## Supplementary Information

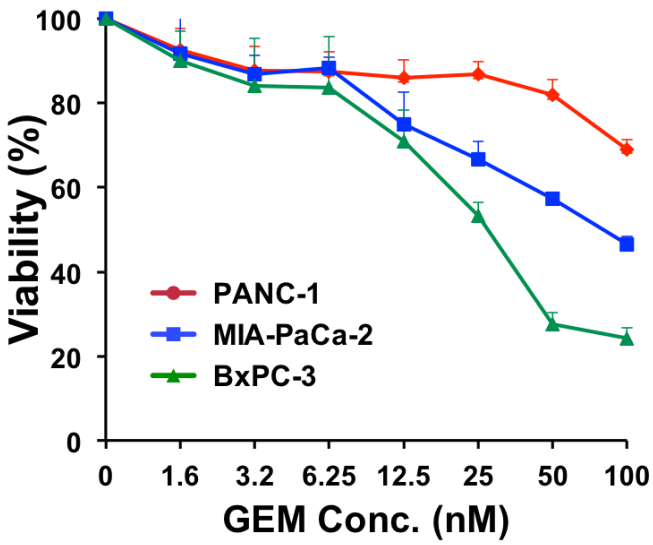


**Fig. S1. GEM-induced changes in PANC-1, MIA PaCa-2, and BxPC-3 cell viability.** Cell viability was measured by MTT assay after 72 h incubation with 1-100 nM GEM, and normalized to untreated cell viability.

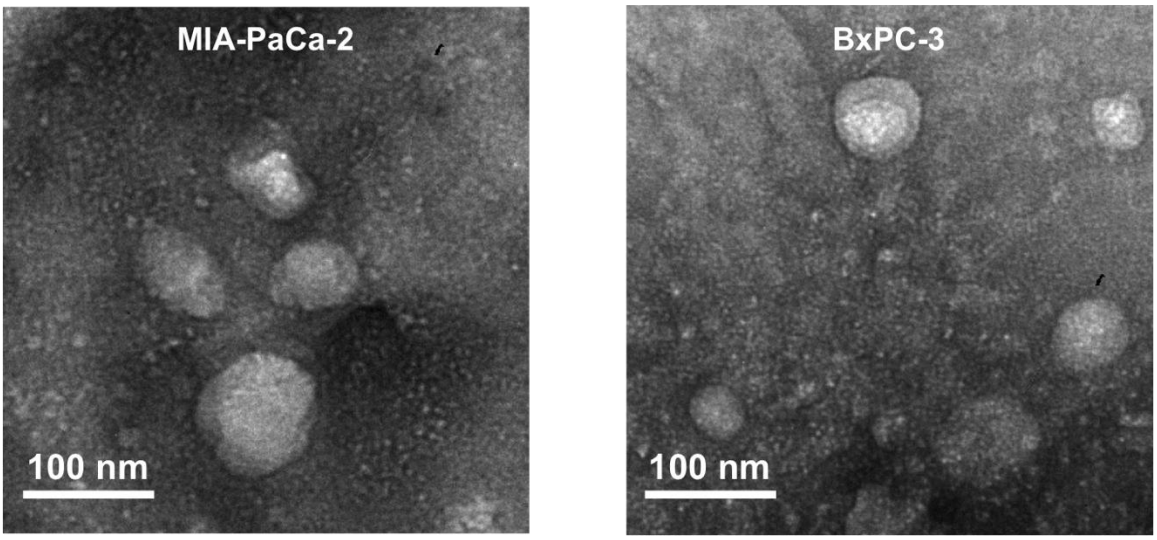


**Fig. S2. TEM images of exosomes purified from MIA PaCa-2 and BxPC-3 cells.** Exosomes were negatively stained by uranyl acetate. The scale bar represents 100 nm.

