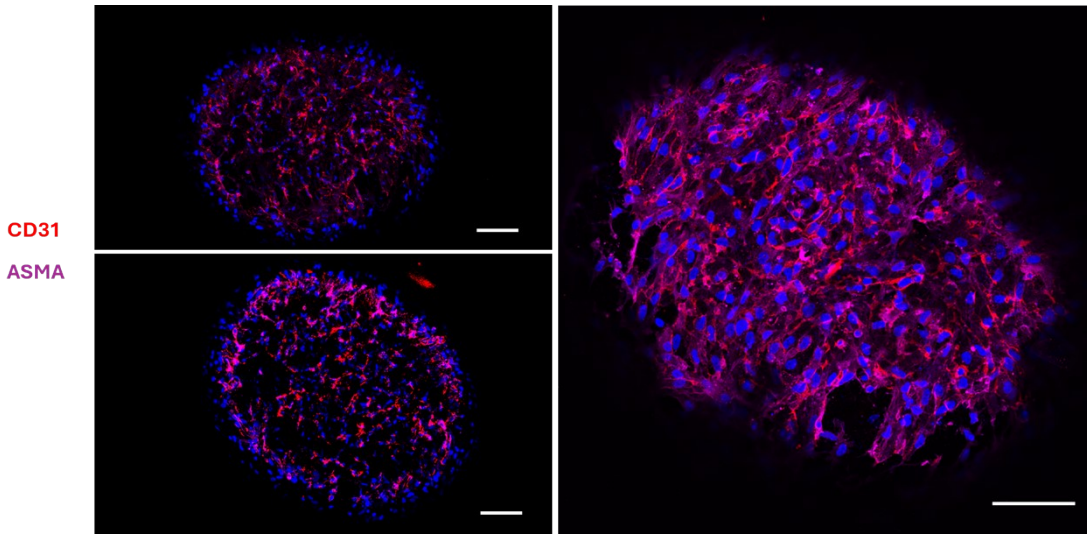

Fig. S1: Immunofluorescence confocal imaging showing CD31+ ECs (red) in vascular networks covered by pericytes (aSMA+, magenta) at day 20 after differentiation Scale bars: 200µm.

