

1. Supplemental Material and Methods

Cell Culture

The human microvascular endothelial cell line (HMEC-1) was purchased from ATCC and was grown in reconstituted MCDB 131. MCDB 131 was supplemented with 10% Foetal bovine serum (FBS), 100 U/mL penicillin, 100 µg/mL streptomycin, 10 ng/mL of epidermal growth factor (EGF) and 1 µg/mL of hydrocortisone.

Human saphenous vein endothelial cells (HSVEC) were donated within the institute and maintained in cell vascular basal medium supplemented with 50 µg/mL ascorbic acid, 5 ng/mL EGF, 5% FBS, 0.75 U/mL heparin sulphate, 10 mM L- glutamine, 1 µg/mL hydrocortisone and 0.2% bovine brain extract.

2. Supplemental Figures

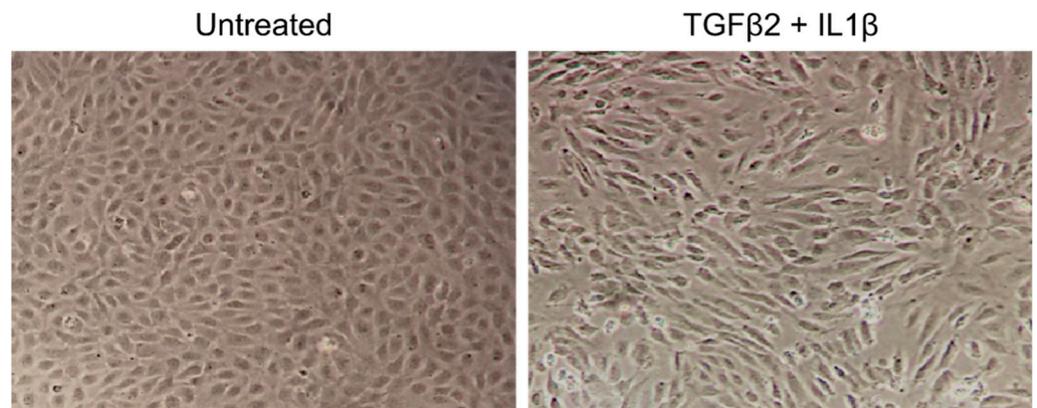


Figure S1. Effect of TGF β 2 and IL1 β treatment on HUVEC morphology.

Cells were treated with TGF β 2 (10 ng/mL) and IL1 β (10 ng/mL) for 24 h. HUVECs normally grow as a monolayer with a cobblestone appearance. Post-treatment, there is a disruption of the monolayer and cells take on a spindle shape morphology.

