



**Supplementary Figure 1. STAT3 silencing resulted in reduced OSCC tumorigenesis/stemness and oncogenic exosomal cargo.** (A) Left, representative micrographs of tumor spheres. Tumor sphere formation assay showed that silencing STAT3 (si) in CAL27 and SCC-15 resulted in a significantly reduced tumor sphere forming ability as compared to their counterparts (nc, negative control). Middle, comparative bar graph of tumor sphere formation. Right, western blots of both STAT3-silenced (si) CAL27 and SCC-15 cells as compared to their control (nc) counterparts. (B) Western blots of EVs isolated from control (nc) and STAT3-silenced (si) OSCC cells. CD63 was used as loading control and marker of EVs. A significantly lower miR-21-5p level in EVs isolated in STAT3-silenced tumor spheres of CAL27 and SCC-15. (C) Migration assay of CAFs transformed by EVs collected from control (nc) OSCC spheres and EVs from STAT3-silenced (si) counterparts. Insert indicates the Western blots showing reduced markers for CAFs, VIM (vimentin) and α-SMA in CAFs transformed by EVs from tumor spheres generated from STAT3-silenced OSCC cells. (D) Cell viability assay comparing CDDP responses in OSCC cells treated with EVs isolated from control tumor spheres (nc) and EVs from tumor spheres with STAT3-silenced. \*\* $p < 0.01$ ; \*\*\* $p < 0.001$ .