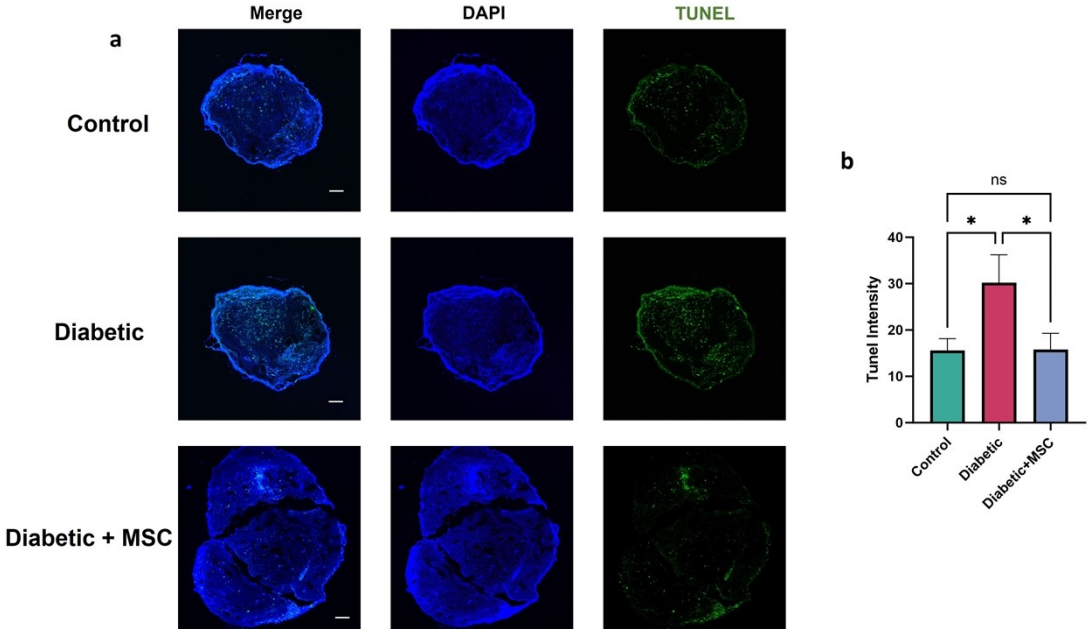

Figure S2: MSC Treatment Reduces Apoptosis in Diabetic Vascular Organoids. a, Representative TUNEL staining images of vascular organoids from the Control, Diabetic, and Diabetic + MSC groups at Day 21 of co-culture. DAPI (blue) marks nuclei, while TUNEL (green) indicates apoptotic cells. Scale bars = 100 um. b, Quantification of TUNEL intensity. Quantification of TUNEL intensity in three different groups. Data are presented as mean ± SEM Statistical significance was assessed using one-way ANOVA ($p < 0.05$, ns = not significant). n=3.

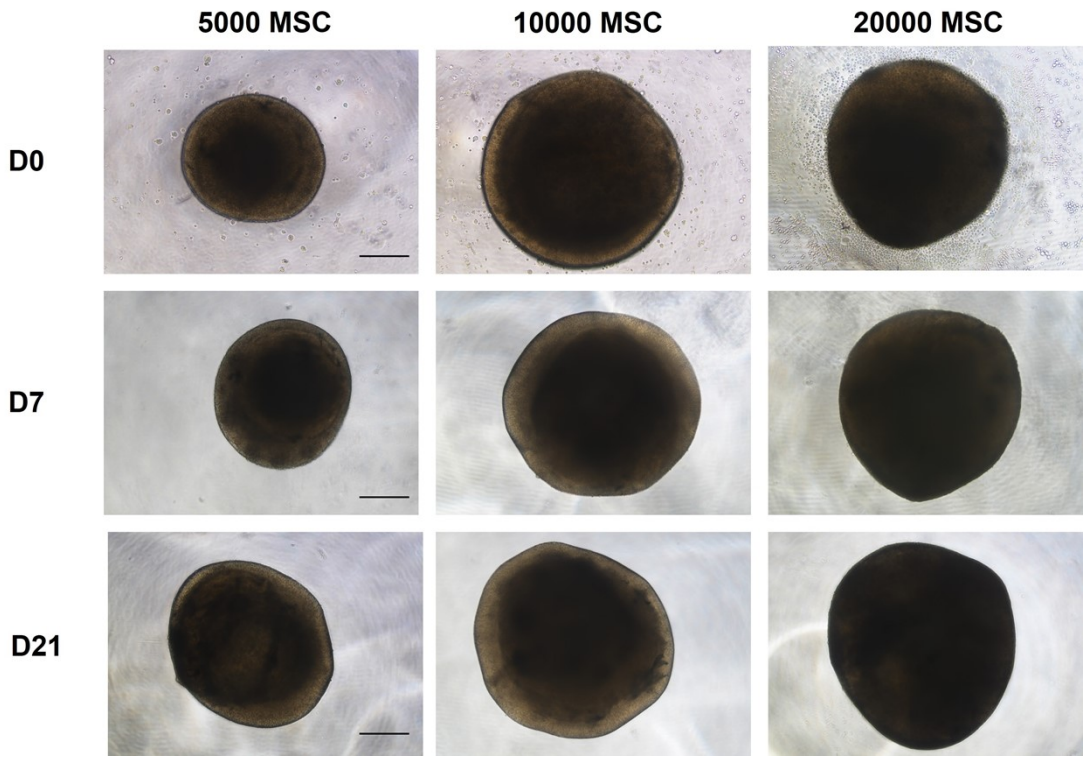

Figure S3: Representative bright-field images showing vascular organoids (BVOs) co-cultured with different numbers of mesenchymal stem cells (MSCs) over time. MSCs were added at three different concentrations: 5,000, 10,000, and 20,000 cells per organoid. Images were captured at Day 0 (D0, immediately after MSC addition), Day 7 (D7), and Day 21 (D21, fully matured BVOs). No significant morphological differences were observed among the different MSC concentrations over time. Scale bars: 500 µm.

