Supplemental Figures:

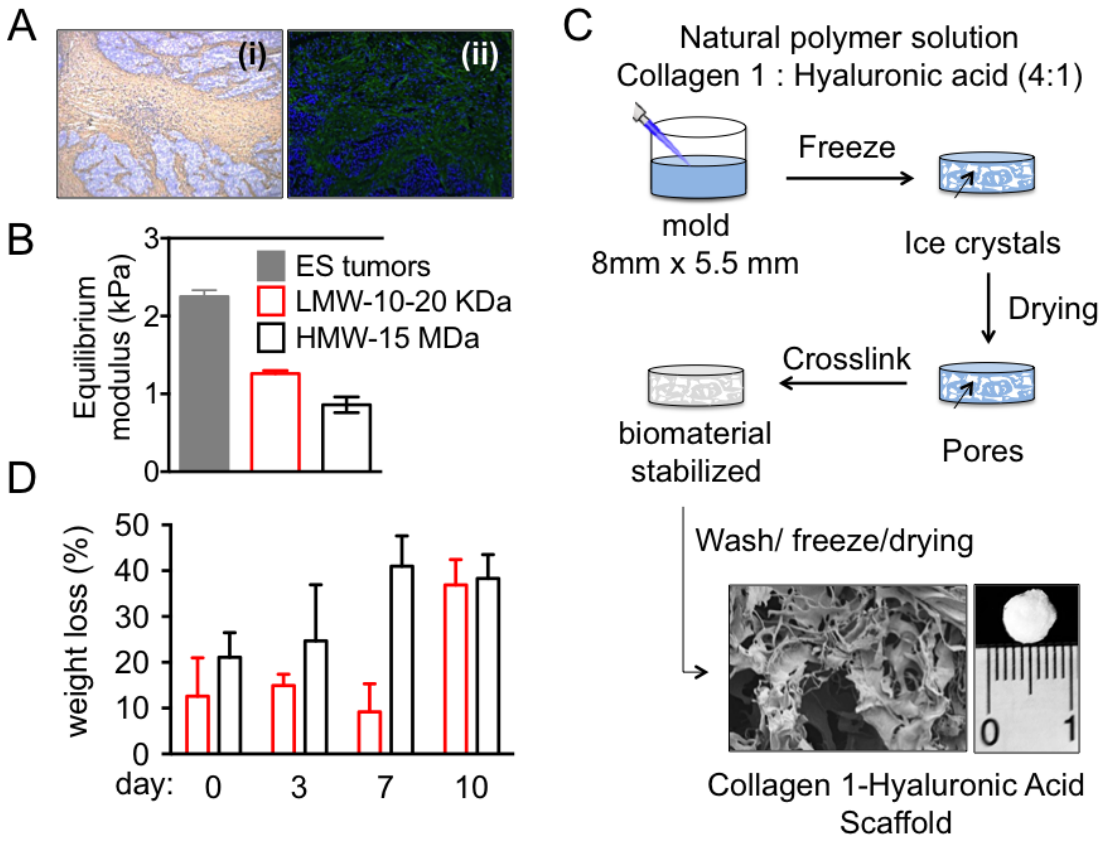

Figure S1. Establishment and characterization of the biomimetic tumor scaffold. **(A)** Characterization of the extracellular matrix composition for Ewing's sarcoma tumors. (i) Immunohistochemical staining for Collagen 1; Counterstaining with hematoxylin QS (blue). (ii) Immunofluorescence image of hyaluronan acid binding protein (green); cell nuclei were stained by Hoechst 33342. Representative images are shown (n=3 per condition). **(B)** Equilibrium modulus of native Ewing's sarcoma tumors (n=3) and (Col1-HA) high molecular weight (HMW) scaffolds (n=3). **(C)** Preparation of Collagen1 - Hyaluronic acid (Col1-HA) scaffolds. **(D)** Degradation of the LMW and HMW Col1-HA scaffolds (n=3 per condition and time point).