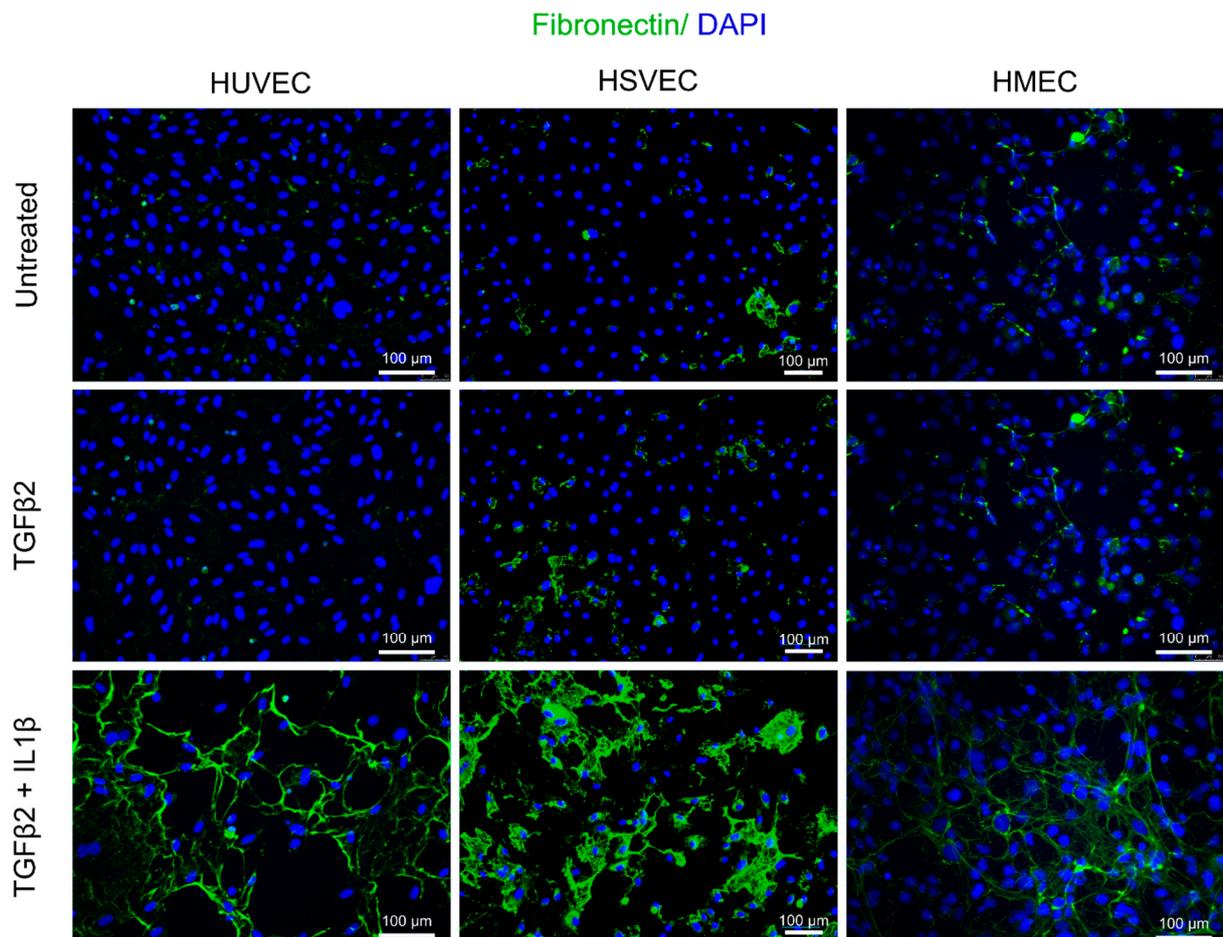


Figure S2. Fibronectin staining in endothelial cells treated with TGF β 2 or TGF β 2 and IL1 β .

Human umbilical vein endothelial cells (HUVEC) ($n = 4$), Human saphenous vein endothelial cells (HSVEC) ($n = 3$) and Human microvascular endothelial cells (HMEC) ($n = 2$) were treated for 6 days

with TGF β 2 (10 ng/mL) or TGF β 2 and IL1 β (10 ng/mL). Cells were stained for fibronectin and counterstained with DAPI.