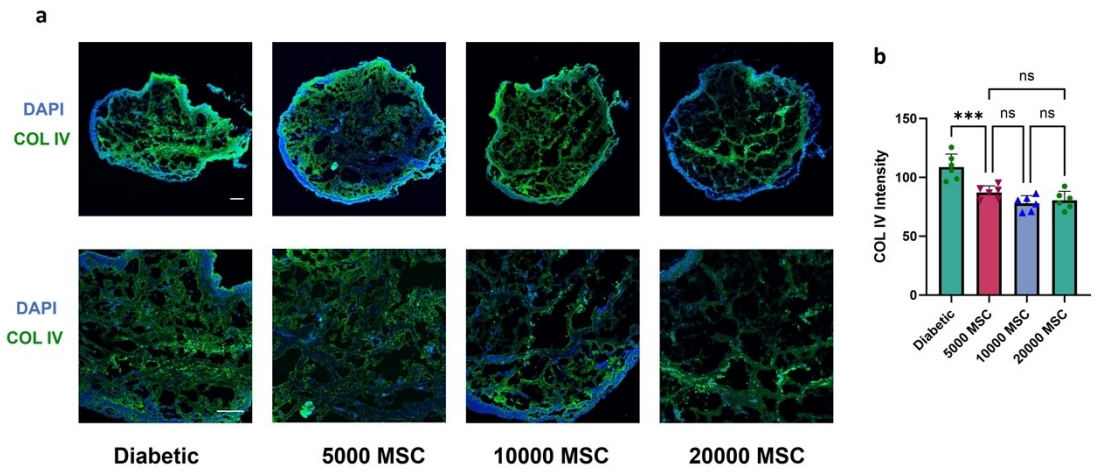

Figure S4: Immunofluorescence analysis of collagen IV (COL IV) expression in vascular organoids (BVOs) at day 21 under different conditions. a, (Top row) Whole-mount images of BVOs from the diabetic group and those treated with 5,000, 10,000, or 20,000 MSCs,

showing overall COL IV (green) deposition. DAPI (blue) marks nuclei. (Bottom row) Higher-magnification images highlighting COL IV distribution and structural organization within the vascular networks. b, Quantification of COL IV intensity across groups. Scale bars: 100um. $p < 0.001$; ns, not significant.

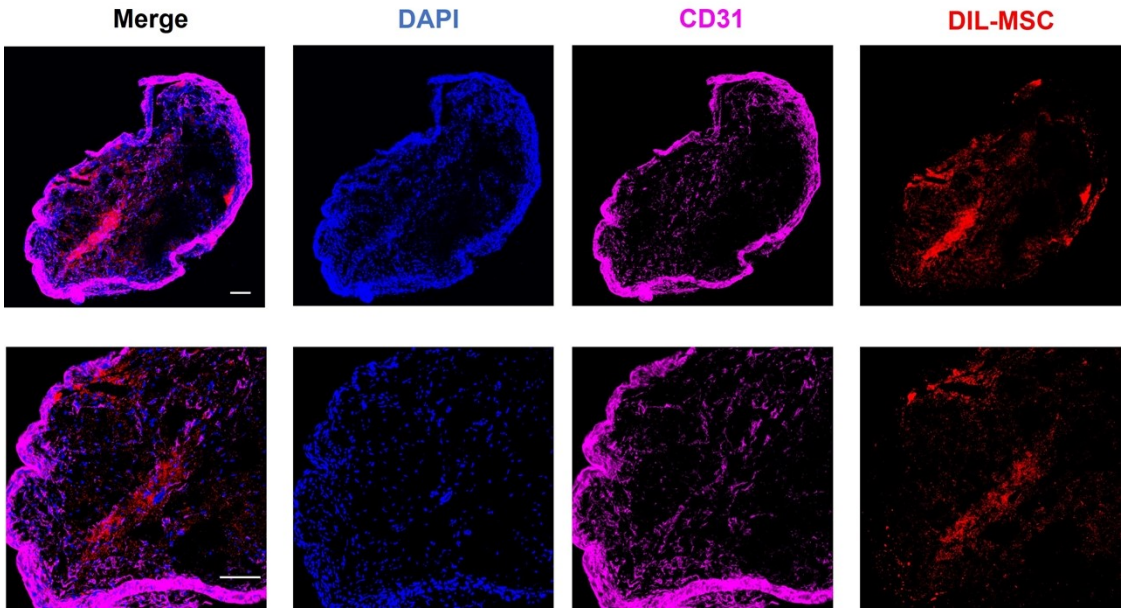

Figure S5: Immunofluorescence staining of vascular organoids (BVOs) co-cultured with DIL-Labeled mesenchymal stem cells (MSCs) after 21 days of co-culture. DAPI (blue) stains nuclei, CD31 (magenta) marks endothelial cells within blood vessels, and DiI (red) labels MSCs. Scale bar: 100 µm.

