Supplementary materials for

Placenta-Specific Drug Delivery by Trophoblast-Targeted Nanoparticles in Mice

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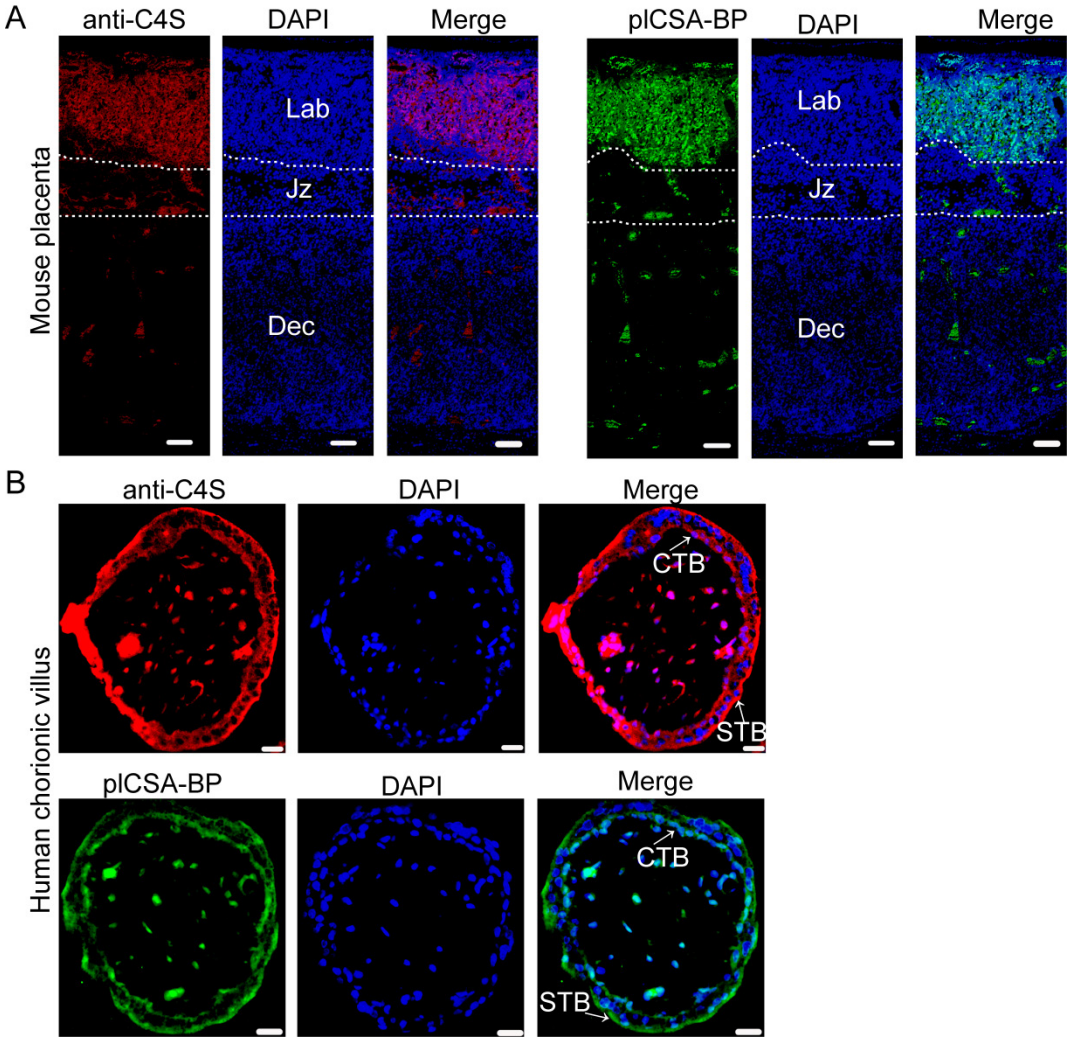

