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Supporting Information

Macrophages-Triggered Sequential Remodeling of Endothelium-Interstitial Matrix to Form Pre-Metastatic Niche in Microfluidic Tumor Microenvironment

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Supporting information

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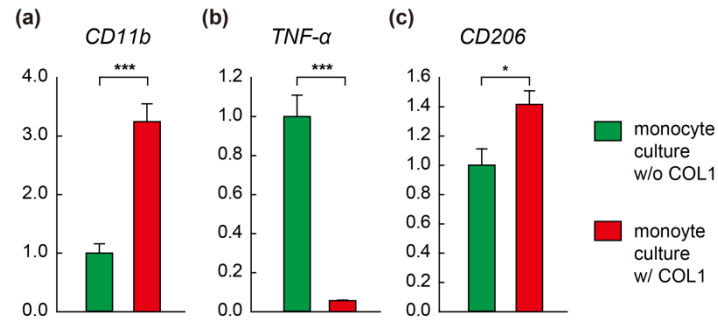
Figure S1. Characterization of monocytes within type 1 collagen hydrogel. a-c) mRNA expression levels of markers for macrophage differentiation (M0), M1 macrophage and M2 macrophage in monocytes under 3D culture embedded in type 1 collagen hydrogel. CD11b a), TNF-α, b) and CD206, c) were used as markers for M0, M1 and M2 macrophage respectively. n = 3 independent experiments. Data represent mean ± S.E.M. *, p<0.05, ***, p<0.001 by Student's t-test
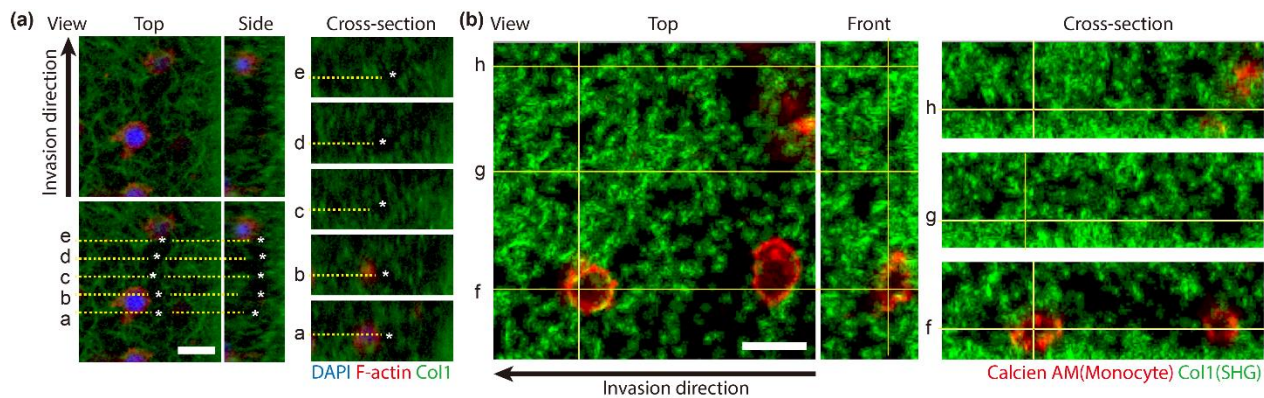
Figure S2. Pre-invaded macrophages induced microtracks in collagen. a) Representative confocal fluorescence images of collagen matrix (green), F-actin (red) and DAPI (nucleus, blue) showing collagen structure in the presence of macrophages. a-e indicate position of cross-section view and each asterisk indicates microtracks within the matrix. Scale bar, 20 μm. b) Representative second-harmonic generation (SHG) microscopy images of collagen matrix. f-h indicate position of cross-section view respectively. Scale bar, 20 μm. Calcein AM (red) and collagen fiber (green).
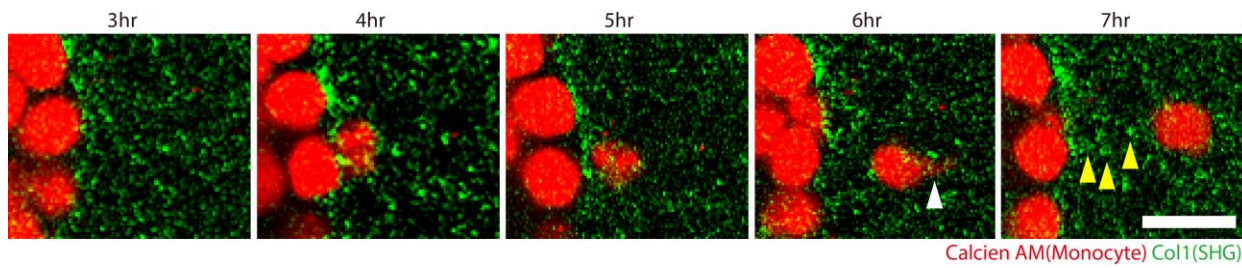
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Calcien AM(Monocyte) Col1(SHG)

Figure S3. Time-lapse SHG microscopy images of migrating monocytes in the collagen matrix (3-7 h after seeding). White arrow head indicates an invadopodia of monocytes and yellow arrow heads indicate deformation of collagen matrix respectively. Calcein AM (red) and collagen fiber (green). Scale bar,20 μm.
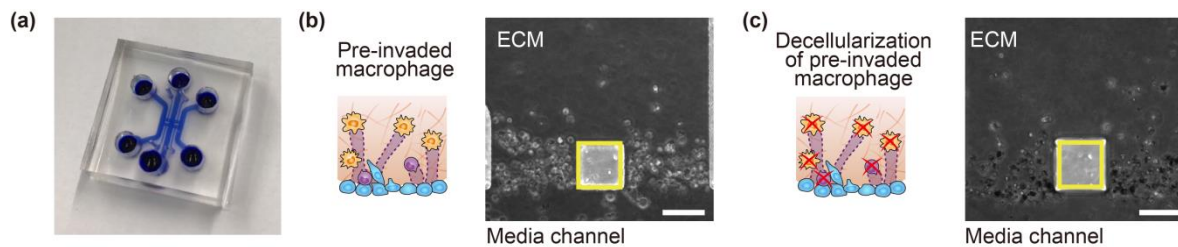
Figure S4. Decellularization of pre-invaded macrophages in microfluidic model. a) To confirm the decellularization with DW, trypan-blue stating was performed on a microfluidic chip. b and c) Illustration of the experiment (left panel) and representative phase images (right panel) of pre-invaded macrophage without (b) or with decellularization process (c). Dead cells were stained with trypan-blue dye. Scale bar, 150 μm.