# Proinflammatory macrophage-derived microvesicles exhibit tumor tropism dependent on CCL2/CCR2 signaling axis and promote drug delivery *via* SNARE-mediated membrane fusion

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## SUPPLEMENTARY FIGURES

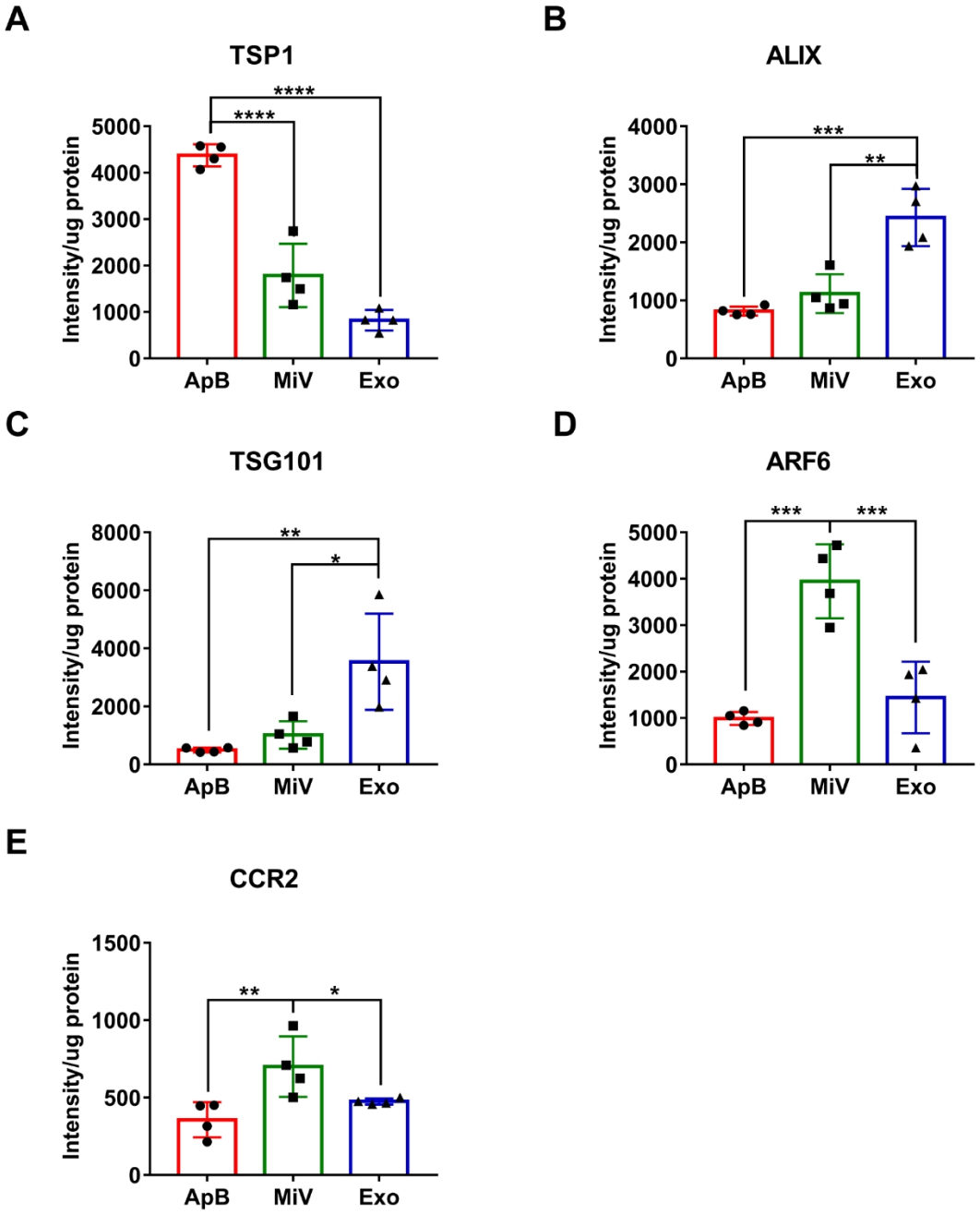


**Figure S1.** (A-E) Quantitative protein expression levels of EV subtypes by western blotting analysis (n = 4). The data were shown as mean ± s.d., * was $p < 0.05$, ** was $p < 0.01$, *** was $p < 0.001$, **** was $p < 0.0001$ by one-way ANOVA test.