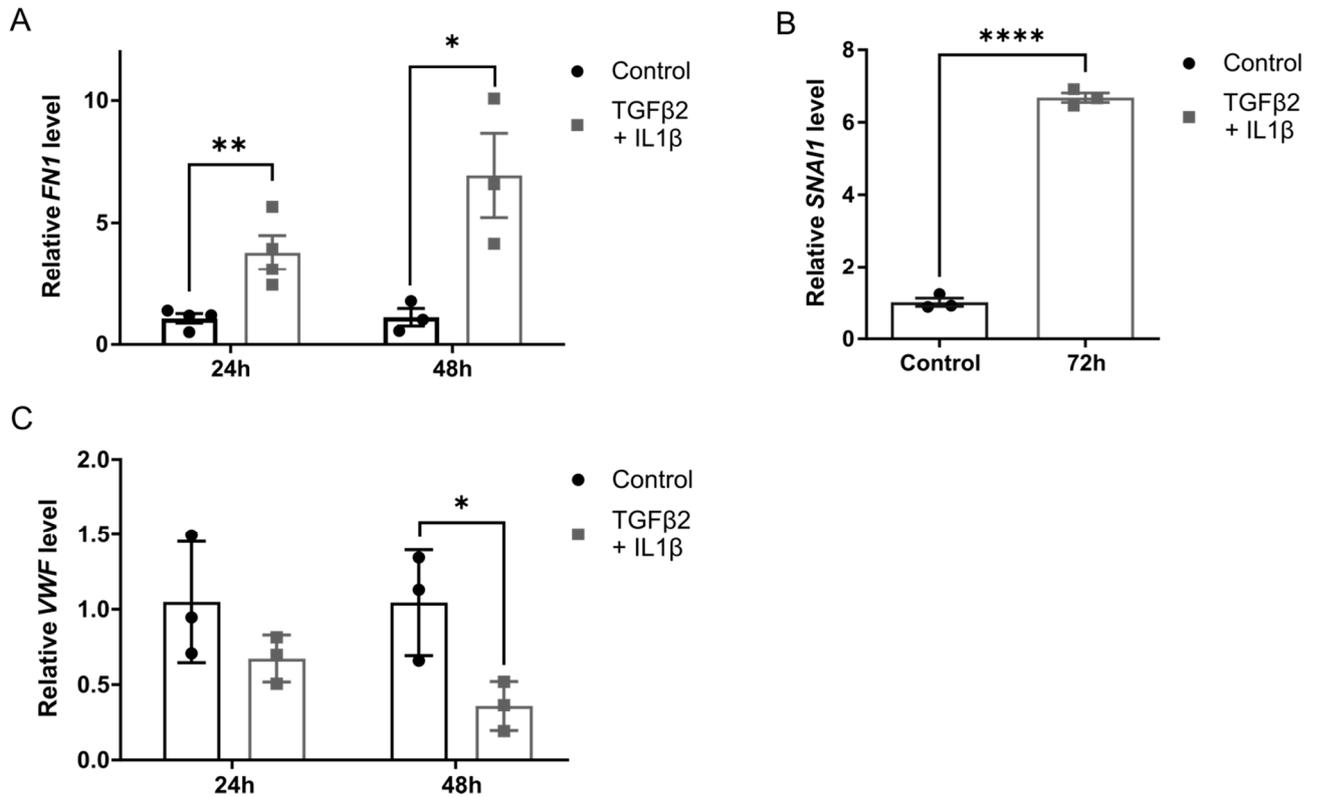


Figure S3. HMEC cells undergo endothelial to mesenchymal transition with TGF β 2 and IL1 β treatment.

HMEC were treated with TGF β 2 (10 ng/mL) or TGF β 2 and IL1 β (10 ng/mL). Gene expression level for fibronectin (A) and vWF (C) was assessed in endothelial cells at 24 and 48 h post-treatment with TGF β 2 and IL1 β . (B) Snail expression was evaluated 72 h post-treatment with TGF β 2 and IL1 β . Expression was normalised to the expression of the housekeeping gene Hprt1 and the error bars are representative of the standard error of the mean. ($n = 3$) Statistical significance was calculated by unpaired Student's *t*-test and one way ANOVA. (* $p < 0.05$; ** $p < 0.01$; **** $p < 0.0001$).

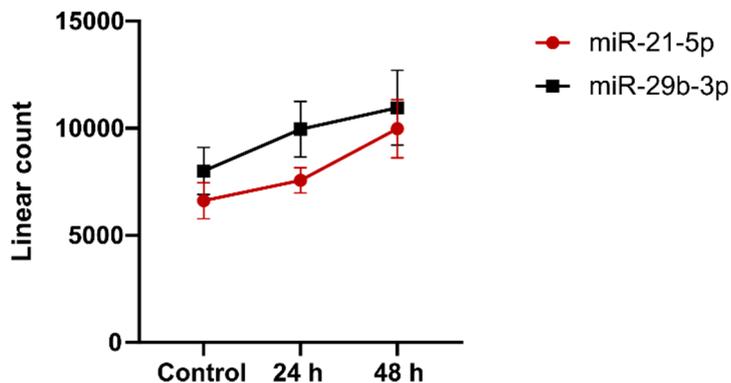


Figure S4. Linear count of miR-21-5p and miR-29b-3p in endothelial cells undergoing EndMT.