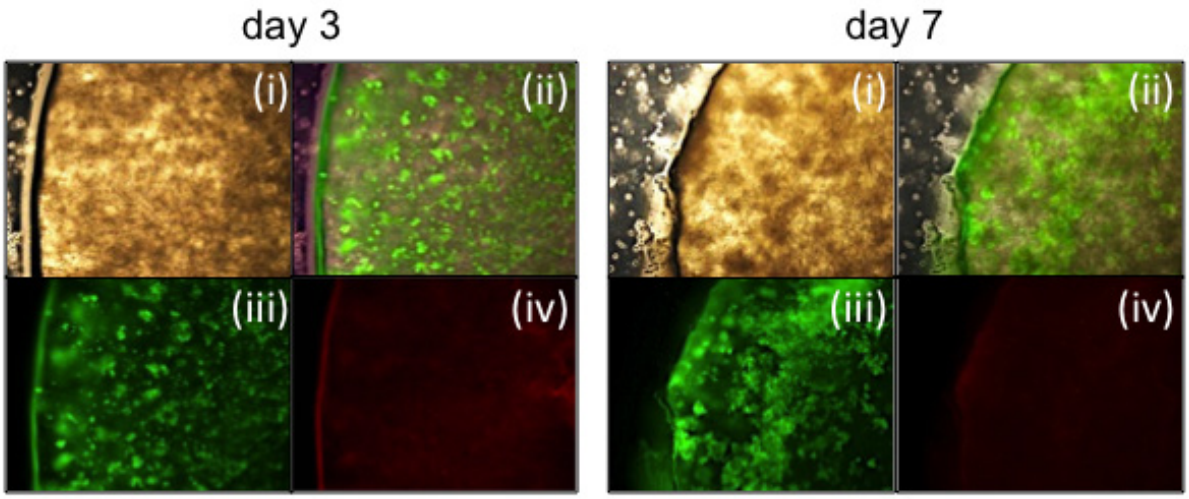

Figure S2. Live/dead staining images of Te-tumor models at day 3 and 7 (n=4). (i) brightfield, (ii) merge, (iii) Calcein staining (green-live cells), (iv) ethidium homodimer-1 staining (red-dead cells).

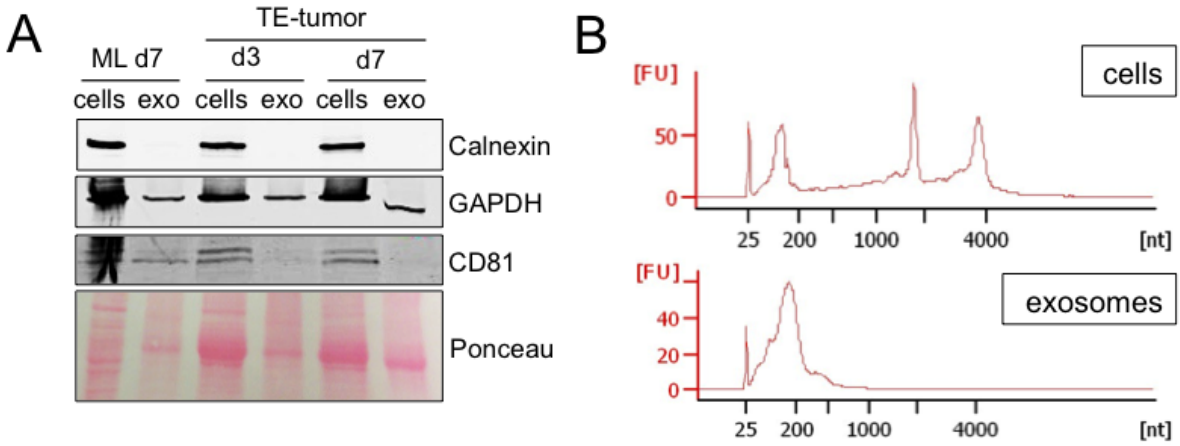

Figure S3. Evaluation of the purity of exosomes preparations. (A) Protein levels of the indicated proteins in cells and exosomes (exo) preparations from monolayer cultures (ML) at day 7 (d7) and TE-tumors at day 3 (d3) and day 7 (d7). **(B)** Electropherograms of total RNA isolated from cells and exosomes in the TE-tumor model at day 7, using the Agilent Bioanalyzer. FU, fluorescent units; nt, nucleotides (RNA size).

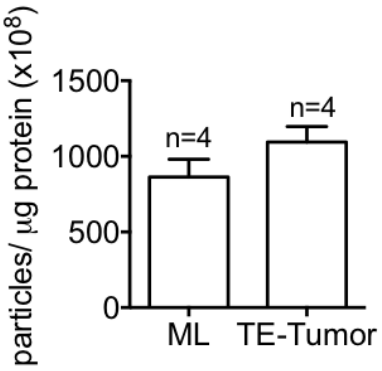

Figure S4. Analysis of the total number of exosomes ($x10^8$) per microgram of protein by NTA in monolayer (ML) or cells cultured in scaffold (TE-tumor) at day 7.