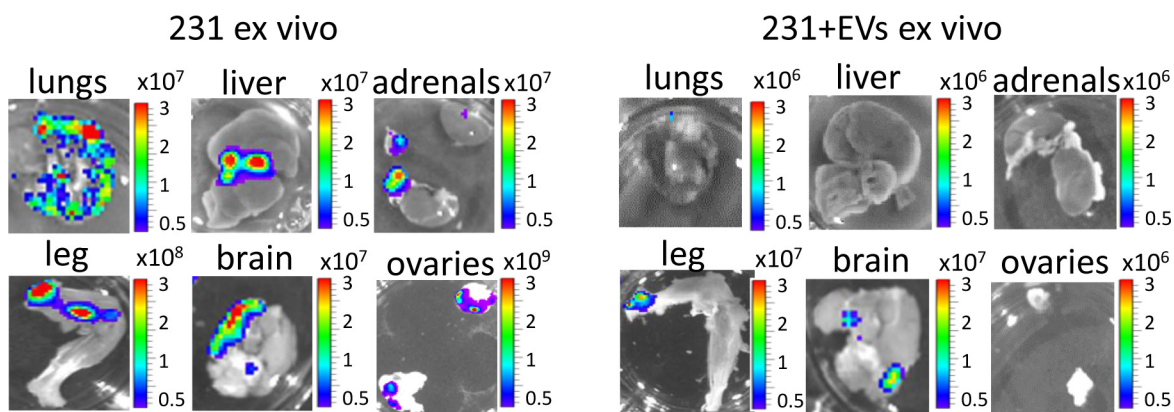
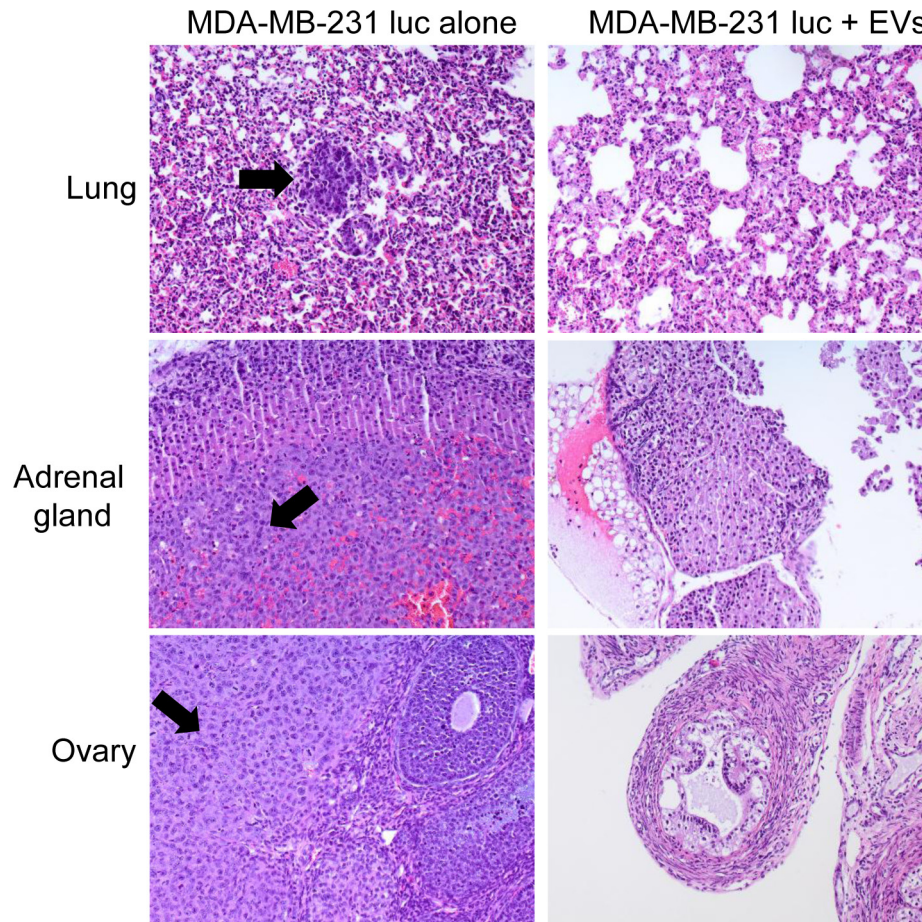


