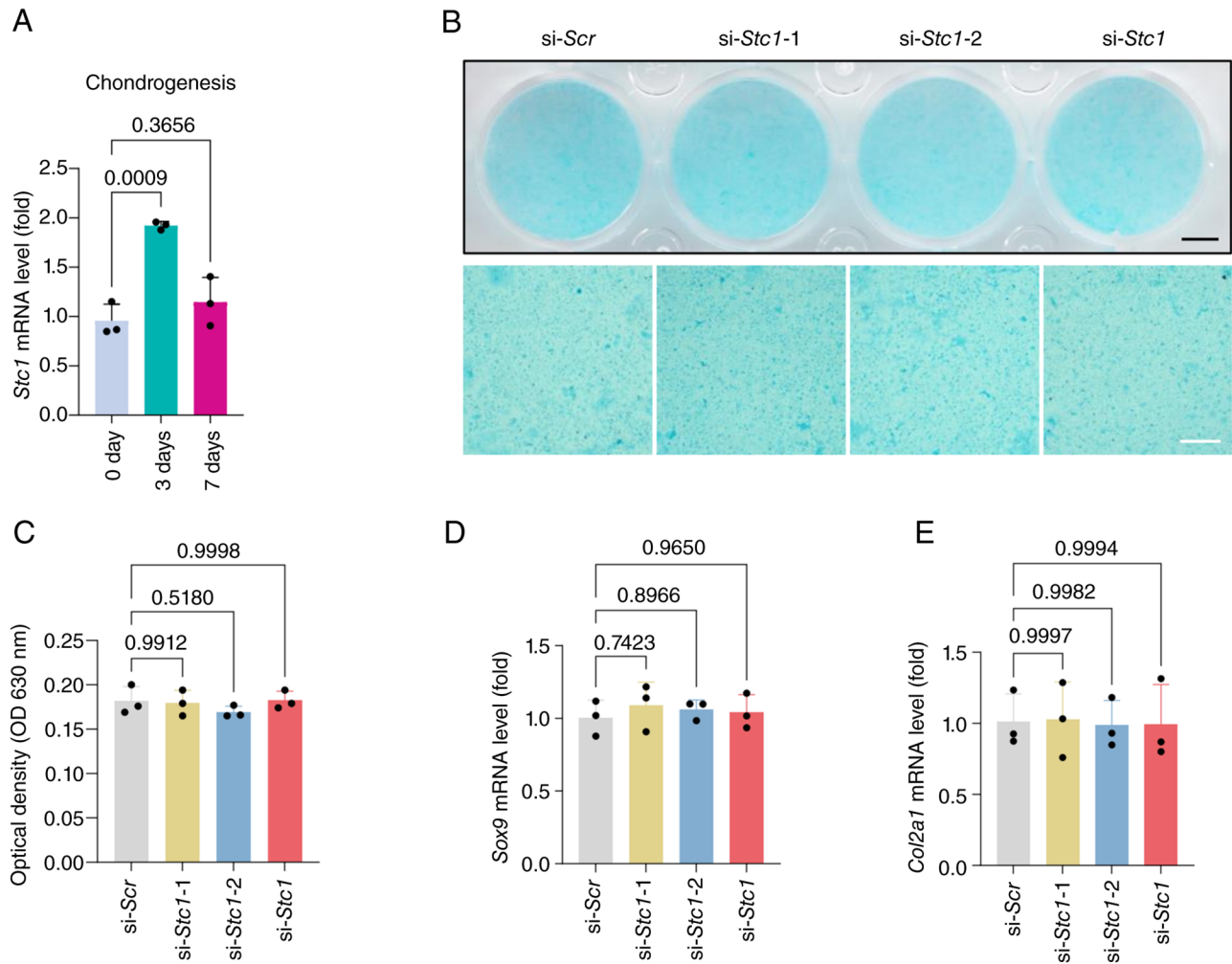


Figure S3. JSH-23 rescues the osteogenic differentiation deficit and further suppresses senescence in STC1-depleted MSCs. (A) Cell counting kit 8 assay of MSCs treated with vehicle or JSH-23 (20 or 50  $\mu$ M). n=3. (B and C) ALP staining and quantitative ALP activity assay of STC1-knockdown MSCs treated with vehicle or JSH-23 (20 or 50  $\mu$ M) upon osteogenic induction. Scale bar, 5 mm. n=3. (D) ARS staining and (E) quantification of extracellular matrix mineralization in STC1-depleted MSCs treated with vehicle or JSH-23 (20 or 50  $\mu$ M) upon osteogenic induction. Scale bar, 5 mm. n=3. (F and G) mRNA expression levels of osteogenic marker genes (F) *Alp* and (G) *Ocn* in STC1-depleted MSCs treated with vehicle or JSH-23 (20 or 50  $\mu$ M) upon osteogenic induction. n=3. (H and I) mRNA expression levels of NF- $\kappa$ B downstream target genes (H) *Tnf- $\alpha$*  and (I) *Il-1 $\alpha$*  in STC1-depleted MSCs treated with vehicle or JSH-23 (20 or 50  $\mu$ M). n=3. (J and K) SA- $\beta$ -Gal staining and the quantitation of positive cells in STC1-depleted MSCs, after treatment with vehicle, JSH-23 (20  $\mu$ M, 50  $\mu$ M). Scale bar, 200  $\mu$ m. n=3. JSH, JSH-23; STC1, stanniocalcin-1; Scr, scrambled; MSCs, mesenchymal stromal cells; SA- $\beta$ -Gal, senescence associate  $\beta$ -galactosidase.

