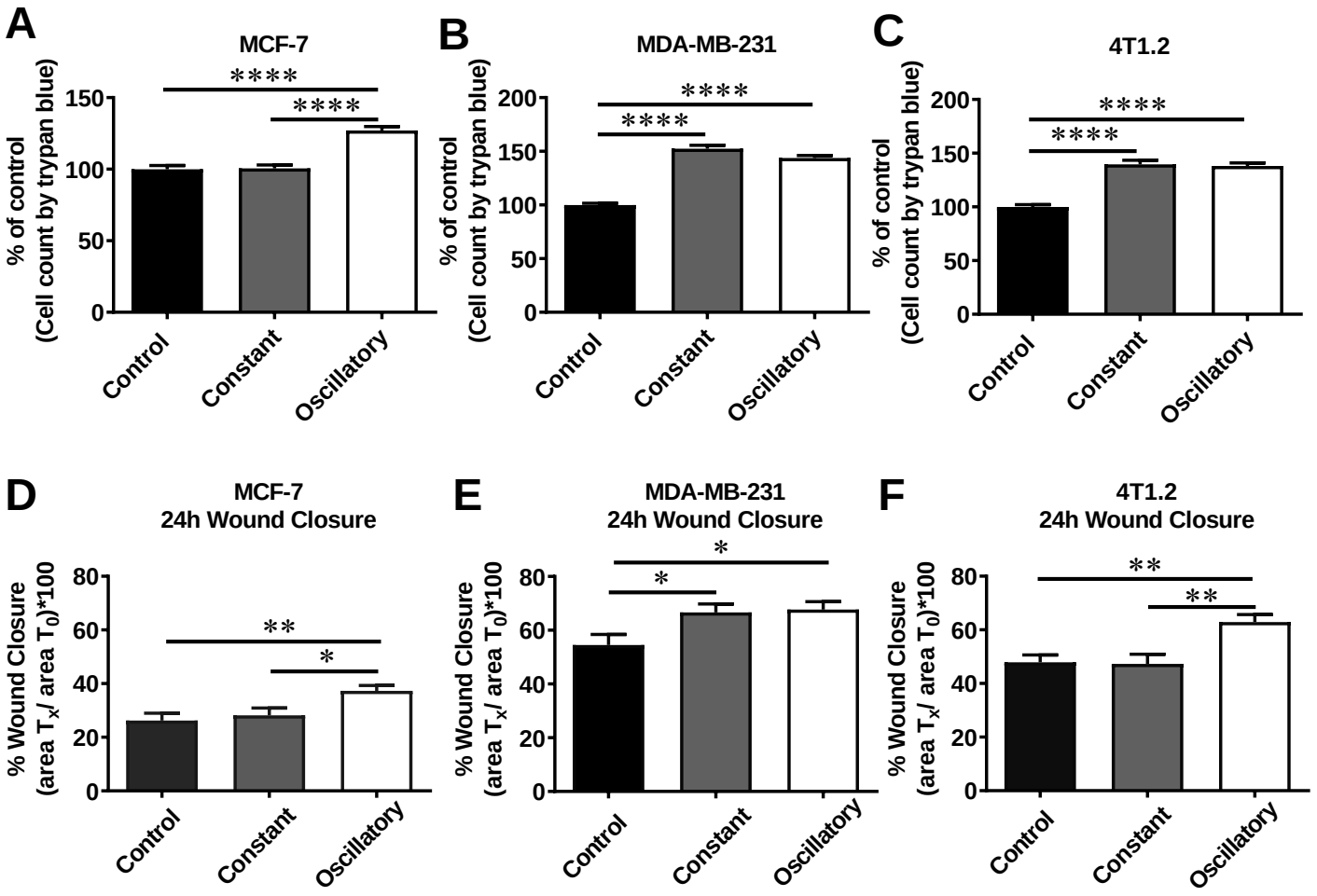
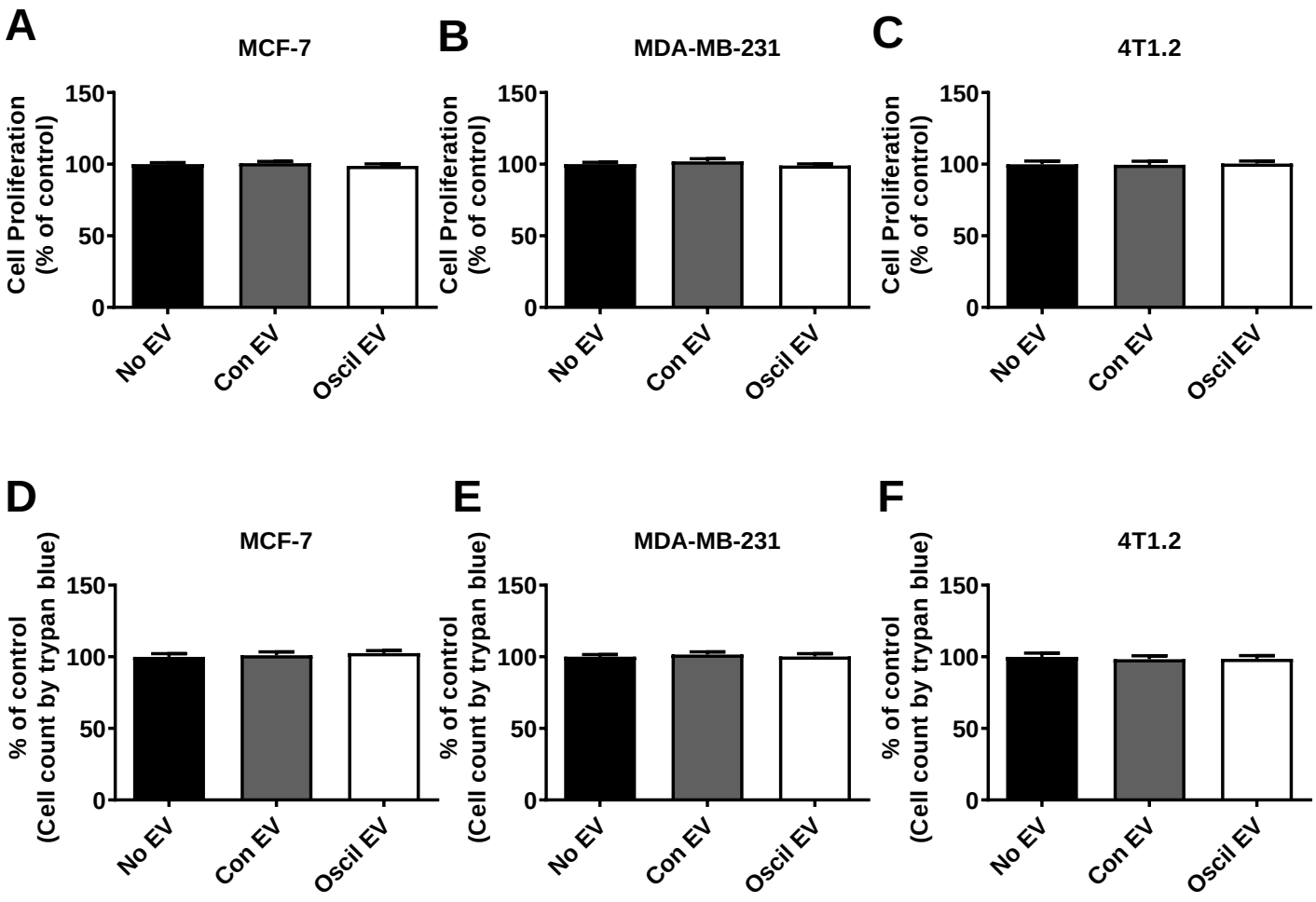
Supplemental Figure 1