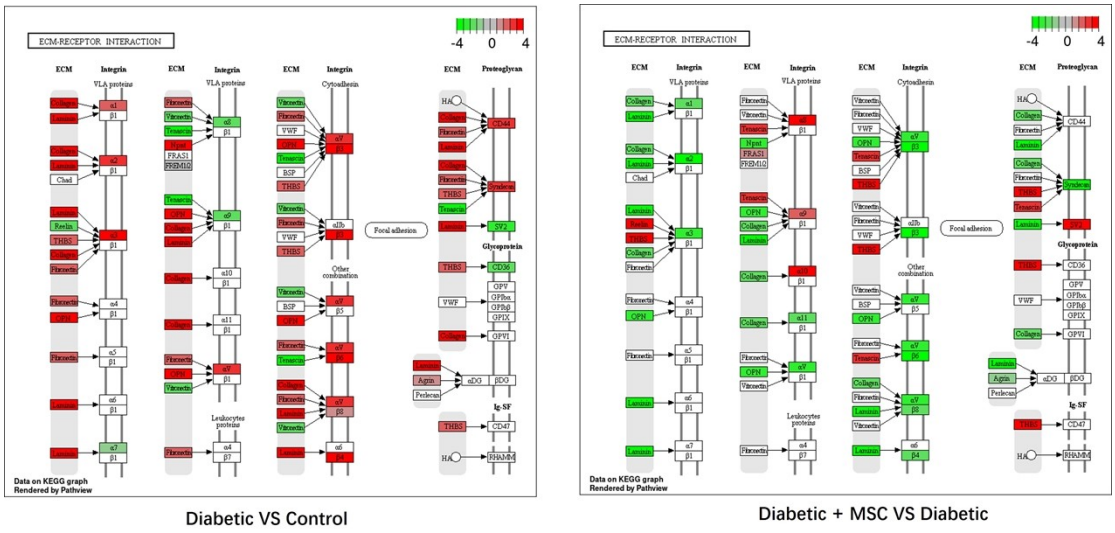

Fig. S6: KEGG Pathway Analysis of ECM-Receptor Interaction. (Left) Diabetic vs. Control: Upregulated ECM components (red) indicate excessive ECM deposition. (Right)

Diabetic + MSC vs. Diabetic: MSC treatment reduces ECM-related gene expression (green), suggesting ECM restoration.

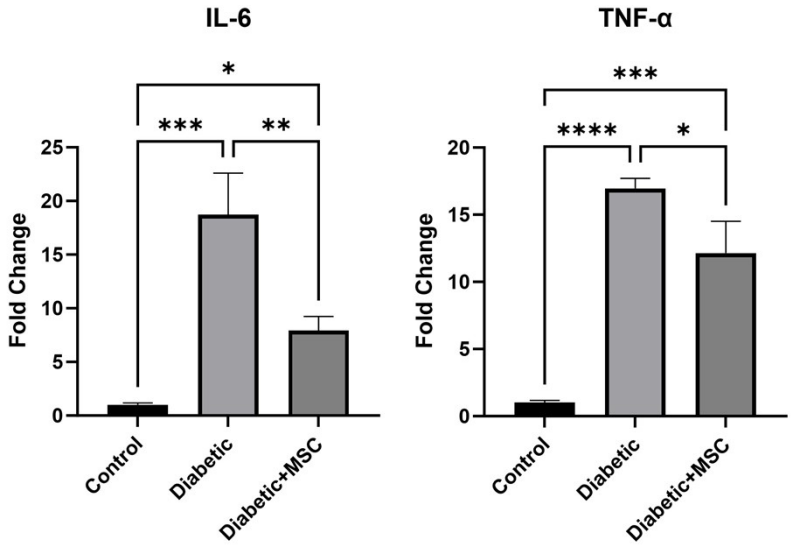

Figure S7: qPCR analysis of IL-6 and TNF-α expression at day 21 co-culture in diabetic vascular organoids. (*p < 0.05, **p < 0.01, ***p < 0.001, ***p < 0.0001; mean ± SEM).