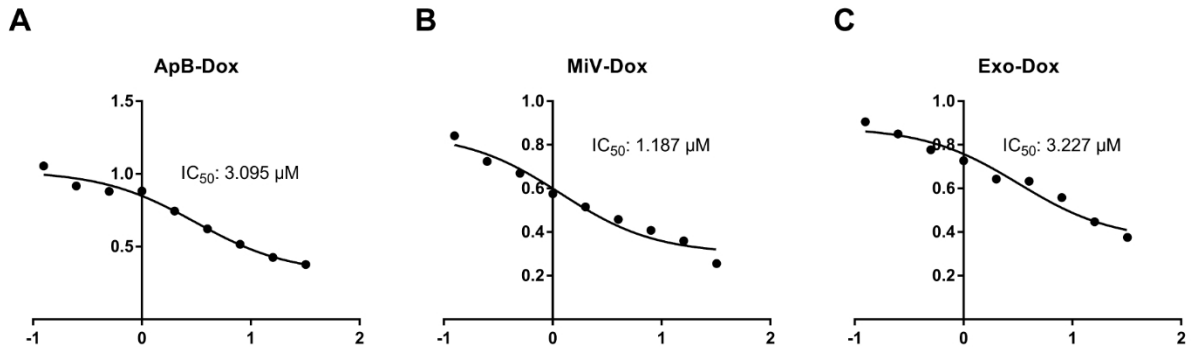


**Figure S2.** The $IC_{50}$ value of ApB-Dox, MiV-Dox and Exo-Dox calculated by the GraphPad Prism7 software.

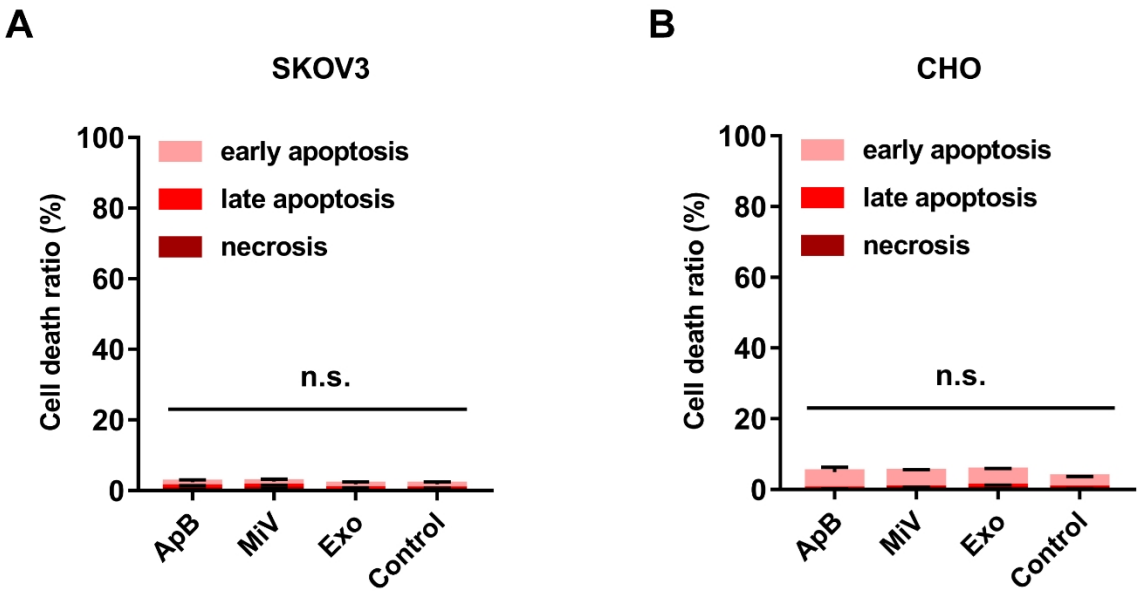


**Figure S3.** Annexin V-FITC/PI assay for apoptosis detection of SKOV3 cells (A) and CHO cells (B) under the treatment of drug-free EVs for 24 h. Quantitative data showed the percentage of early apoptosis, late apoptosis and necrosis cells. The data were shown as mean ± s.d., n.s. was $p > 0.05$ by one-way ANOVA test.