Supplemental Figure 2



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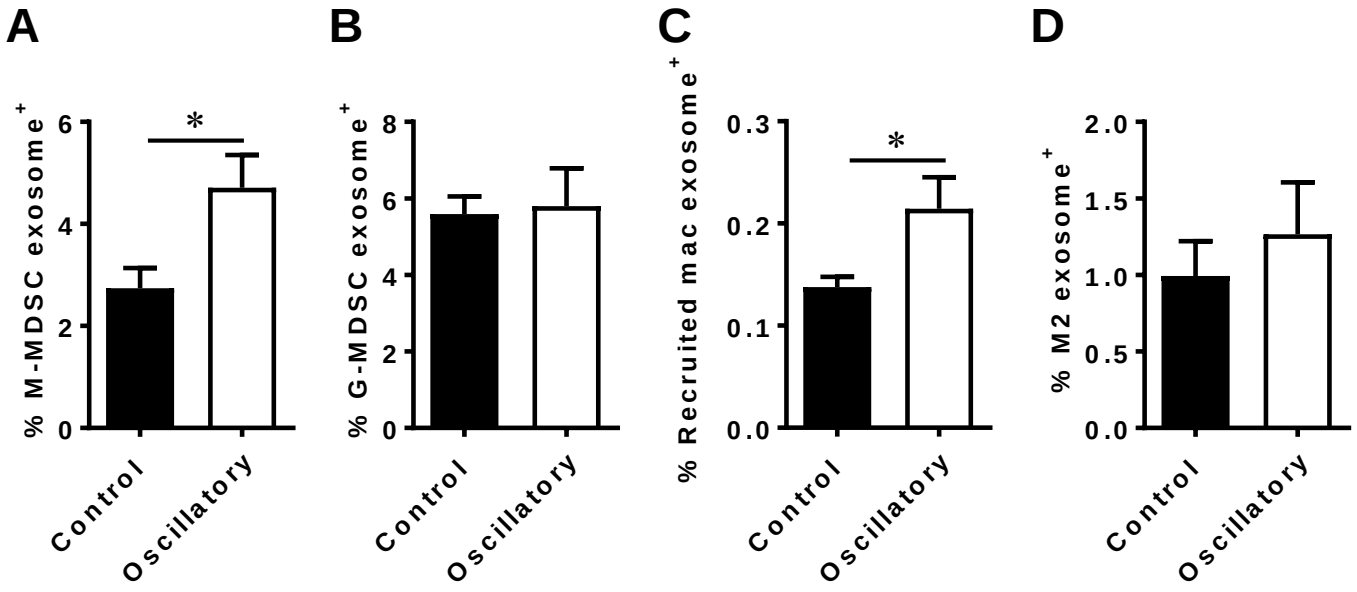

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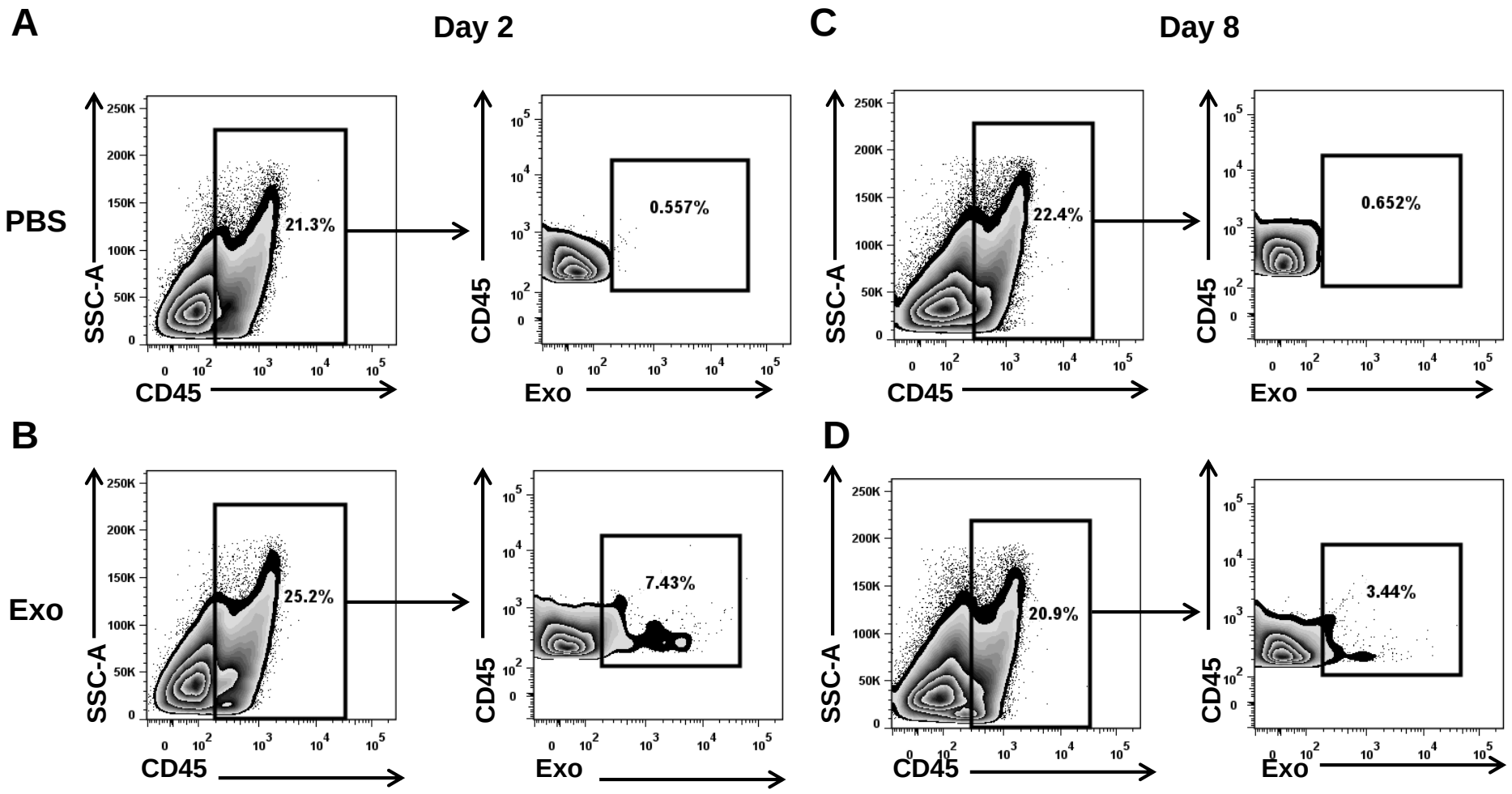