Stromal cell extracellular vesicular cargo mediated regulation of breast cancer cell metastasis via Ubiquitin Conjugating Enzyme E2 N pathway

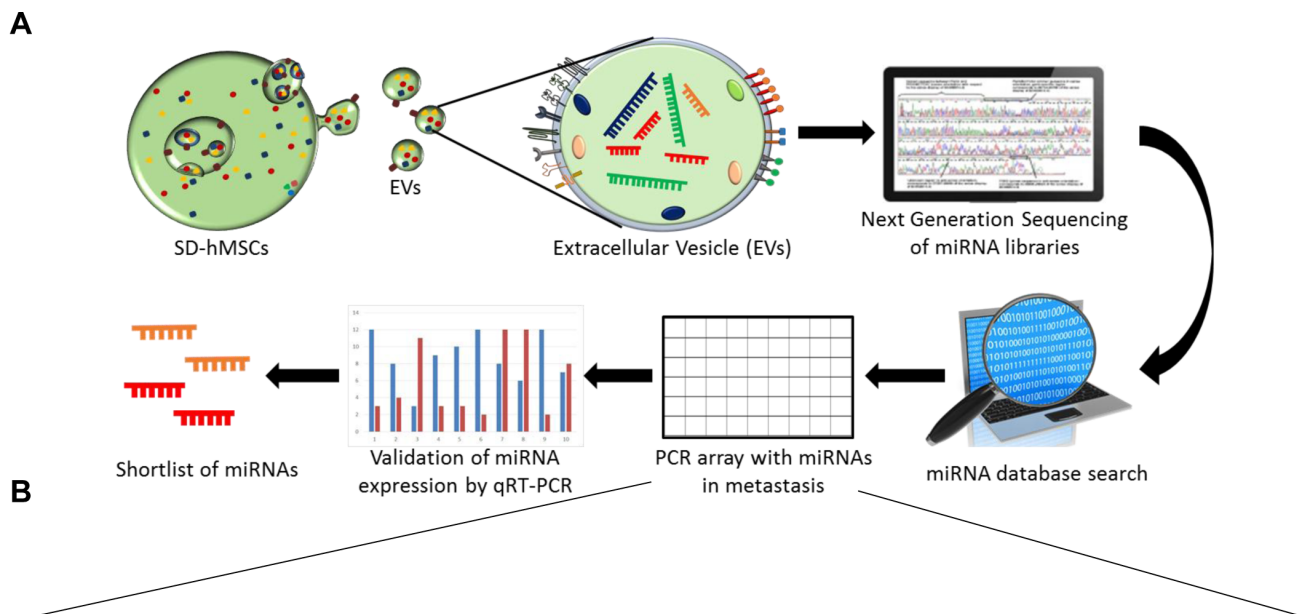
SUPPLEMENTARY MATERIALS



Supplementary Figure 1: 5×10^5 MDA-MB-231 cells and hMSC-EV-primed MDA-MB-231 cells were intracardially injected into nude mice. At the endpoint, mice were sacrificed and the total photon of lungs, liver, adrenals, legs, brain, and ovaries were measured, $n = 8$.