Figure S1.plCSA-BP and anti-C4S are colocalized, shown by adjacent section immune staining. Mouse (A) and human (B) placental tissue sections (5μm) stained using biotin-plCSA-BP (green) and anti-C4S (red) and counter-stained with DAPI (blue). Images representative of n=5. The scale bar represents 100 μm (A) and 20 μm (B). Lab, labyrinth; Jz, junctional zone; Dec, decidua. CTB, cytotrophoblasts; STB, syncytiotrophoblasts. **Related to Figure 1.**

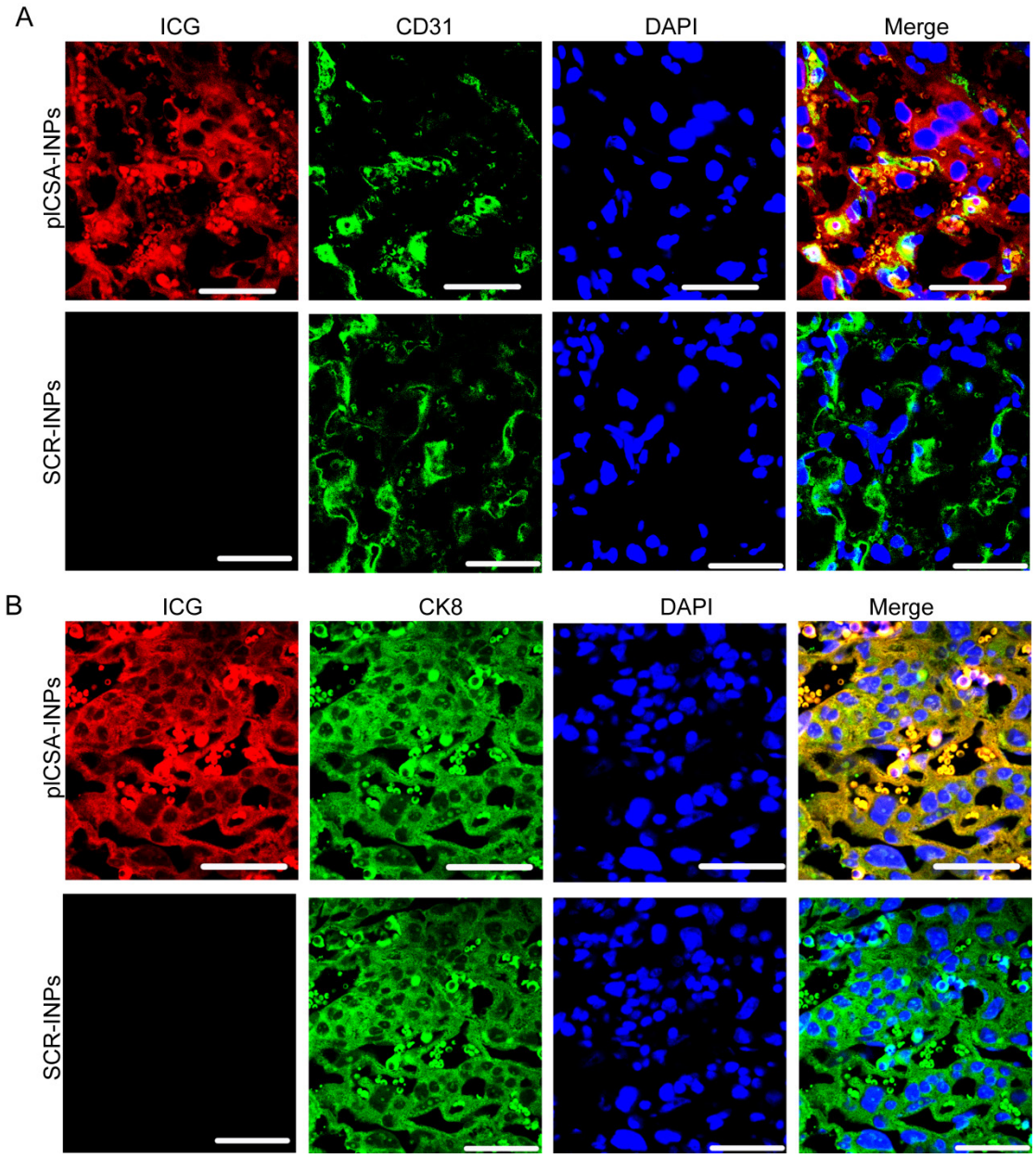

Figure S2. plCSA-INPs accumulate in mouse placental trophoblast cells. Placenta tissues immunostained for CK8 (green) and CD31 (green) and counter-stained with DAPI (blue) as in Figure 4(D-E).These sections are 100 μm away from the placental center sections. Images representative of n=6. The scale bar represents 50 μm. **Related to Figure 4.**