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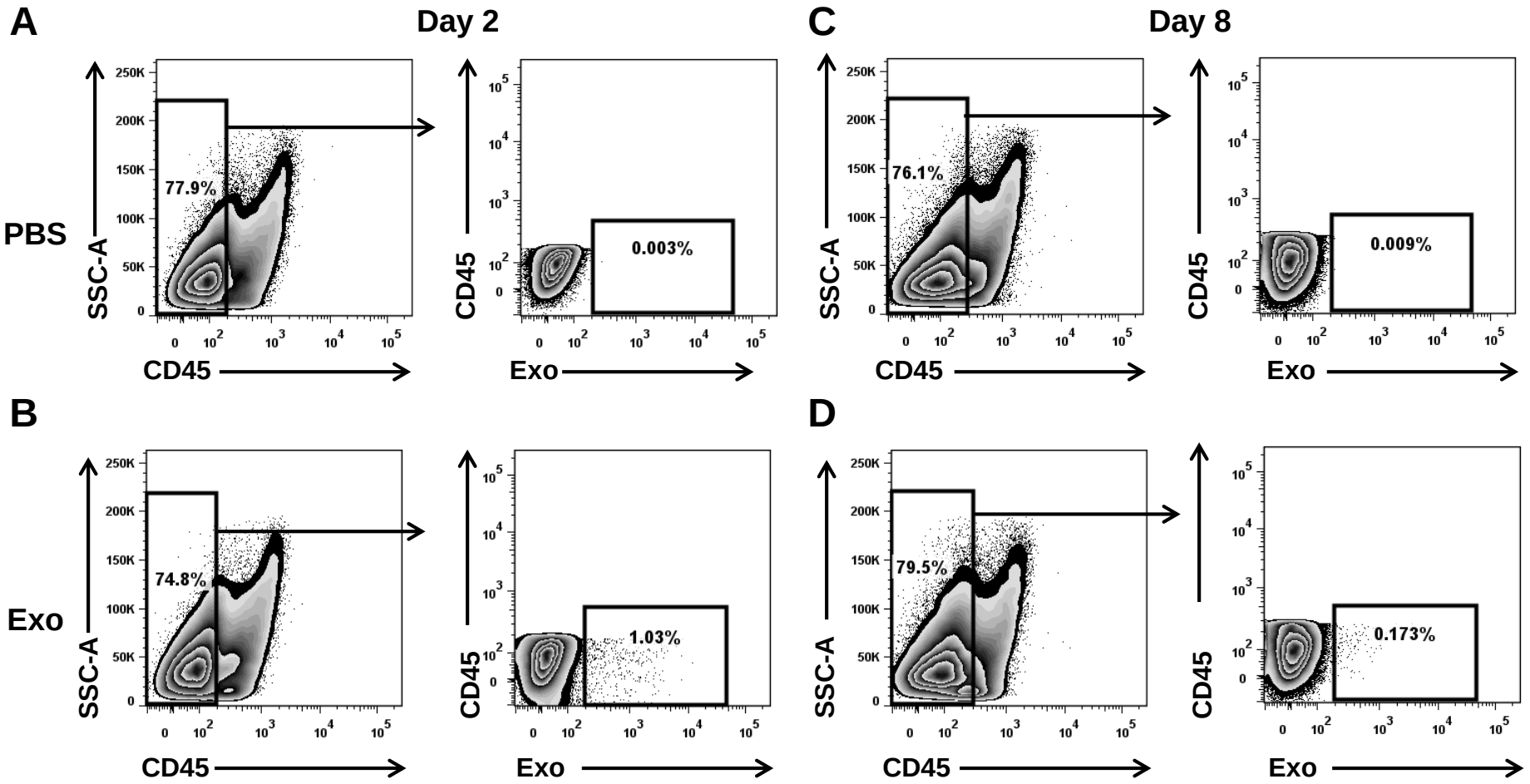

