Supporting Information

Genetically-Engineered Protein Prodrug-like Nanoconjugates for Tumor-Targeting Biomimetic Delivery via a SHEATH Strategy

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Figure S1 Legumain-mediated cleavage of rTCS-PTN-ABD determined by SDS-PAGE analysis.



Figure S2 Cellular uptake of protein toxins in 4T1 cells, Scale bar, 50 µm.



Figure S3 The influence of ABD to albumin cellular uptake.



Figure S4 The cellular uptake by the blood monocyte macrophages (RAW 264.7). The conjugates of rTCS-PTN-ABD/HSA showed the reduced cellular capture.



Figure S5 Plasma

concentration-time profile of rTCS, rTCS-ABD, and the pre-formed nanoconjugates of rTCS-ABD/HSA measured in rats.



Figure S6 The intratumor legumain-activated measurement. rTCS-PTN-ABD was labeled with Cy5 and HSA labeled with QSY21. The increased fluorescence intensity indicated the legumain-mediated cleavage and the release of TCS.



Figure S7 Legumain expression in different tissues detected by immunohistochemical staining (A) and Western blotting (B).



Figure S8 Histochemical examination of major organs dissected from the mice after treatment. Scale bar, $50 \mu m$.