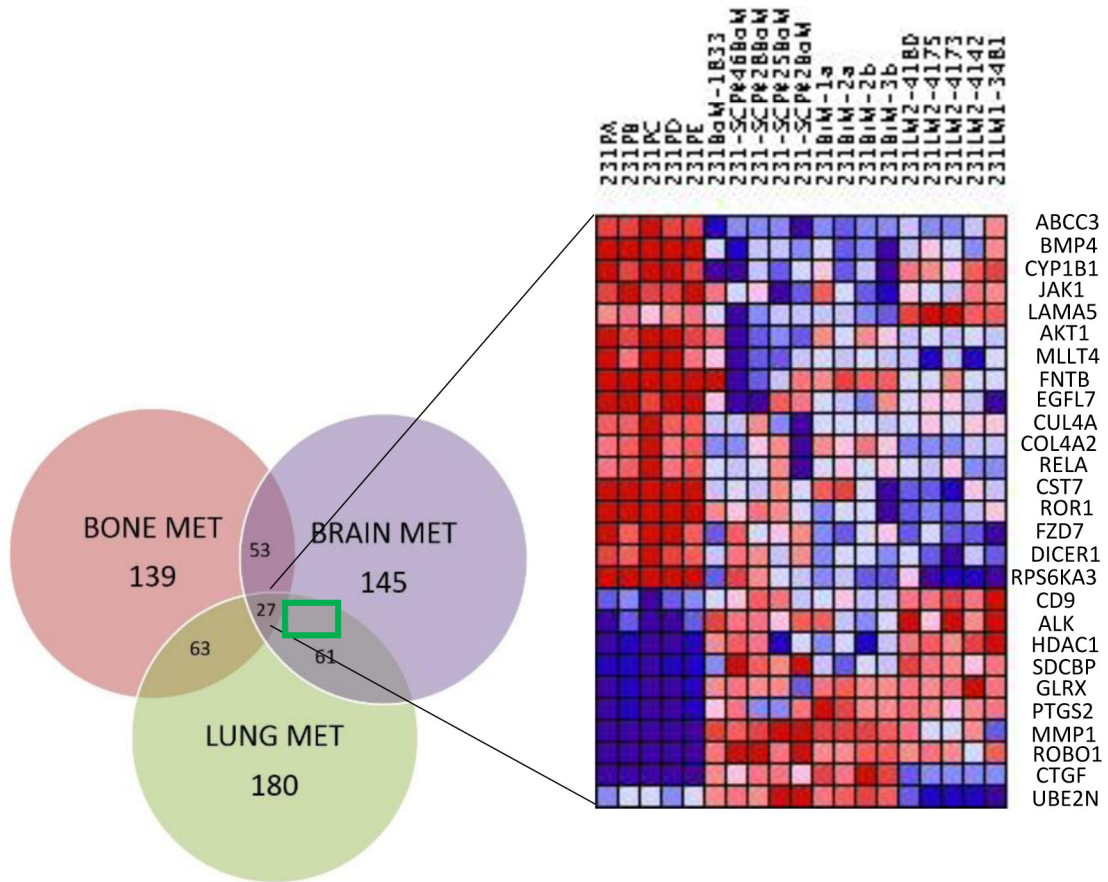


Supplementary Figure 2: Representative images of hematoxylin and eosin staining of tumor sections showing higher grade of tumors (arrows) in mice that received untreated cells compared with the hMSC-s-EV-primed cancer cells.