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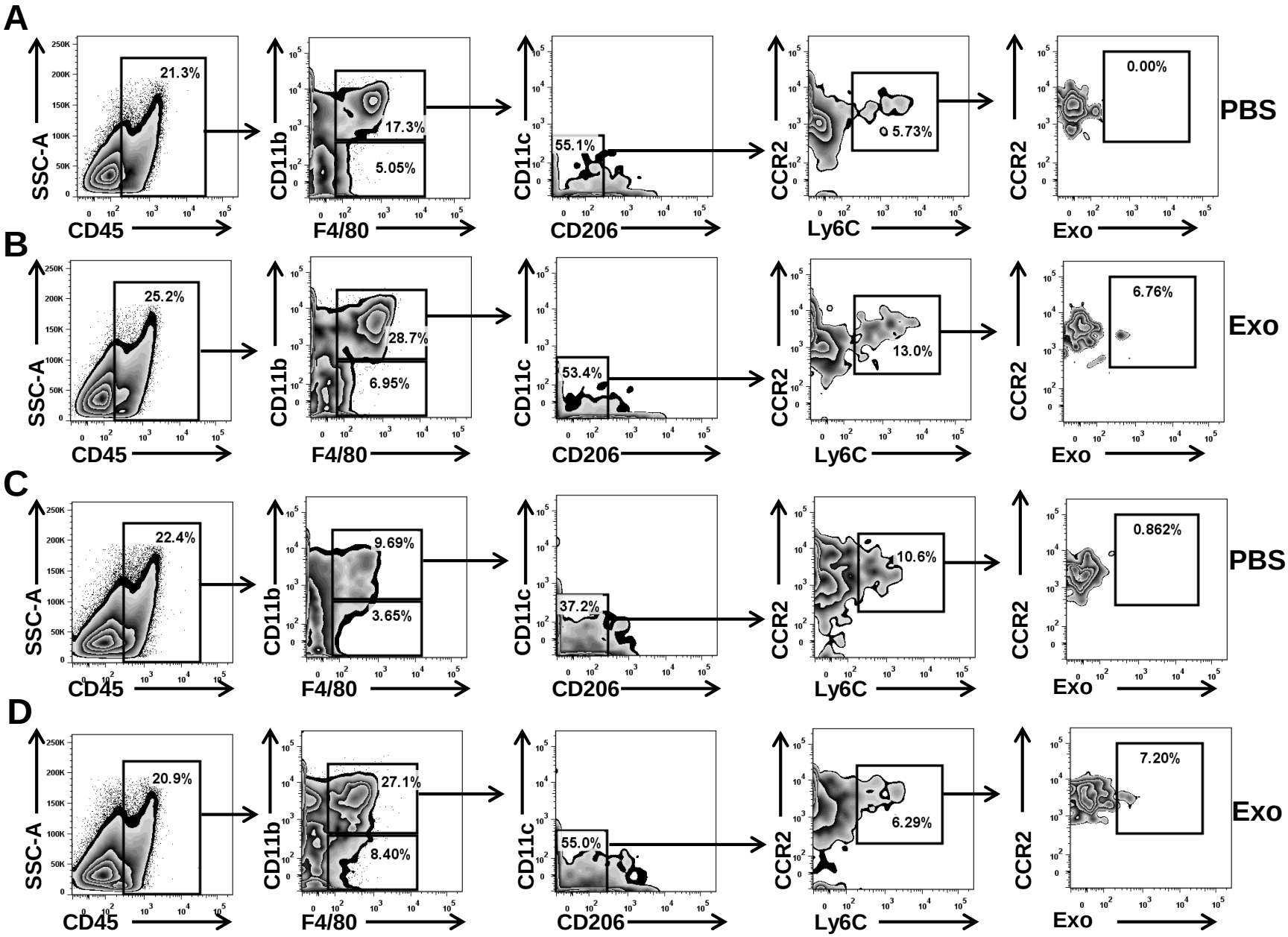