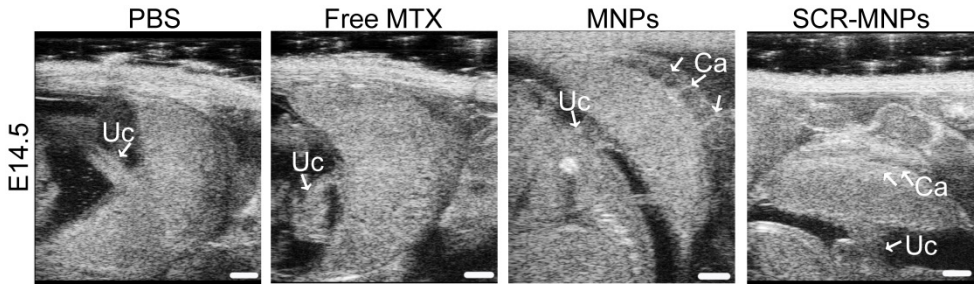

Figure S3. Representative B-mode images of embryo placenta at E14.5. The placenta is visualized as a homogenous mass in the PBS and free MTX groups (n=6). The placentas display hyperechogenic calcification deposits (Ca, arrows) in MNP and SCR-MNP groups. **Related to Figure 6.**

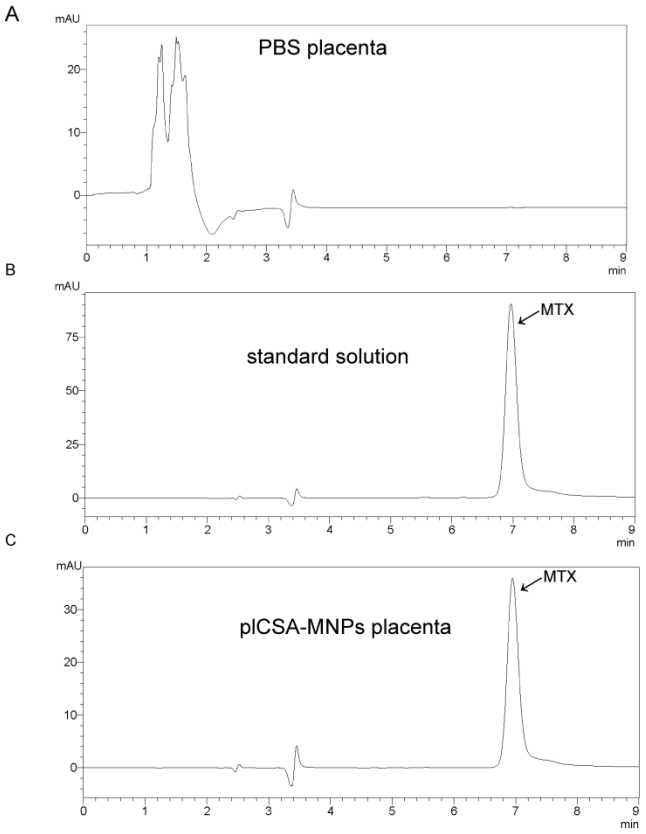

Figure S4. Representative HPLC chromatograms of a plCSA-MNP group placental sample. (A) PBS placental sample. (B) Standard solution of 25 μg/ml MTX, with UV detection at 313 nm; retention time for MTX was 7 min. (C) Placental sample 24 h post-plCSA-MNP injection in tail vein. **Related to Figure 7.**