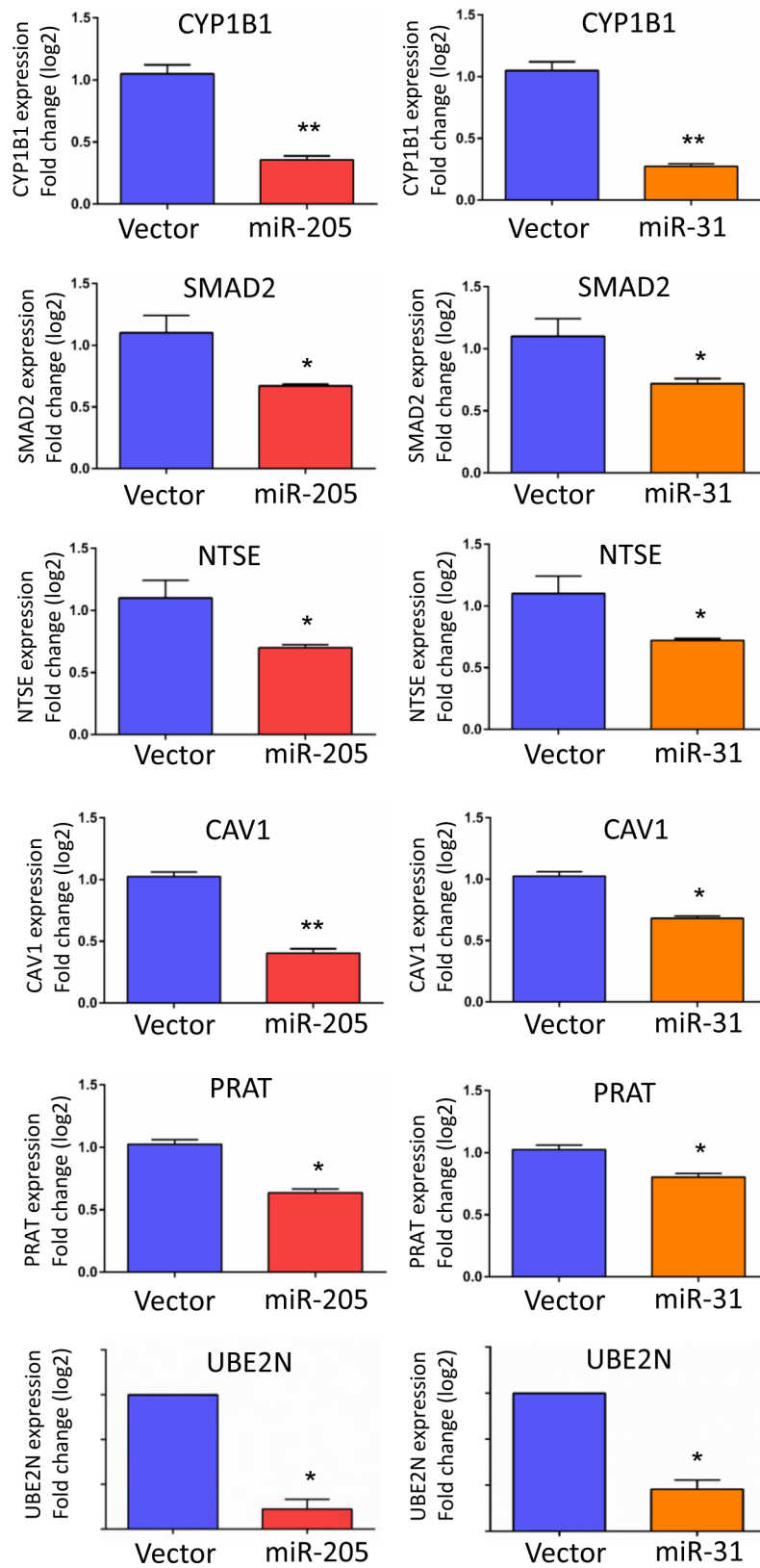


miR-30a	miR-100	miR-107	miR-10b	miR-124	miR-1258	miR-125b	miR-126	miR-127	miR-132
miR-143	miR-145	miR-146a	miR-146b	miR-148a	miR-149	miR-183	miR-185	miR-191	miR-193b
miR-195	miR-19a	miR-200c	miR-205	miR-22	miR-26a	miR-26b	miR-31	miR-335	miR-339
miR-34c	miR-379	miR-497	miR-517a	miR-9	miR-99a	5sRNA	18sRNA	RNU6-2	SNORD68

Supplementary Figure 3: (A) Schematic overview of the in silico procedures used to shortlist the miRNAs in metastasis. The experimental approach used to validate the shortlisted miRNAs is also depicted. (B) The panel of 36 miRNAs that have a known role in metastasis.



