

Response to Editorial Comments:

1. Please review Figure 1E. The boxes around parts of the figure look like image artifacts. If possible, can this Figure 1E be recreated?

Answer: Thank you for your suggestion. This has been revised as following.

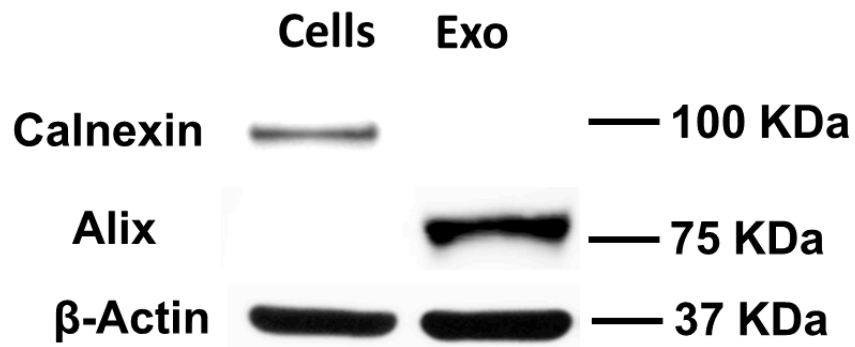


Figure 1: (E) Western Blot show that CB-SC-derived exosomes display the exosome-specific markers Alix, but negative for the endoplasmic reticulum(ER)-associated marker Calnexin.

Responses to Reviewer 4:

1. I didn't receive the video about the process of this new method.

Answer: Many thanks for your comment. The video will be scheduled to produce after this manuscript is accepted for publication.

2. In section of Result, there are no images demonstrating that exosomes released from CB-SC tagged with Dio into PBMC.

Answer: Many thanks. We performed this experiment according to your comments. PBMC were treated with 3, 3'-Diocetadecyloxycarbocyanine perchlorate (Dio)-labeled CB-SC-derived exosomes for 4 hours at 37°C in 5% CO₂ in the non-tissue culture-treated 24-well plate. The microscopy observation demonstrated the direct interaction of Dio-labeled exosomes with PBMC (**Figure 2A**). To better define which cell population interacted with the Dio-labeled exosomes, different cell compartments were gated with cell-specific markers such as CD3 for T cells, CD11c for myeloid dendritic cells (DC), CD14 for monocytes, CD19 for B cells, and CD56 for NK cells (**Figure 2B**). After an incubation for 4 hr, flow cytometry demonstrated that different blood cell compartments displayed at different median fluorescence intensity (MFI) of Dio-positive exosomes (**Figure 2C**). Notably, monocytes exhibited higher median fluorescence intensity of Dio-positive exosomes than those of other immune cells (**Figure 2C**), highlighting the monocytes were primarily targeted by the CB-SC-derived exosomes.

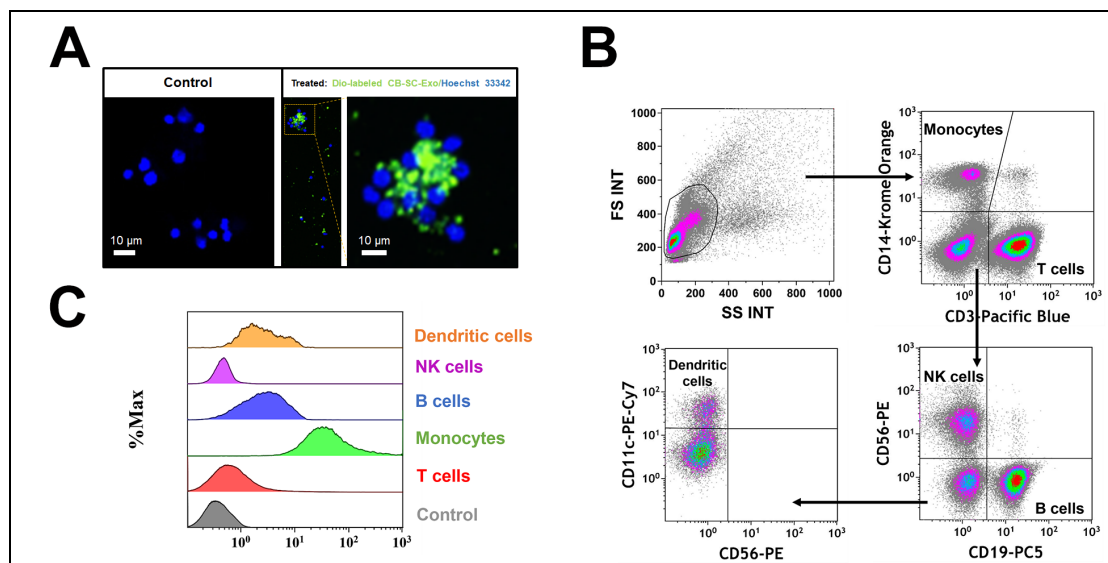


Figure 2: Interaction of CB-SC-derived exosomes with different population of PBMC. (A) The interaction of Dio-labeled CB-SC-derived exosomes (green) with PBMC (blue, nuclear staining with Hoechst 33342) was photographed with Nikon Eclipse Ti2 microscope with NIS-Elements software version 5.11.02, with a high magnification showing the distribution of Dio-labeled exosomes (green) in the PBMC cells after the co-incubation for 4 hours 5% CO₂ in the tissue culture-treated 24-well plate. *n* = 2. (B) Gating strategy for flow cytometry analysis with cell-specific surface markers for different subpopulation in PBMC, including CD3 for T cells, CD14 for monocytes, CD19 for B cells, CD56 for NK cells and CD11c for DCs. (C) Display different median fluorescence intensity (MFI) of Dio-labeled exosome among different PBMC subpopulations (e.g., T cells, Monocytes, B cells, NK cells, DCs).

3. **There are still many grammatical mistakes in this draft manuscript. It would greatly benefit from English language editing.**

Answer: Thanks for your comments. The manuscript has been revised by English editing.