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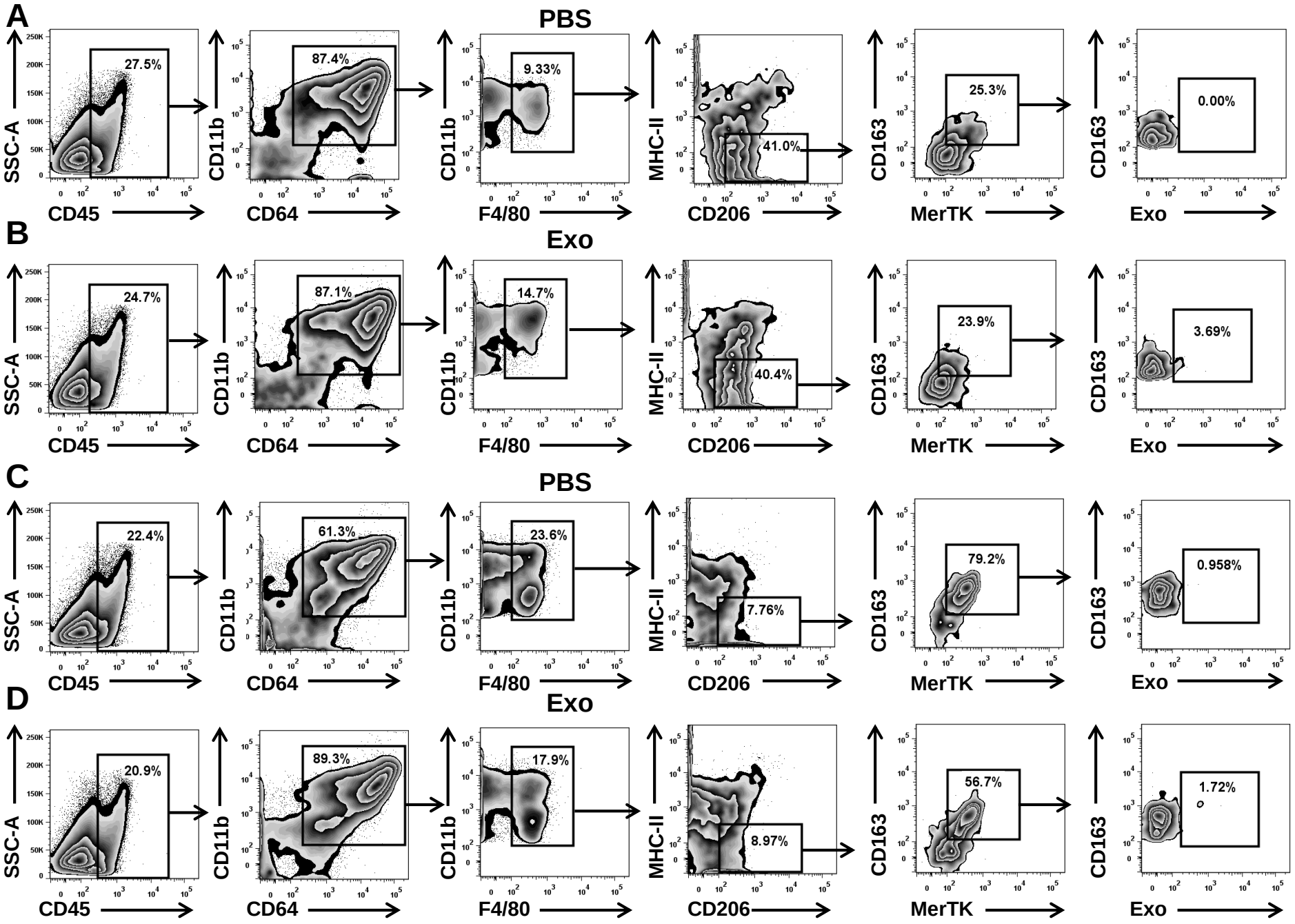
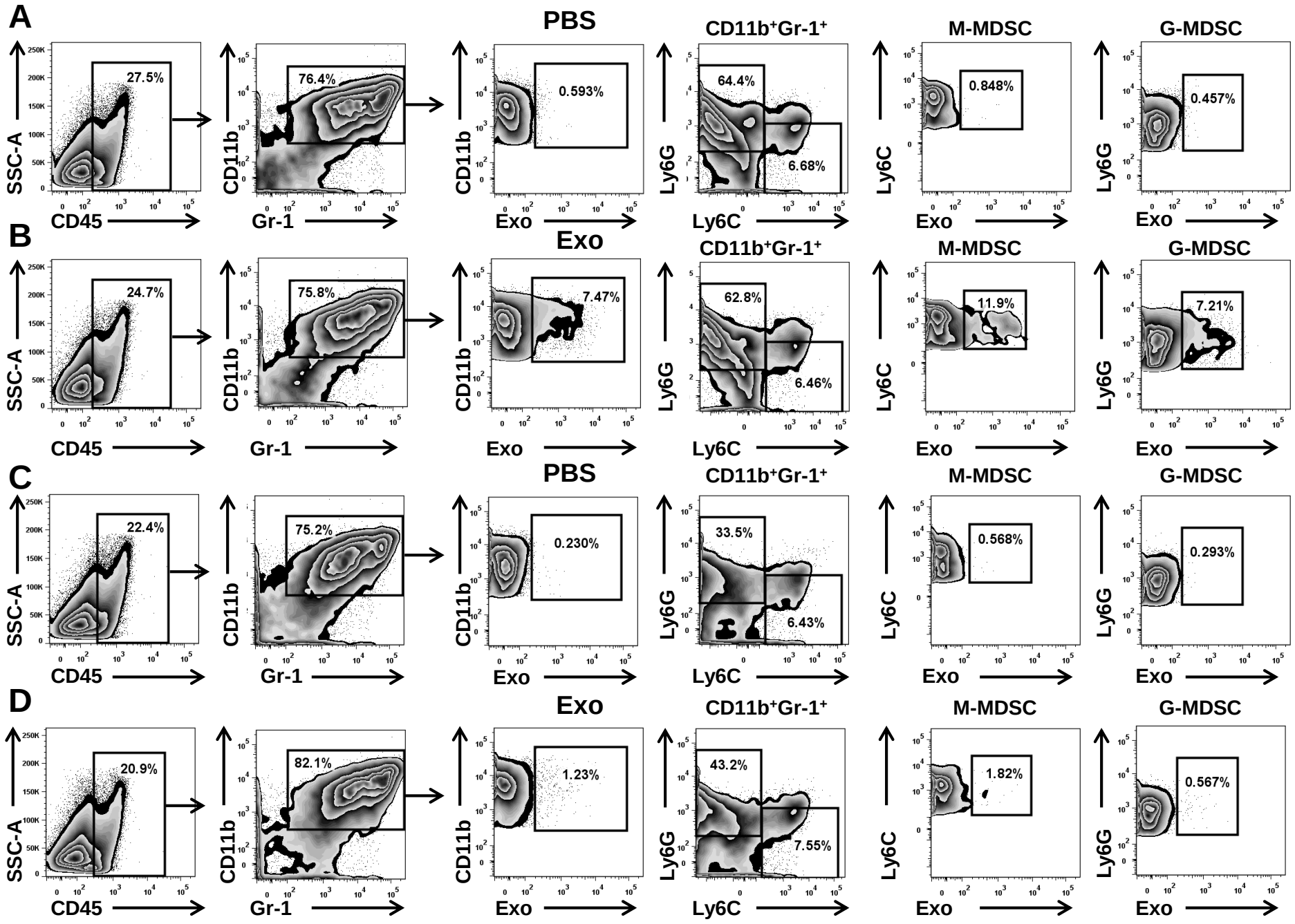
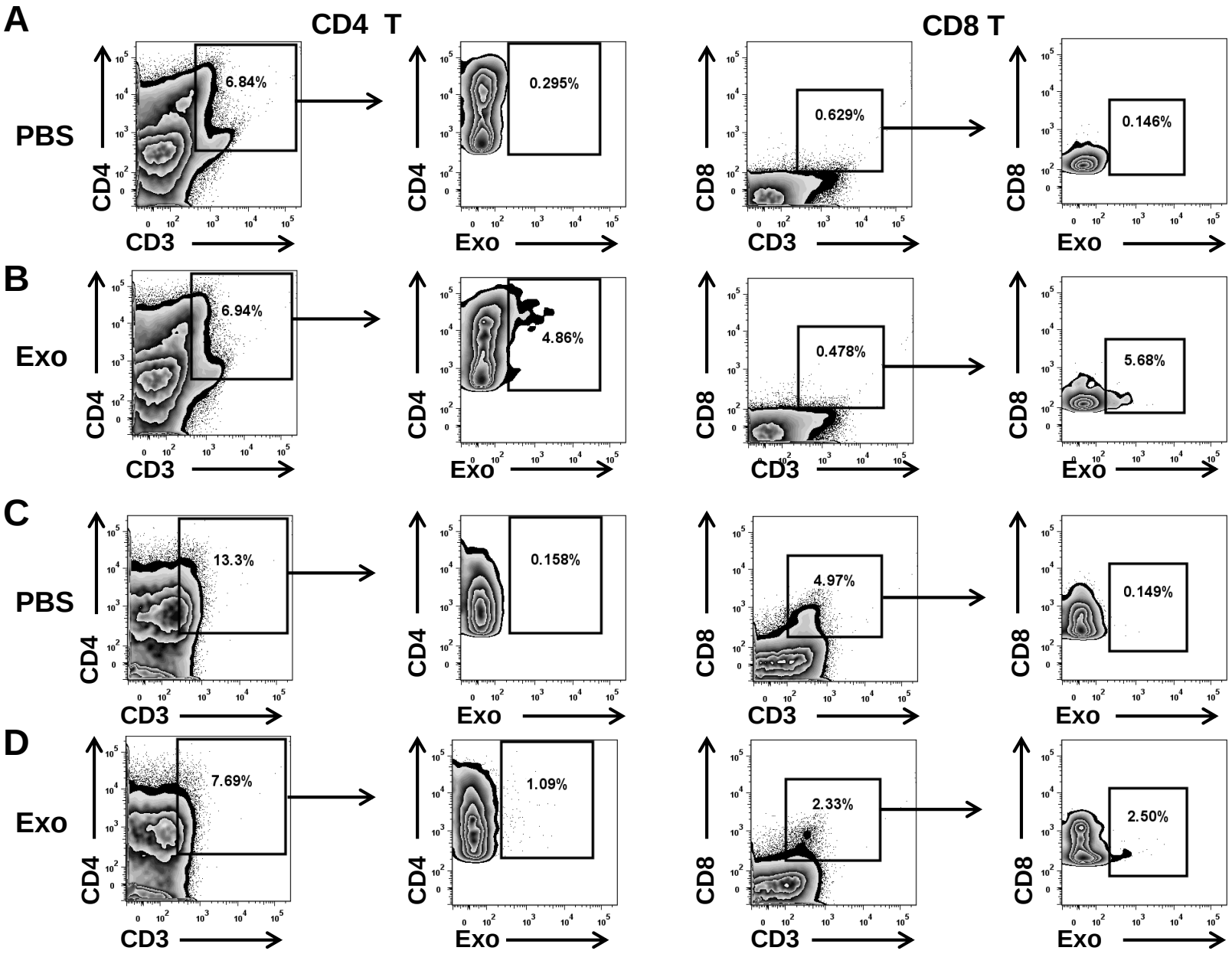


