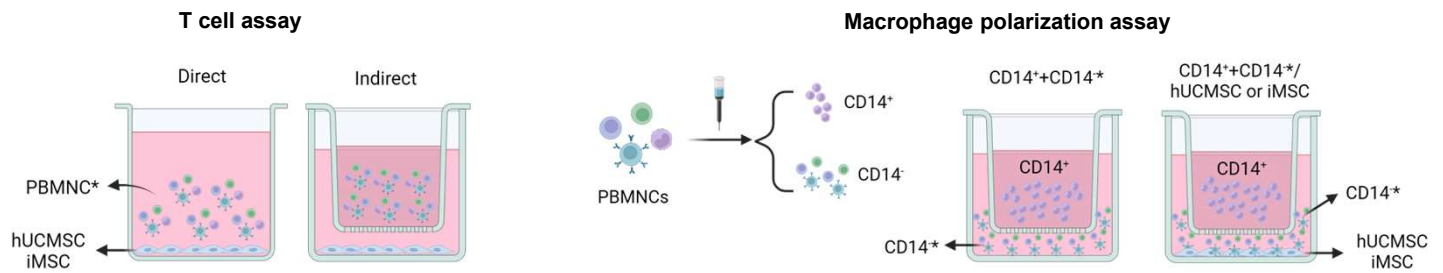


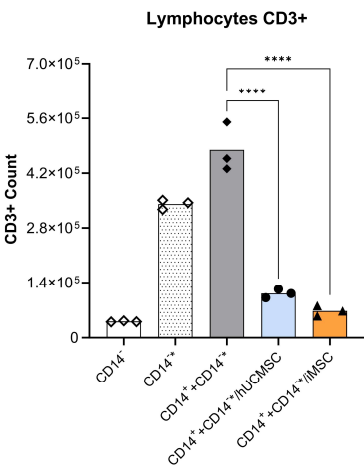
Supplemental Figure 1.

A.



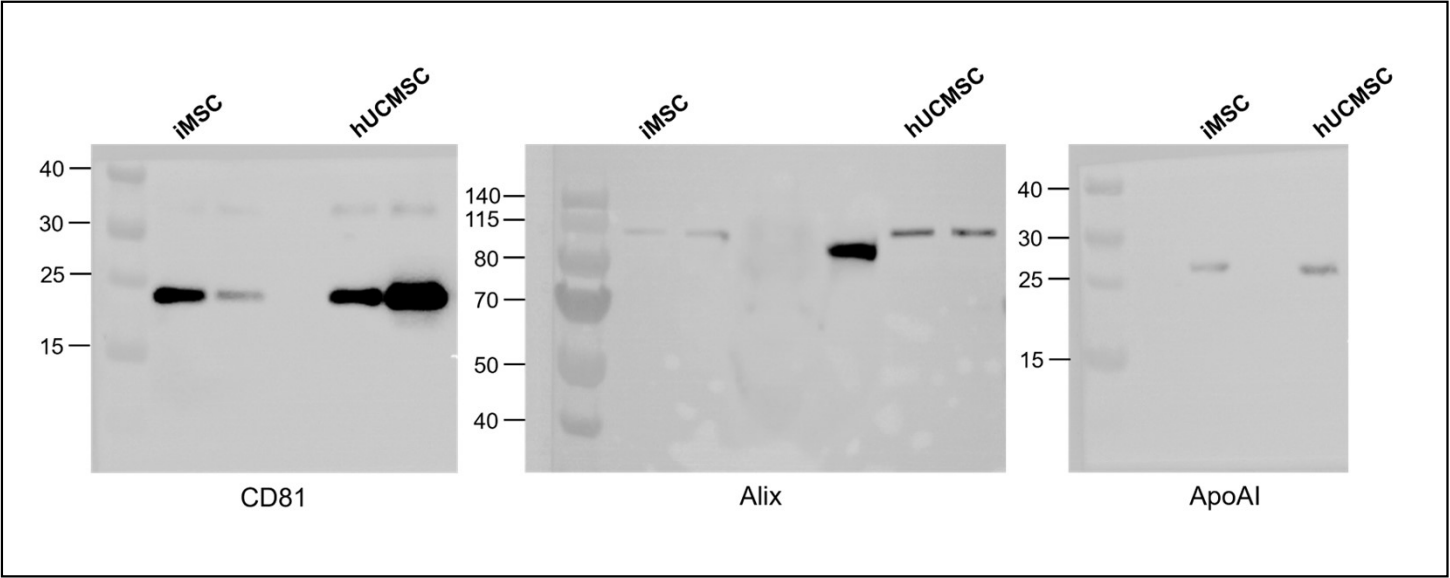
Convention	Description
PBMNC*	Bead-activated PBMNCs
PBMNC*+MSC	Bead-activated PBMNCs in co-culture with hUCMSCs or iMSCs
CD14+	Monocytes isolated from PBMNCs
CD14-	Monocytes-depleted PBMNCs
CD14+*	Monocytes-depleted PBMNCs activated with beads
CD14++CD14-*	Co-culture reference
CD14++CD14-*/MSC	Co-cultures with hUCMSCs or iMSCs

B.