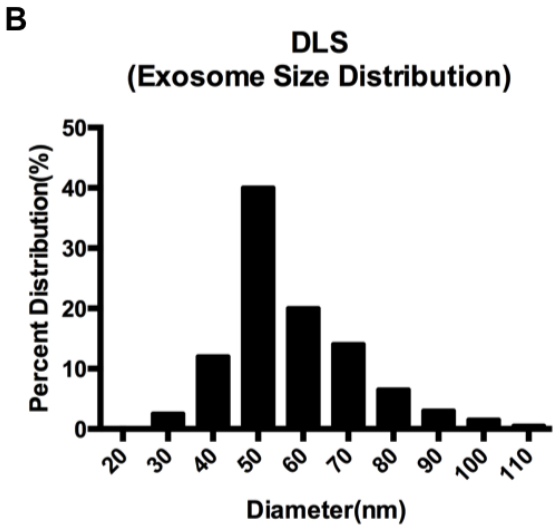


**Fig. S3. Size distribution of PANC-1 isolated exosomes.** Exosome size was determined by Dynamic Light Scattering, yielding a mean diameter of 50.75 ± 20 nm.

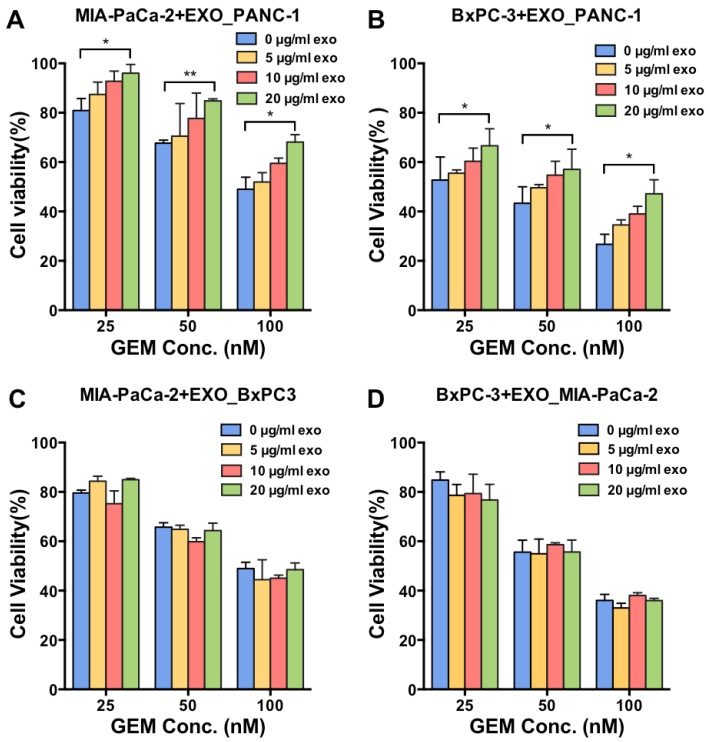


**Fig. S4. GEM cytotoxicity in MIA PaCa-2 and BxPC-3 cells cultured with exosomes isolated from PANC-1, MIA PaCa-2 or BxPC-3 cells.** GEM-induced cell viability of (**A**) MIA-PaCa-2 cells and (**B**) BxPC-3 cells after incubation with PANC-1 exosomes and (**C**) MIA-PaCa-2 cells exposed to BxPC-3 exosomes and (**D**) BxPC-3 cells exposed to MIA-PaCa-2 exosomes. Data indicate mean±SD; n=6; *$p$<0.05; **$p$<0.01.

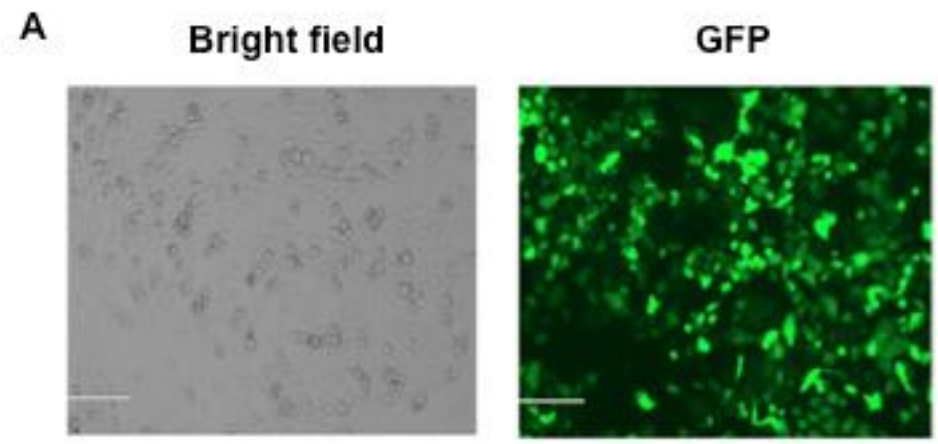


**Fig. S5. Representative PANC-1 transduction with a GFP-shRNA-expressing lentivirus construct.** Phase contrast (left) and fluorescence microscope (right) images of PANC-1 cells transduced with a lentivirus expressing GFP and EphA2_shRNA_1 after 48 h selection with 10 µg/mL puromycin. Scale Bar: 20 µm