Endothelial cells were treated 24 and 48 h with TGF β 2 and IL1 β to induce EndMT. MiR-21-5p and miR-29b-3p expression level was evaluated with a nCounter assay ($n = 2$).

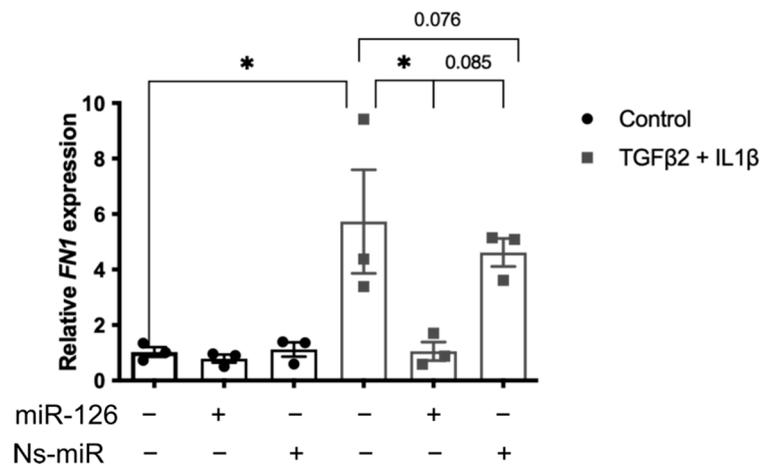


Figure S5. Gene expression of fibronectin after miR-126-3p transfection in HMECs undergoing EndMT.

HMECs were transfected with 50 nM of miR-126-3p mimics using lipofectamine followed by TGF β 2 and IL1 β (10 ng/mL) treatment for 48 h. Transfection of non-specific miRNA (50 nM) was used as a control. The gene expression levels of fibronectin were assessed in endothelial cells post-transfection and post-treatment. Expression was normalised to the expression of the housekeeping gene Hprt1 and error bars are representative of the standard error of the mean. Statistical significance was assessed by one-way ANOVA followed by the Tukey test ($* p < 0.05$) ($n = 3$).