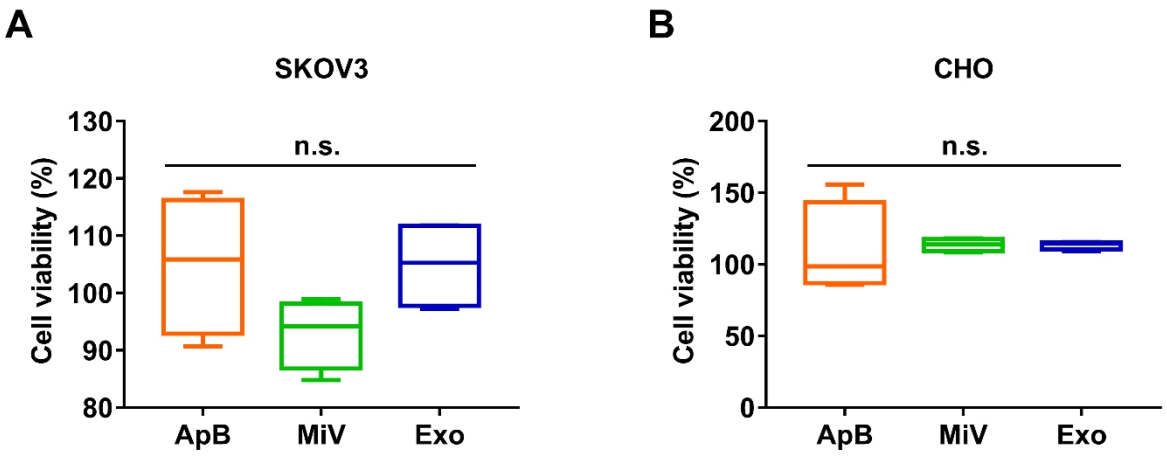


**Figure S4.** Cell viability of SKOV3 cells (A) and CHO cells (B) treated with drug-free EVs for 24 h. The data were shown as mean ± s.d., n.s. was $p > 0.05$ by one-way ANOVA test.

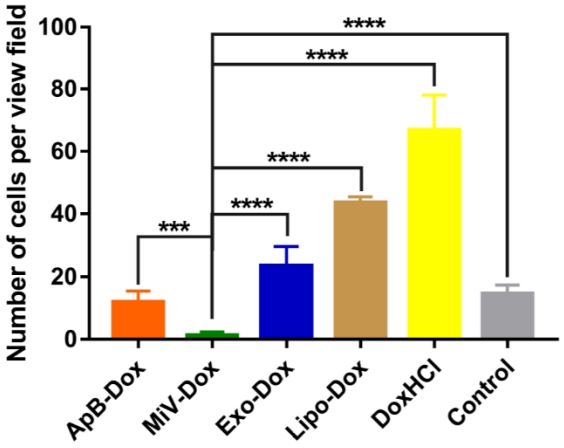


**Figure S5.** Quantification of the number of live cells per each view field from corresponding fluorescence images present in Figure 4I (n = 11). The data were shown as mean ± s.d., *** was $p < 0.001$, **** was $p < 0.0001$ by one-way ANOVA test.