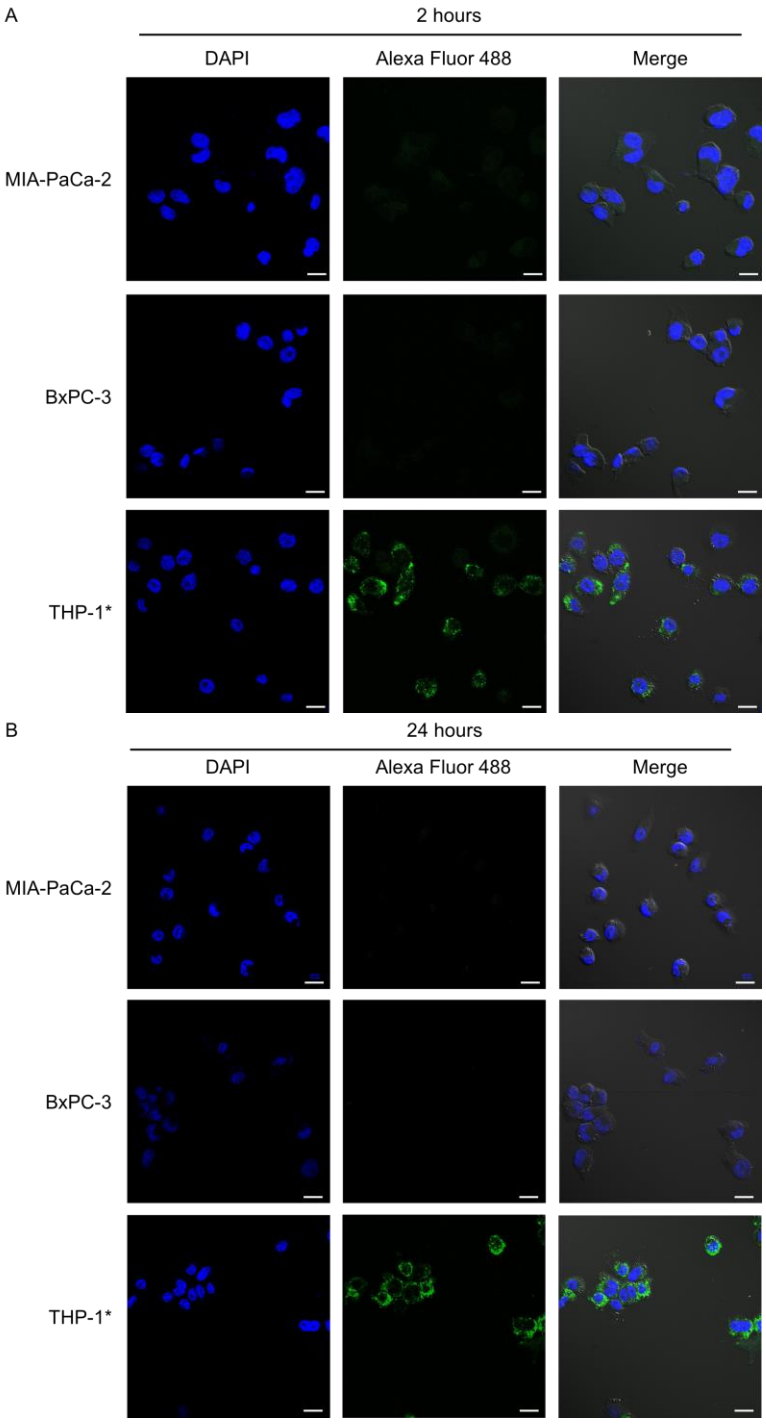


**Figure S6. Recombinant EphA2 internalization.** EphA2 internalization in MIA PaCa-2, BxPC-3 and THP-1 differentiated macrophage cells after (A) 2 hours, and (B) 24 hours incubation with fluorescent-labeled EphA2 and then staining with DAPI for nuclear visualization. Bar indicates 10 µm.