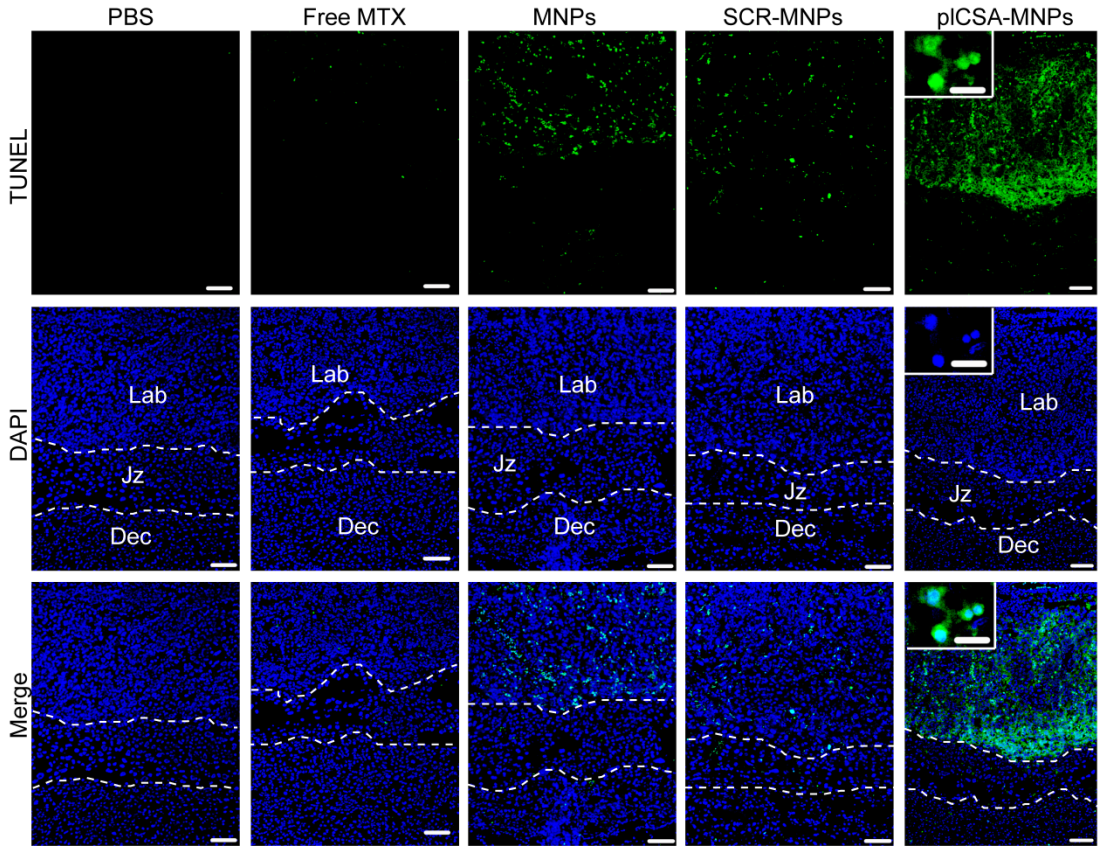

Figure S5. Apoptosis is induced by plCSA-MNPs in the placenta, as confirmed by TUNEL assay. Section selected 100 μm away from the middle sections stained using the TUNEL (green) method; blue indicates DAPI-stained nuclei. Lab, labyrinth; Jz, junctional zone; Dec, decidua. Scale bar=100 μm, and white boxes represent magnifications of the indicated areas (scale bar 20 μm). Images representative of n=6. **Related to Figure 8.**