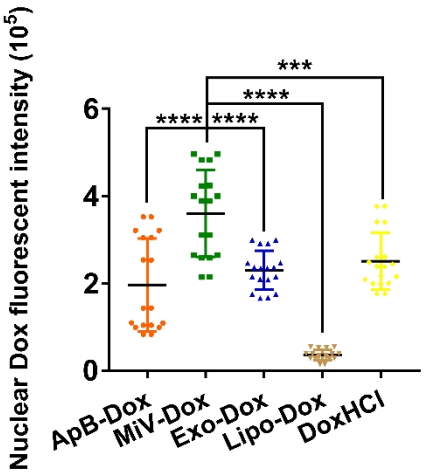


**Figure S6.** The Dox fluorescence signal in SKOV3 nuclei was quantificationally analyzed by ImageJ software (n = 20). The data were shown as mean ± s.d., *** was $p < 0.001$, **** was $p < 0.0001$ by one-way ANOVA test.

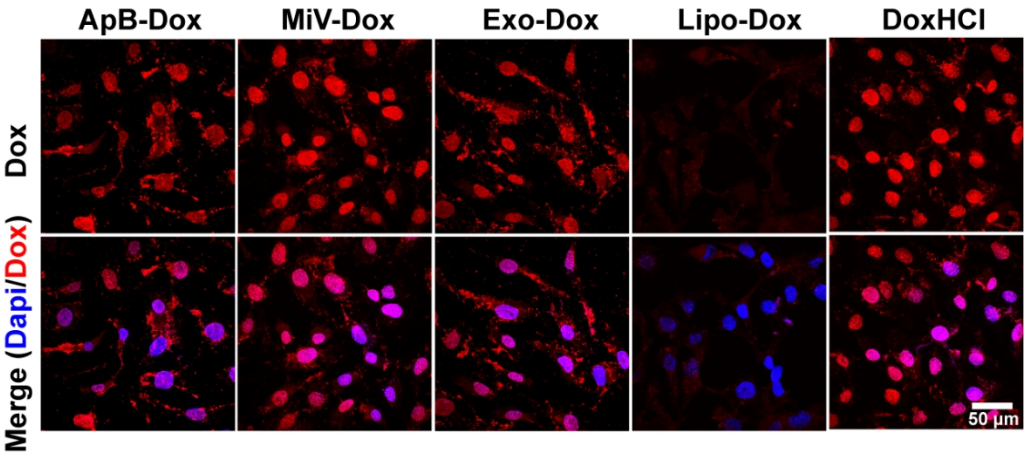


**Figure S7.** Confocal laser scanning microscopy images showed the intracellular distribution of Dox of SKOV3 cells after treated with various formulations at 4 h. The nuclei were stained with DAPI (blue). Dox produced the red fluorescence. The merged images were the overlay of two individual images. Scale bar was 50 μm.