Supplemental Figure 8



Supplemental Figure 9



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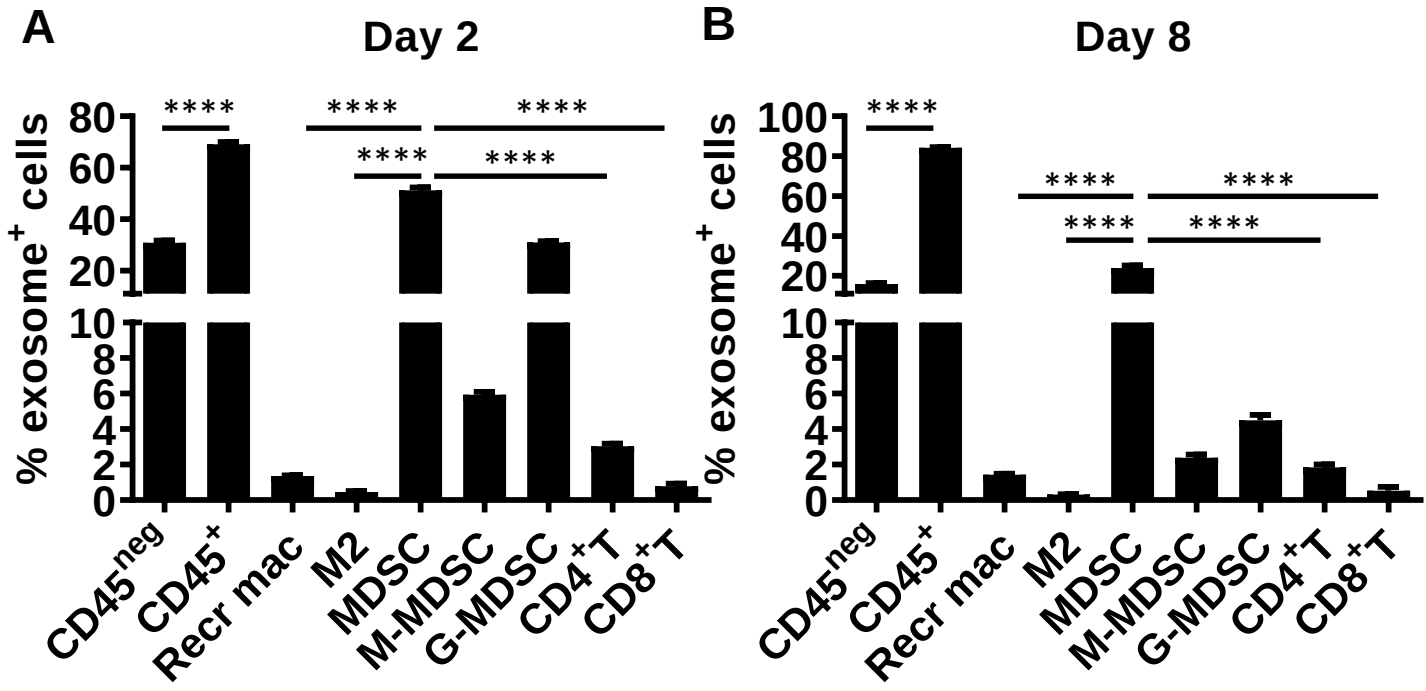
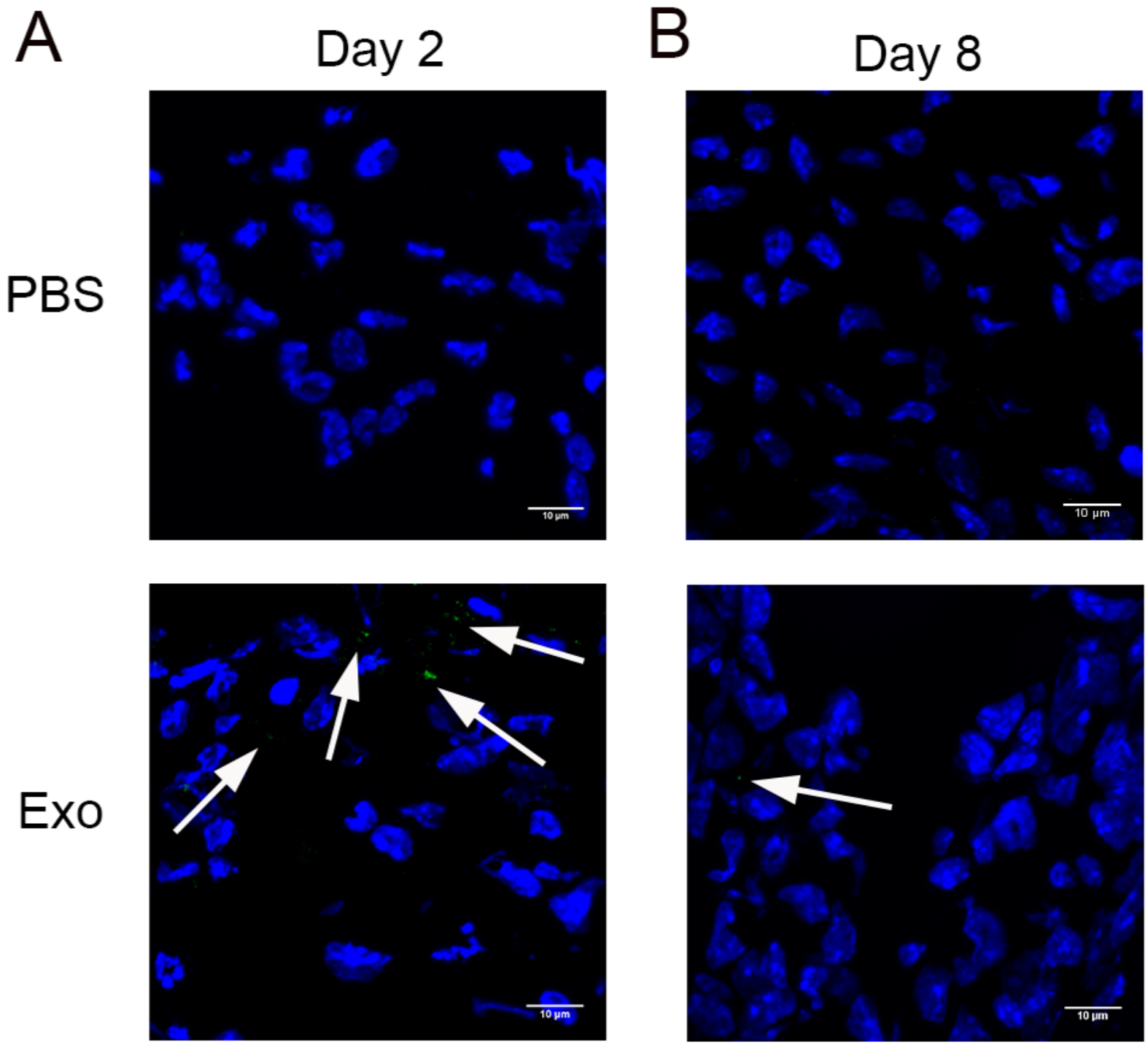


