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**Legend Figure S1.** (A) CD73, CD90, CD105, CD146 and SSEA4 frequency from NBM-MSC (n=3-23) or HS27A cell line (n=3-7). Dot plot represents percentage of positive cells quantified in independent experiments. (B) Representative pictures from adipocytes (left panel), osteoblasts (right panel) differentiated from NBM-MSC or HS27A cell line. Adipocytes were revealed by Oil red O staining (Scale bar, 50µm) and osteoblast by Alizarin red staining (Scale bar, 1000µm) (C) Representative picture from clones derived from NBM-MSC or HS27A cell line CFU-F assays (Scale bar, 100µm).



**Legend Figure S2.** Related to Figure 1 (A) Schematic protocol of osteoblastic differentiation. (B) Representative pictures from 3D systems incubated in control medium (left) or osteoblastic differentiation medium (right). Top panel: Disposition of inserts in 6-well plates. Lower panels: Final structure recovery after 21 days of culture. (C) Representative pictures from HS27A-3D systems at day 28, stained with Sirius Red (left panel). and Alizarin red (right panel).



**Legend Figure S3.** Related to Figure 2. (A) Tests of different culture media for HS27A, HMEC-1 and KG1A cells. (B) Schematic diagram of the protocol of 3D co-culture of HS27A, HMEC1 and KG1A cells. (C) Representative pictures from recovered 3D systems showing fluorescent HS27A (turquoise) in blue, HMEC-1 (orange) in red and KG1A (GFP) in green at day 28, following introduction of KG1A cells at day 21. Scale Bar, 100µm. (D) Immunofluorescence representative pictures from CD45, CD34 and CD38 staining of 3D systems with KG1A cells. (E) Representative FACS plots of Turquoise/Orange<sup>+</sup> and GFP<sup>+</sup> cells present in dissociated 3D systems generated with KG1A cells. (F) Representative pictures from cultured cells recovered from dissociated 3D systems generated. Left panel: bright field. Right panel: fluorescence analysis; Scale Bar, 100µm.



**Legend Figure S4.** Related to Figure 2 (A) Proportion of CD34 positive cells among CD45A cells counted after 7 days in the 3D structure. (B) Immunofluorescence representative pictures from CD45, and Ki67 staining of 3D systems with NBM mononuclear cells. Proportion of Kl67 positive cells among CD45A cells counted after 7 days in the 3D structure (n=3). (C) 3D structure incubated one week with primary MNC BM cells were stained by ICH for H3K27me3 (D) Dot plot showing GATA2 relative expression from input MNC (black) or CD34+ (blue) subsets at day 0 before seeding or day7 from dissociated 3D systems. Individual data are from independent experiments (n=4). (E) Representative FACS plots of CD41/CD14 cells present at day 0 before seeding (left panel) or day7 from dissociated 3D systems (right panel) generated with NBM CD34+ cells. F. Frequency of CD14+ cells recovered after one week of culture in the 3D system. All Scale bars represent 100µm.

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**Legend Figure S5.** Related to Figure 3. (A) Representative images of sections stained for E-cadherin, CD44 and Vimentin from systems produced with T47D (top panel) or MDA-MB-231 (bottom panel) cells. (B). Representative images of COL-3 and Fibronectin- stained sections of 3D systems produced after one week, of incubation with T47D (top panel) and MDA-MD-231 (bottom panel) cells. Scale bar: 100µm.(C). Dot plots showing measured area of Collagen III and Fibronectin in the structure following one week of incubation with T47D or MDA-MB-231 cells.



**Legend Figure S6.** Related to Figure 4. (A) Representative images of Collagen III- and Fibronectin- stained sections of 3D systems produced without hematological cells as control or with MEG-01, KG1A or MEG-01 + KG1A cells. Scale bar, 100µm. (B) Dot plots showing measured levels of Collagen III or Fibronectin after one week in presence of hematological cells as indicated. Individual data are from independent experiments (n=3). (C) Representative images of CD45-stained sections of 3D systems produced with CD34+ from NBM (left panel) or AML (right panel) cells. Scale bar, 100µm. (D) Dot plots showing measured levels of Collagen 1 or Fibronectin in NBM or AML MNC or CD34+. Individual data are from independent experiments (n=3 to 7) recovered from systems produced with MNC (open circles/squares) or CD34+ (closed circles/squares).