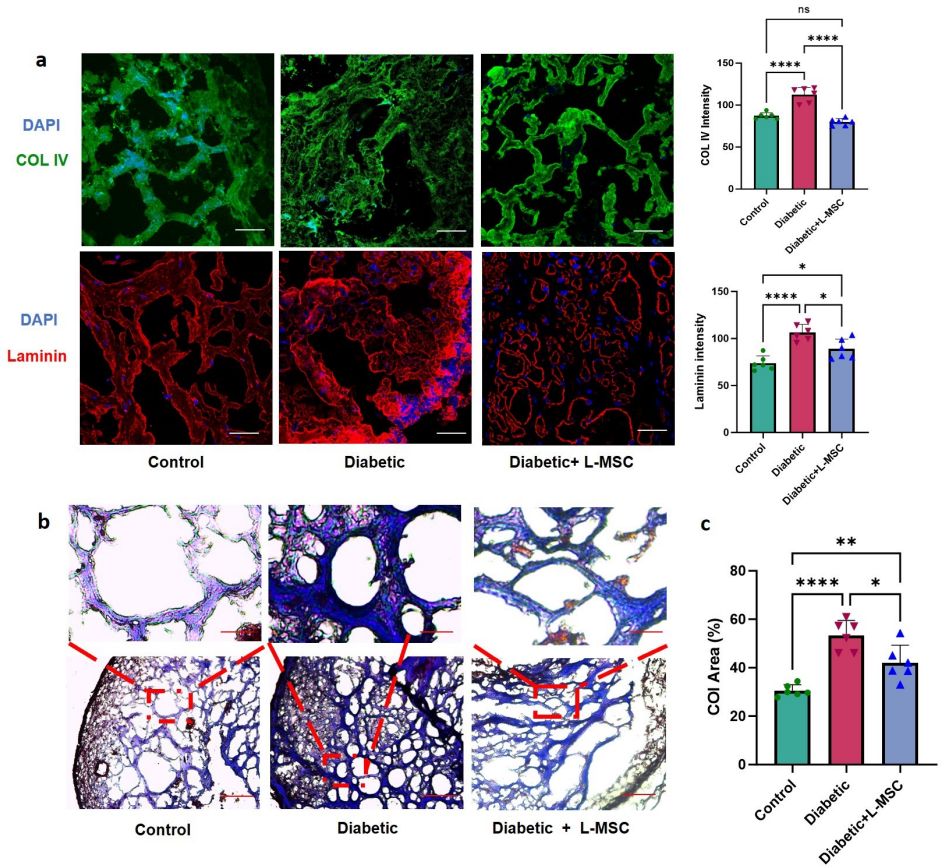

Figure S8: Late MSC Administration Mitigates ECM Accumulation in Diabetic Vascular

Organoids. a, Representative images of collagen type IV (green) and laminin (red) in different groups. Scale bars: 50 μm. n=3 independent experiments. quantification of collagen type IV and laminin expression from a were measured. n=6 biological sample per group. For each group, 6 imaging windows are randomly chosen. Data are demonstrated with mean ± sd. (b) Masson's trichrome staining showing collagen deposition in the three groups. (c) Quantification of collagen area from Masson's trichrome staining, Data are represented as mean ± SEM (n = 6 per group). Statistical significance was determined using one-way ANOVA (*p < 0.05, **p < 0.01, ****p < 0.0001).

Table S1. List of qPCR Primers and Their Sequences

Gene name	Sequence
COL4A1	Forward: TGCTGTTGAAAGGTGAAAGAG Reverse: CTTGGTGGCGAAGTCTCC
COL4A2	Forward: ACAGCAAGGCAACAGAGG Reverse: GAGTAGGCAGGTAGTCCAG
LAMA4	Forward: TTCGAACACCAGCTGACAAC Reverse: AGGTAACCATTGCGCATTTC
IL-6	Forward: CCACACAGACAGCCACTCAC Reverse: CCAGATTGGAAGCATCCATC
TNF-α	Forward: GAGGCCAAGCCCTGGTATG Reverse: CGGGCCGATTGATCTCAGC
GADPH	Forward: CCACTTTGTGAGCTCATTTCCTT Reverse: TTCGTCCTCCTCTGGTGCTCT