

**Supplementary Fig. S3. Succinate induces phenotypic switching of SMCs.** (a) Real-time PCR analysis of the mRNA expression of SMCs marker ( $\alpha$ -SMA, SM22 $\alpha$ , Calponin) and endothelial marker (CD144, vWF, CD31, eNOS) in the indicated times after succinate treatments. GAPDH serves as the internal control. (b) IB analysis of expression of p-ERK1/2, ERK1/2, p-Elk1, Elk1 and nuclear-KLF4 in PBSMCs treated by SFC-MI-PDBC#1/#3, with or without SUCNR1 inhibitor 4C and MAPK/ERK inhibitor PD98059. GAPDH served as the loading control. H3 serve as a loading control for nuclear protein. (c) IB analysis of expression of SLC13A3, SLC13A2, SLC13A5, SLC25A10, MCT1, MCT2 and MCT4 in the indicated PBSMCs. GAPDH served as the loading control. (d) <sup>13</sup>C<sub>4</sub>-succinate uptake was measured in the PBSMCs that treated with control, succinate or SFC/MI-PDBC#1 transduced with or without MCT1 siRNA. (e) Real-time PCR analysis of the mRNA expression of iNOS in the indicated times after succinate or SFC-MI-PDBC#1 treatments. GAPDH serves as the internal control. (f) Co-IP/IB analysis of succinylated iNOS in the indicated cells. (g) Co-IP/IB analysis of succinylated iNOS in the cells transduced with FLAG-wild-type-iNOS, iNOS-K22R, iNOS-K505R, iNOS-K516R and iNOS-K613R. (h) IB analysis of the protein degradation rate of iNOS in the cells that transduced with FLAG-wild-type-iNOS or iNOS-K22R. (i) Co-IP/IB analysis of the level of polyubiquitinated iNOS-WT and iNOS-K22R. Each error bar in a, d and e represents the mean  $\pm$  SD of three independent experiments. Statistical analysis was performed using Two-way ANOVA with Šídák's multiple comparisons test for (d), and one-way ANOVA with Dunnett's multiple comparison tests for (e). \*\*\* $P < 0.001$ ; ns, not significant.

### Supplementary Fig. S3