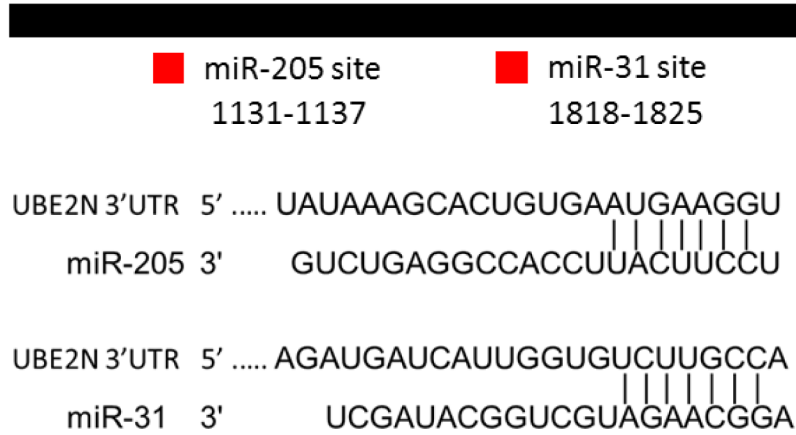
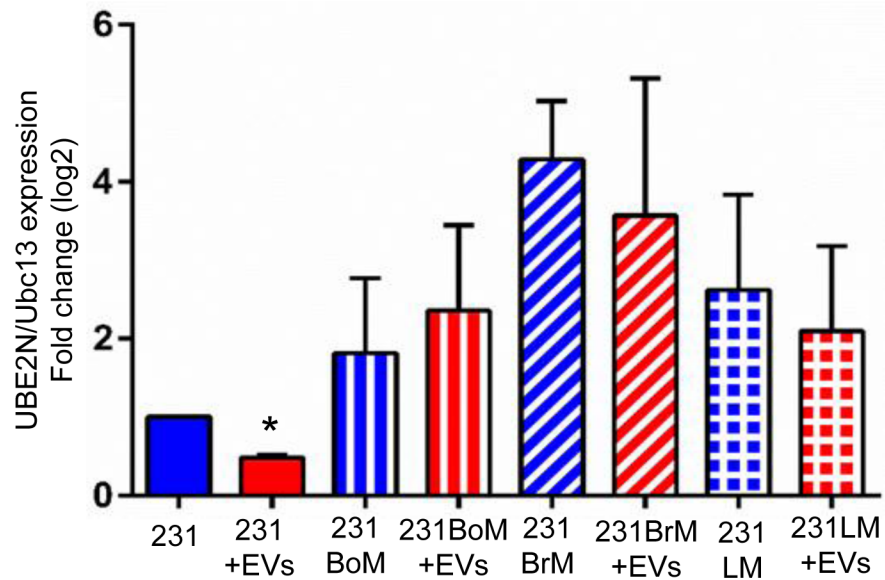
Supplementary Figure 4: Microarray clustering analysis of GEO datasets. A heat map was generated for the 27 genes out of 281 that were significantly up- or downregulated in the metastatic sublines compared with parental cells (MDA-MB-231).



Supplementary Figure 5: Real-time PCR data showing the significant down-regulation of the target genes upon expression of miR-205 and miR-31 by lentiviral transductions.

A

Human UBE2N 3'UTR (length:5179)

**B**

Supplementary Figure 6: (A) Schematic representation of the UBE2N 3'-UTR with binding sites for miR-205 and miR-31 and sequence alignment of predicted miR-205 and 31 binding sites on UBE2N 3'-UTR. Complementary sequences of miR-205 and 31 to mammalian UBE2N 3'-UTR are shaded red. (B) MDA-MB-231, 231-BM, 231-BrM, and 231-LM cells were treated with hMSC-EVs, and the UBE2N/Ubc13 levels were measured by RT-PCR.