Supplementary Fig. S6. TGFβ3/SMAD2 pathway promotes SQOR expression and SMCs-to-ELCs transdifferentiation. (**a**).The mRNA (Left) and protein (Right) expression of SQOR in the MI-PDBCs#1 and UMUC3 cells treated with TβRI&II inhibitor, or anti-TGFβ1, or anti-TGFβ2 antibody or anti-TGFβ3 antibody. (**b**) The relative CoQH2/CoQ ratio in the bladder cancer cells (left), and *in vitro* tube formation capability in PBSMCs educated by SFC from the indicated cells (right). (**c**) IB analysis of expression of the endothelial marker CD31, CD144 and vWF in PBSMCs treated with SFC derived from TGFβ3-overexpressed, TGFβ3-silenced and control cells. (**d**) The relative ubiquinol/ubiquinone (CoQH2/CoQ) ratio in the bladder cancer cells (left), and tube formation capability in PBSMCs educated by SFC from the indicated cells (right). Scale bars, 20 μm. (**e**) The relative CoQH2/CoQ ratio in the bladder cancer cells (left), and *in vitro* tube formation capability in PBSMCs educated by SFC from the indicated cells (right). (**f**) Quantification of pulmonary metastatic nodules, TGFβ3 level, TGFβ3 level and intramuscular $CD31^+$ or $\alpha\text{-SMA}^+\,CD31^+$ vessels in the indicated mice. (**g**) Kaplan–Meier curves analysis of metastasis-free survival in mice bearing the indicated orthotopic bladder tumors. (**h**) Kaplan-Meier analysis of overall survival and distant-metastasis free survival in 178 MIBC patients with high or low TGFβ3 expression. (**i**) Representative immunostaining images of PCNA, CD31 and α-SMA, and quantification of intramuscular $\alpha\text{-SMA}^+\,CD31^+$ vessels in human bladder cancer specimens with high (n=138) or low TGFβ3 (n=42) expression. Scale bars, 500 μm; Scale bars insets, 10 μm. Each error bar in a, b, d and e represents the mean ± SD of three independent experiments, error bar in f represents as the mean ± SD of n = 6 mice per group. Statistical analysis was performed using two-way ANOVA with Šídák's multiple comparisons test for (a, b, d and e), unpaired two-tailed t tests for (f and i), and Kaplan-Meier method for (g and h). ***$P < 0.001$; ns, not significant.

Supplementary Fig. S6