Supplemental Figure 11



Supplementary figure legends

Supplemental Fig. 1 Cell count and wound closure of breast cancer cells changes in response to strain. MCF-7 cells, MDA-MB-231 cells, and 4T1.2 cell were exposed to 10% uniaxial constant or oscillatory strains for 48 hours. 5 x 10^4 MCF-7 cells (**a**), 2.5 x 10^4 MDA-MB-231 cells (**b**) and 4T1.2 cells (**c**) were seeded into 96-well plates and cultured for 48 hours. Live cells were measured by trypan blue exclusion. Cell counts were normalized with those of control cells without exposure to strain. Migration of breast cancer cells were measured by scratch assay. Percentages of wound closure were measured under microscope 24 hours after MCF-7 cells (**d**), MDA-MB-231 cells (**e**) and 4T1.2 cells (**f**) grew confluent and made the scratch. ∗ $P < 0.05$; ∗∗, $P < 0.01$; ∗∗∗, $P < 0.001$.

Supplemental Fig. 2 Proliferation and cell count of breast cancer cells co-cultured with exosomes derived from breast cancer cells with or without exposure to oscillatory strain. Exosomes were isolation from conditioned media of MCF-7 cells, MDA-MB-231 or 4T1.2 cells with or without exposure to oscillatory strain by using the Total Exosome Isolation kit. 5 x 10^4 MCF-7 cells, 2.5 x 10^4 MDA-MB-231 cells and 4T1.2 cells were co-cultured in the absence or presence of exosomes derived from cancer cells with or without exposure to oscillatory strain at 10:1 ratio (10 exosomes per cell) for 48 hours. Cell proliferation was evaluated by MTT assay. The cell proliferation rates were normalized to those of the control cells cultured in the absence of exosomes. **a** The cell proliferation rates of MCF-7 cells co-cultured with exosomes derived from MCF-7 with or without exposure to

oscillatory strain. **b** The cell proliferation rates of MDA-MB-231 cells co-cultured with exosomes derived from MDA-MB-231 cells with or without exposure to oscillatory strain. **c** The cell proliferation rates of 4T1.2 cells co-cultured with exosomes derived from 4T1.2 cells with or without exposure to oscillatory strain. 5 x 10^4 MCF-7 cells (**d**), 2.5 x 10^4 MDA-MB-231 cells (**e**) and 4T1.2 cells (**f**) were co-cultured with or without exosomes as described above. Live cells were measured by trypan blue exclusion. Cell counts were normalized with those of control cells cultured in the absence of exosomes.