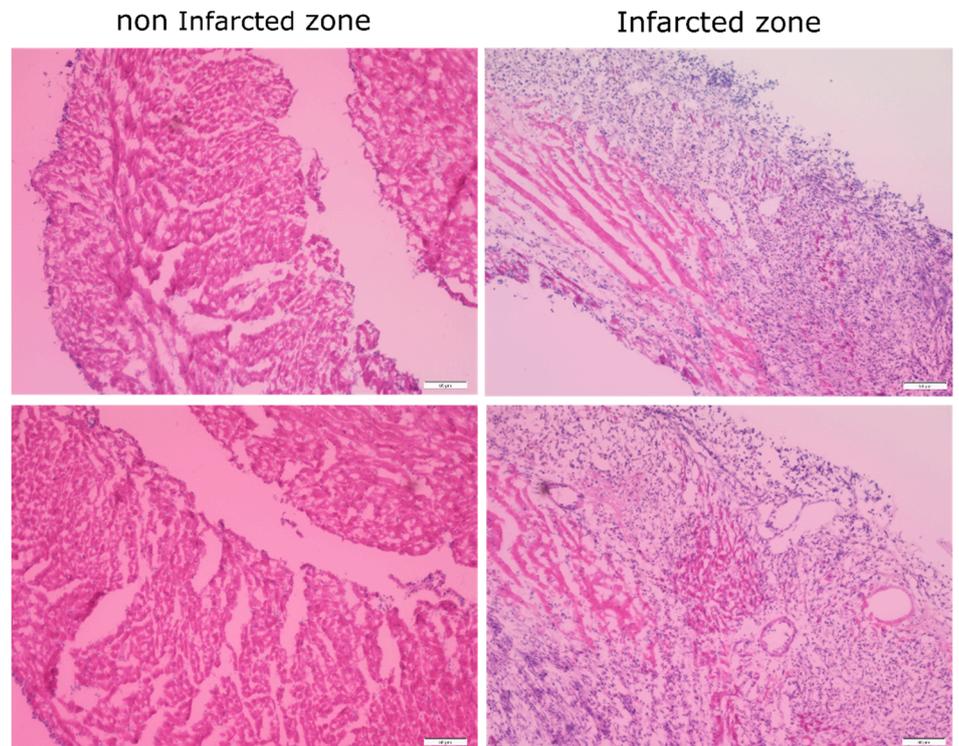


Figure S6. Haematoxylin-eosin staining of transverse sections of MI mice heart.

Infiltration of immune cells and the presence of fibrous tissue can be observed in the infarcted zone compared to the non-infarcted zone suggesting severe cardiac injury. Scale bars : 50µm.

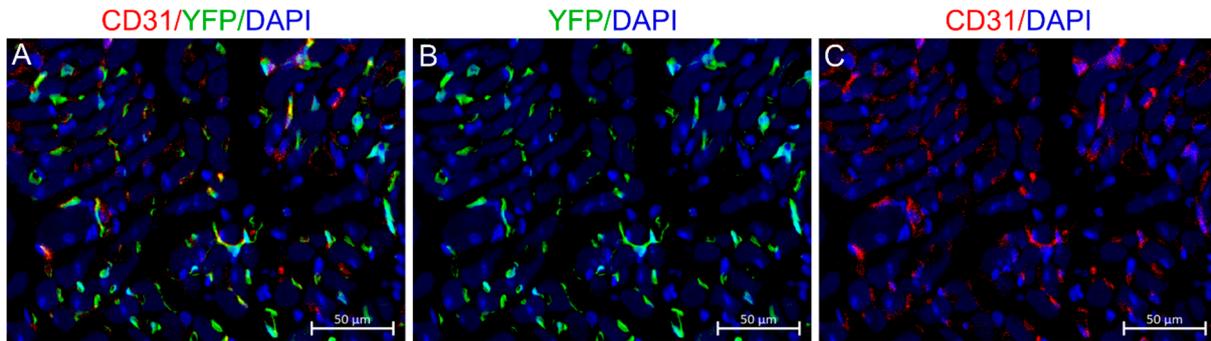


Figure S7. Lineage tracing of endothelial cells in the non-infarcted area of the mouse heart.

Staining for YFP (endothelial origin) (B) and CD31 (C) were performed on frozen sections of *Cdh5-Cre;Rosa26R-YFP* T/T mouse heart to evaluate the lineage tracing of endothelial cells (A). Tissues were counterstained with DAPI.