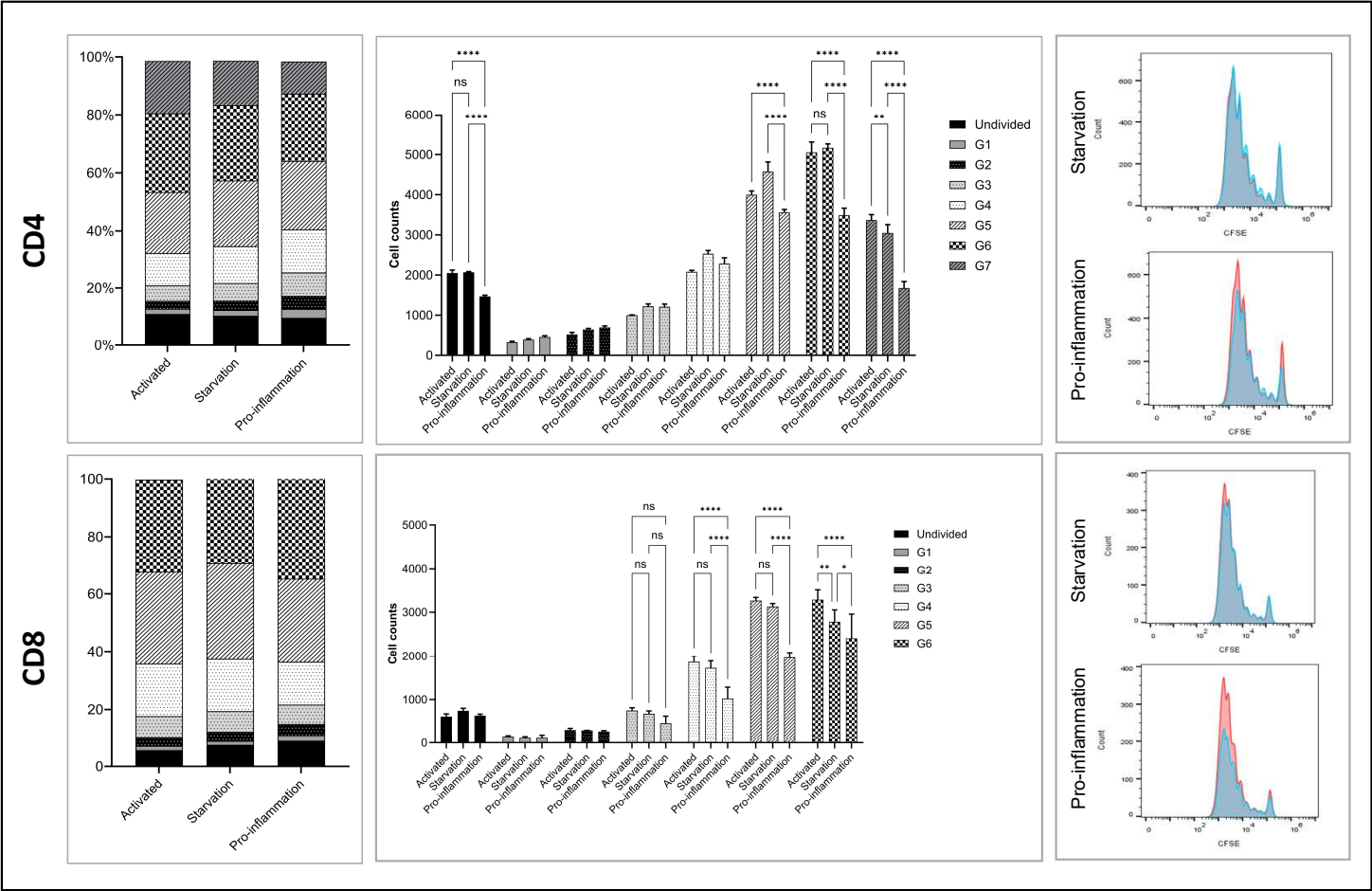
Supplemental Figure 1. (A) Diagram of the cell co-culture systems to assess T cell proliferation in direct (cell to cell) and indirect (transwell) contact with MSCs (hUCMSCs or iMSCs, left panel), and macrophage polarization (right panel). For the T cell assay MSCs were seeded into wells and after 24 h bead-stimulated PBMNC were added directly to the MSCs or in the upper camber of 0.4 μ m-pore transwell inserts. For macrophage polarization, MSCs were also seeded into wells and after 24 h bead-stimulated PBMNCs (CD14⁺) were added in the upper chamber of 0.4 μ m-pore transwell inserts. Subsequently, monocytes cells (CD14⁺) purified from PBMNCs using a positive selection magnetic were added in the upper chamber of 0.4 μ m-pore transwell inserts. **(B)** CD3⁺ T cell counts in the macrophage polarization assay. Changes in the CD3⁺ counts for monocytes (CD14⁺) co-cultured with hUCMSCs (n=3, blue bar) or iMSCs (n=3, orange bar) under an inflammation condition (CD14⁺*) were compared with the co-culture CD14⁺*CD14⁺* without MSCs. All data are presented as mean. ****: p<0.0001 by one-way ANOVA followed by Dunnett's test.

Supplemental Figure 2.



Supplemental Figure 2. Immunoblotting for CD81, Alix, and APO A I in hUCMSCs and iMSC-EVs. Original blots and images.

Supplemental Figure 3.



Supplemental Figure 3. Change in the proliferation profile of CD4+ T cells and CD8+ T cells by hUCMSCs-EVs (n=3). A detailed representation is showing the percentage of the total population in each cell division cycle (indicated as G#, left panel), as well as a total cell counts (middle panel) and representative histograms (right panel). PBMCs underwent staining with carboxyfluorescein succinimidyl ester (CFSE), were subsequently stimulated with beads, and were cultivated alongside EVs obtained from conditioned medium harvested following starvation and pro-inflammation culture conditions. After 5 days cells were stained with anti-CD3, anti-CD4 and anti-CD8 antibodies and quantified for CFSE dilution by flow cytometry. All data are presented as mean $\pm$ SD. *: $p<0.05$, **: $p<0.01$, ***: $p<0.0001$ by two-way ANOVA followed by Tukey's multiple comparisons test.

Supplemental Figure 4.