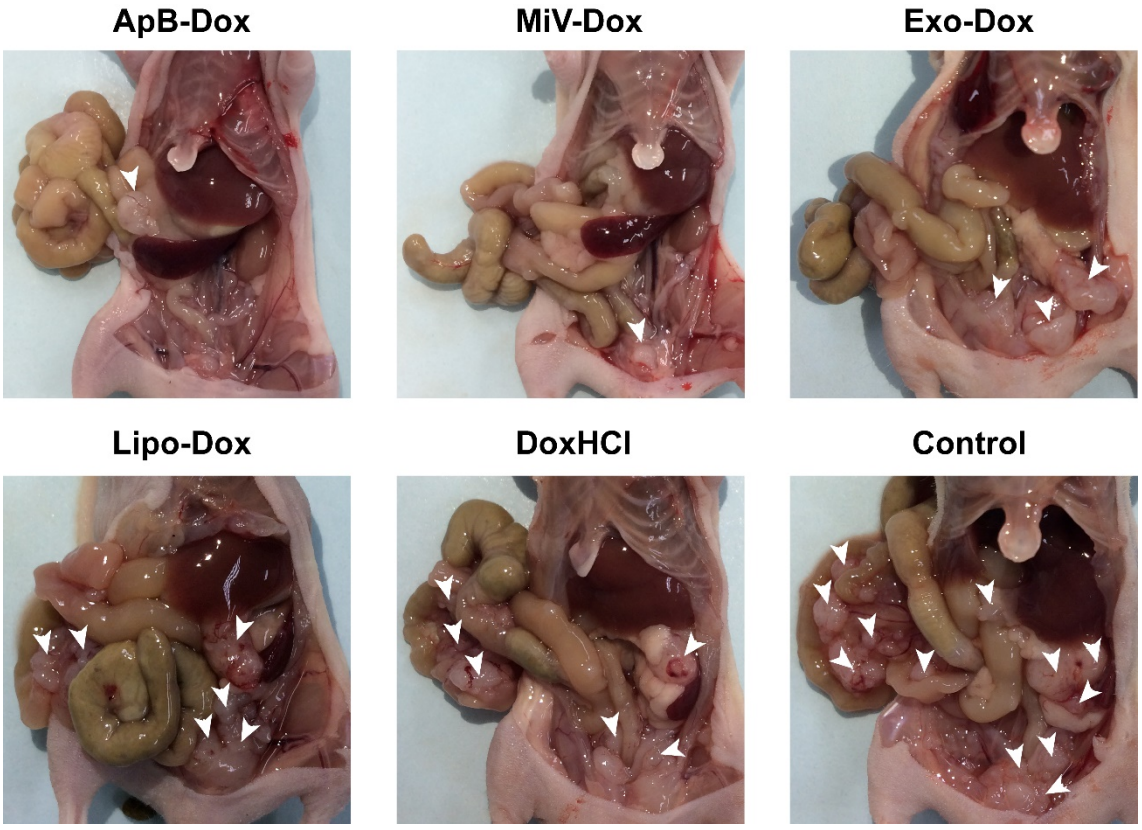


**Figure S8.** Representative microscopic images of peritoneal cavity in mice from six experimental groups on the 28th treatment day. White arrow head indicated tumor nodules.

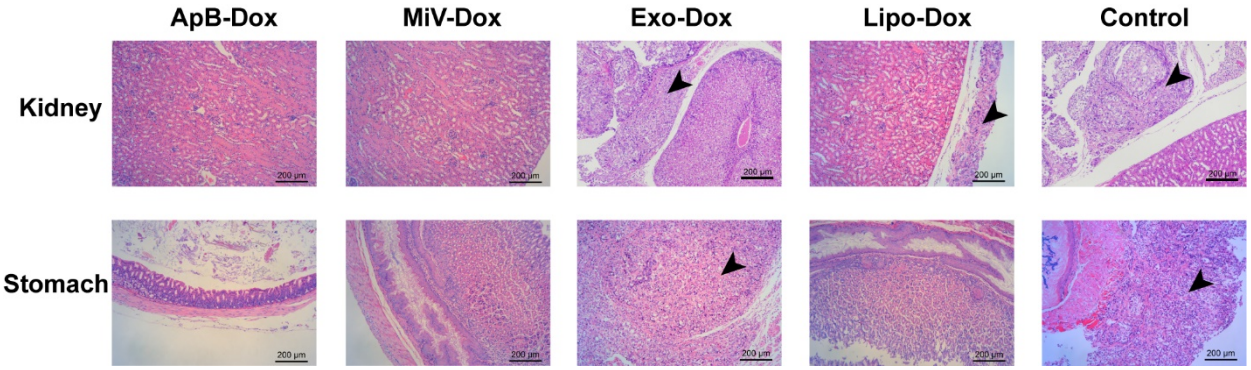


**Figure S9.** H&E stained kidneys and stomachs from control and treated tumor-bearing mice on day 28. Tumor nodules were indicated by arrow heads. Scales bar were shown in each image.


**Figure S10.** *In vivo* safety and toxicity evaluation in mice. $1 \times 10^7$ SKOV3 cells were injected into the abdomen of the BALB/c nude mice followed by serial imaging studies in 3-days intervals from day 7.

**Table S1.** Encapsulation efficiency (EE) of Dox in each EV subtype.

| | ApB | MiV | Exo |
|---|---|---|---|
| EE (%) | 96.70 ± 0.38 | 97.69 ± 0.91 | 96.95 ± 1.47 |