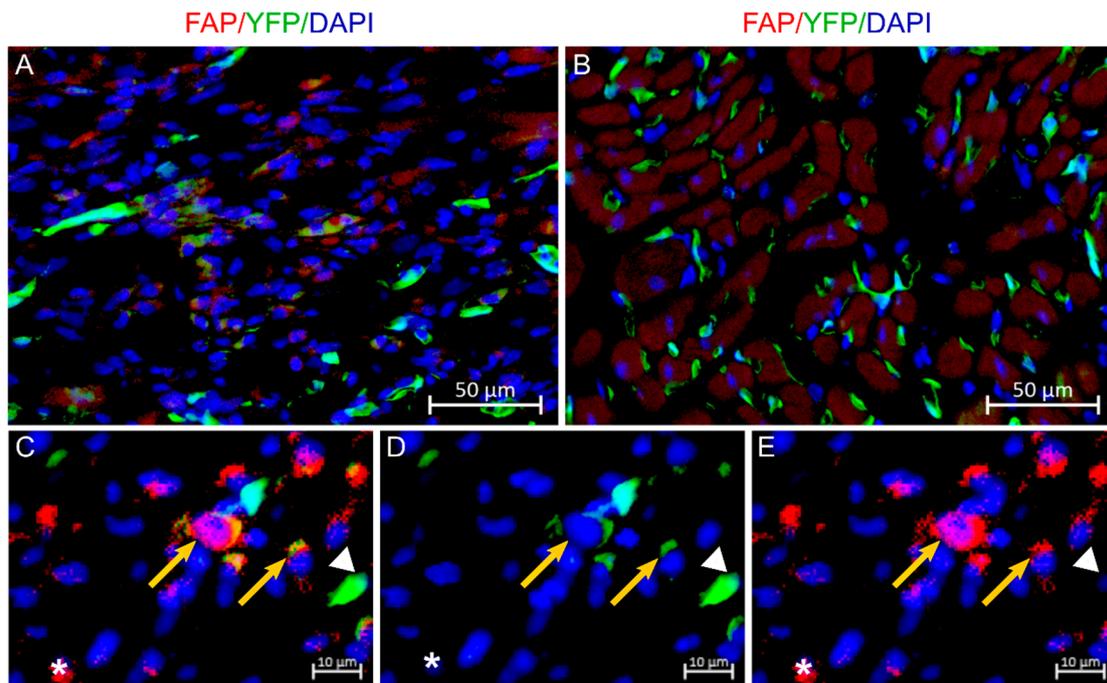


Figure S8. Endothelial-to-mesenchymal transition is present in fibrotic hearts.

Cdh5-Cre-ERT2;Rosa26R-stop-YFP mice underwent MI and were sacrificed 5 days later. Transverse sections of mouse heart post-MI were stained for FAP and YFP (endothelial cell origin). Micrographs show an infarcted area (A) and a non-infarcted area (B). A higher magnification of the infarcted area is shown in the lower panel (C,D,E) YFP+ FAP+ cells were indicated with a yellow arrow. Single YFP+ or FAP+ cells were designated by the white arrowhead or white star, respectively ($n = 2$).

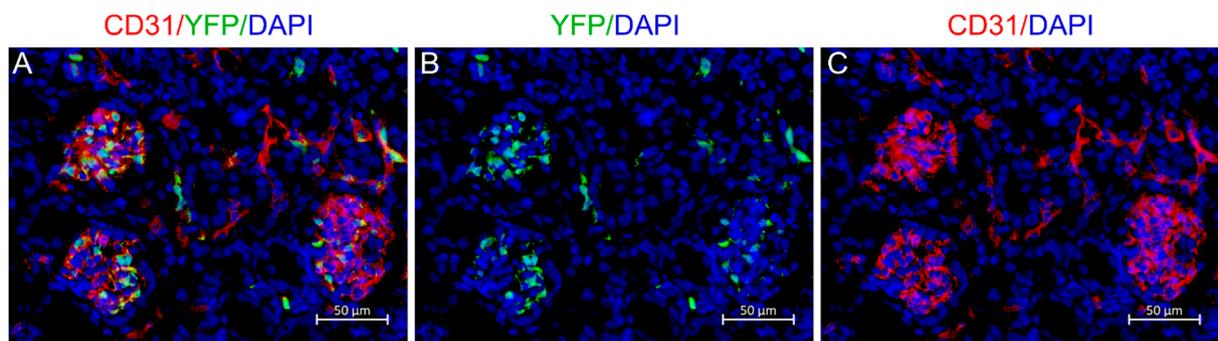


Figure S9. Lineage tracing of endothelial cells in healthy mouse kidney.

Cryosections of *Cdh5-Cre; Rosa26R-YFP* T/T mouse kidney were stained YFP (endothelial origin) (B) and for CD31 (C) to assess the accuracy of the endothelial lineage tracing (A). Nuclei were stained with DAPI.