Supplemental Fig. 3 Exosomes are internalized by immunosuppressive cells in the TME. Six- to eight-week-old female BALB/c mice were injected in the fourth mammary fat pad with 5 x 10^5 PKH67 labeled 4T1.2 cells preconditioned with oscillatory strain or unstrained cells. The internalization of exosomes by immunosuppressive cells in the TME was measured by PKH67 positive signal in MDSCs and macrophages by FACS analysis on day 14 after tumor implantation. **a** The percentage of exosome$^+$ M-MDSC in the TME was determined by FACS analysis on day 14 post tumor challenge (n = 5 mice/group). **b** The percentage of exosome$^+$ G-MDSC in the TME was evaluated by FACS analysis on day 14 post tumor challenge (n = 5 mice/group). **c** The percentage of exosome$^+$ recruited macrophages in the TME was determined by FACS analysis on day 14 post tumor challenge (n = 5 mice/group). **d** The percentage of exosome$^+$ M2 macrophages in the TME was evaluated by FACS analysis on day 14 post tumor challenge (n = 5 mice/group). Statistical significance was determined using unpaired t tests. * $P < 0.05$.

Supplemental Fig. 4 Internalization of exosomes by $CD45^+$ cells. Six to eight-week-old female BALB/c mice were injected in the fourth mammary fat pad with 5 x 10^5 4T1.2 cells. At day 6, 7.5 x 10^8 PKH67-labeled 4T1.2 cell-derived exosomes or PBS were injected into the tumor nodule. On day 2 (**a** and **b**) and day 8 (**c** and **d**) after exosome injection, tumor tissues were harvested. The internalization of exosomes by $CD45^+$ cells was determined by FACS analyses.

Supplemental Fig. 5 Internalization of exosomes by $CD45^-$ cells. Six to eight-week-old female BALB/c mice were injected in the fourth mammary fat pad with 5 x 10^5 4T1.2 cells. On day 6, 7.5 x 10^8 PKH67-labeled 4T1.2 cell-derived exosomes or PBS were injected into the tumor nodule. On day 2 (**a** and **b**) and day 8 (**c** and **d**) after exosome injection, tumor tissues were harvested. The internalization of exosomes by $CD45^-$ cells was determined by FACS analyses.

Supplemental Fig. 6 Internalization of exosomes by recruited macrophages. Six to eight-week-old female BALB/c mice were injected in the fourth mammary fat pad with 5 x 10^5 4T1.2 cells. On day 6, 7.5 x 10^8 PKH67-labeled 4T1.2 cell-derived exosomes or PBS were injected into the tumor nodule. On day 2 (**a** and **b**) and day 8 (**c** and **d**) after exosome injection, tumor tissues were harvested. The internalization of exosomes by recruited macrophages was determined by FACS analyses. Recruited macrophages were identified as $CD45^+CD11b^+F4/80^+CD11c^{neg}CD206^{neg}CCR2^+Ly6c^+$ cells.

Supplemental Fig. 7 Internalization of exosomes by M2 macrophages. Six to eight-week-old female BALB/c mice were injected in the fourth mammary fat pad with 5 x 10^5 4T1.2 cells. On day 6, 7.5 x 10^8 PKH67-labeled 4T1.2 cell-derived exosomes or PBS were injected into the tumor nodule. On day 2 (**a** and **b**) and day 8 (**c** and **d**) after exosome injection, tumor tissues were harvested. The internalization of exosomes by M2 macrophages was determined by FACS analyses. M2 macrophages were identified as $CD45^+CD11b^+CD64^+F4/80^+CD206^+MHC\text{-}II^{neg}MerTK^+CD163^+$ cells.

Supplemental Fig. 8 Internalization of exosomes by MDSCs. Six to eight-week-old female BALB/c mice were injected in the fourth mammary fat pad with 5 x 10^5 4T1.2 cells. On day 6, 7.5 x 10^8 PKH67-labeled 4T1.2-derived exosomes or PBS were injected into the tumor nodule. On day 2 (**a** and **b**) and day 8 (**c** and **d**) after exosome injection, tumor tissues were harvested. The internalization of exosomes by M-MDSCs and G-MDSCs were determined by FACS analyses. M-MDSCs were identified as $CD45^+CD11b^+Gr\text{-}1^+Ly6C^+Ly6G^-$ while G-MDSCs were identified as $CD45^+CD11b^+Gr\text{-}1^+Ly6C^-Ly6G^+$ cells.

Supplemental Fig. 9 Internalization of exosomes by T cells. Six to eight-week-old female BALB/c mice were injected in the fourth mammary fat pad with 5 x 10^5 4T1.2 cells. On day 6, 7.5 x 10^8 PKH67-labeled 4T1.2-derived exosomes or PBS were injected into the tumor nodule. On day 2 (**a** and **b**) and day 8 (**c** and **d**) after exosome injection, tumor tissues were harvested. The internalization of exosomes by $CD4^+$ T cells and $CD8^+$ T cells (**b** and **d**) were determined by FACS analyses.

Supplemental Fig. 10 Frequencies of cell subpopulations in exosomes-positive cells. Six to eight-week-old female BALB/c mice were injected in the fourth mammary fat pad with 5 x 10^5 4T1.2 cells. On day 6, 7.5 x 10^8 PKH67-labeled 4T1.2-derived exosomes or PBS were injected into the tumor nodule. On day 2 (**a**) and day 8 (**b**) after exosome injection, tumor tissues were harvested. In exosome-positive cells, the frequencies of $CD45^{neg}$ cells, $CD45^+$ cells, recruited macrophages, M2 macrophages, MDSCs, M-MDSCs, G-MDSCs, $CD4^+$ T cells and $CD8^+$ T cells were determined by FACS analyses. Statistical significance was determined by one-way ANOVA with Tukey's multiple comparisons test. ****, $P < 0.001$.

Supplemental Fig. 11 PKH67-labeled exosomes in the tumor sections. Six to eight-week-old female BALB/c mice were injected in the fourth mammary fat pad with 5 x 10^5 4T1.2 cells. On day 6, 7.5 x 10^8 PKH67-labeled 4T1.2-derived exosomes or PBS were injected into the tumor nodule. On day 2 (**a**) and day 8 (**b**) after PBS or exosome injection, tumor tissues were harvested and frozen in OCT. 6 μm sections were cut and stained with DAPI (blue). PKH67-labeled exosomes were identified as green signal. Images were taken by confocal microscopy.