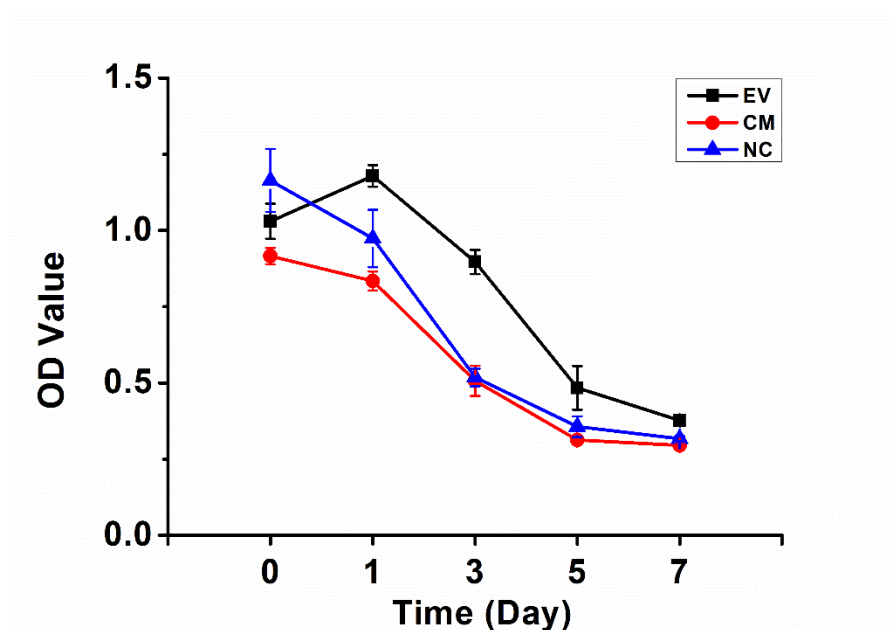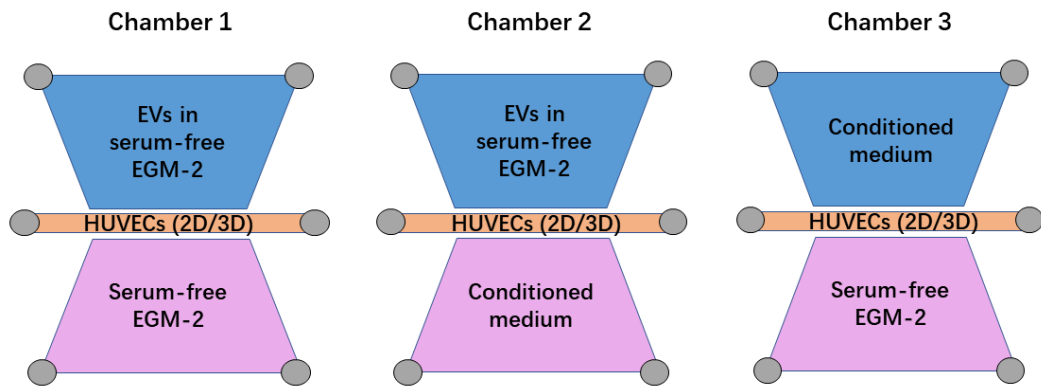**Supplementary Figure S1.** Flow cytometry analysis of the immunotype of DPSCs. The mesenchymal markers (CD73, CD105) and the cell adhesion molecules (CD90) were positive, whereas the hematopoietic lineage markers (CD45, CD34, CD11b, CD79a and HLA-DR) were negative. Please note: Multicolor approach caused a slight shift in the histograms for CD45 and CD11b due to a spill over. Stated values represent the positive fraction after compensation calculation.

Supplementary Figure S2. The XTT test of HUVECs grew in fibrin gels alone.

Chamber 1	Chamber 2	Chamber 3
EVs in serum-free EGM-2	EVs in serum-free EGM-2	Conditioned medium
HUVECs (2D/3D)	HUVECs (2D/3D)	HUVECs (2D/3D)
Serum-free EGM-2	Conditioned medium	Serum-free EGM-2

Supplementary Figure S3. The schematic diagram of chemotaxis assay set up. The Ibidi μ-slide has a thin channel connecting the center chamber to two opposing medium reservoirs. The experiment was set up with three groups each for the 2D and 3D systems: EV/negative, CM/negative and EV/CM in EGM-2.

Supplementary Table S1. VEGF concentration in EV lysate, CM and EV-depleted CM (pg/mL, mean ± S.E.M.).

	VEGF Concentration
EV lysate	36.1 ± 2.8
CM	5447.4 ± 82.3
EV-depleted CM	4768.7 ± 115.9

Supplementary Table S2. Protein concentration in EV lysate (pg/mL, mean ± S.E.M.).

	TNFα	IGF1	VEGF	IL6	FGFb	TGFβ	EGF	Leptin
EV lysate	10.8 ± 1.0	4.46 ± 0.3	34.6 ± 2.2	not detectable	138.8 ± 4.6	38.9 ± 1.0	41.1 ± 2.3	707.4 ± 6.5

Supplementary Table S3. Antibodies List.

Antibody	Company	Dilution	Clone Number	Catalog Number
Primary Antibody				
mouse anti-CD31	Sigma	1:100	Mouse monoclonal, WM-59	P 8590
rabbit anti-collagen I	Acris	1:100	Rabbit polyclonal	R 1038
rabbit anti-collagen III	Acris	1:100	Rabbit polyclonal	R 1040
rabbit anti-collagen IV	Acris	1:100	Rabbit polyclonal	BP 5031
Secondary Antibody				
goat anti-mouse Alexa Fluor 594	Thermo Fisher Scientific	1:400	Goat polyclonal	A 11005
goat anti-rabbit Alexa Fluor 594	Thermo Fisher Scientific	1:400	Goat polyclonal	A 11012
goat anti-rabbit Alexa Fluor 488	Thermo Fisher Scientific	1:400	Goat polyclonal	A 11008