Supplementary Figures and supplementary figure legends

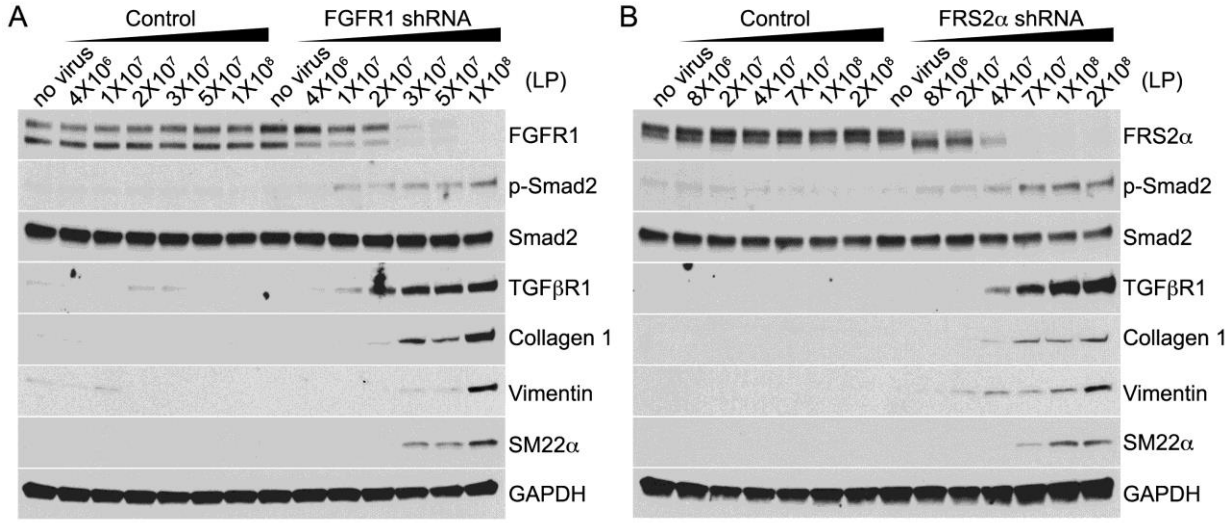


Figure S1. Effect of different percentage of FGF signaling knockdown on TGFβ signaling and EndMT marker gene expression.

HUVECs were subjected to different concentrations of control, FGFR1 shRNA, or FRS2α shRNA for four days. Blots are representative of three independent experiments. LP: Lentiviral particles.

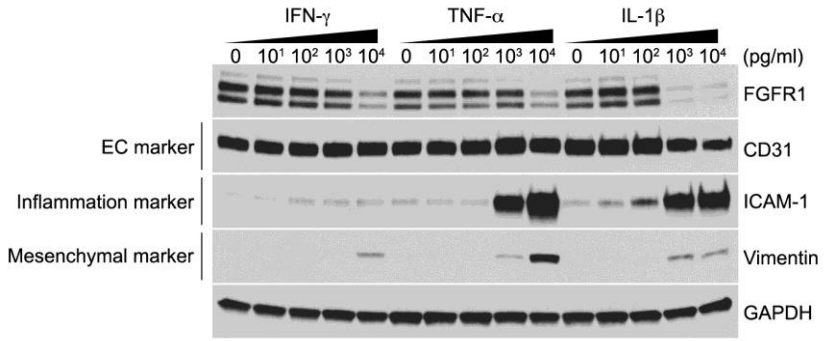


Figure S2. Effect of different cytokine concentration on FGFR1 expression in HUVEC. HUVECs were treated with three different cytokine concentration for 6 days. Immunoblot analysis of different concentration of cytokine treated HUVECs. Blots are representative of three independent experiments.

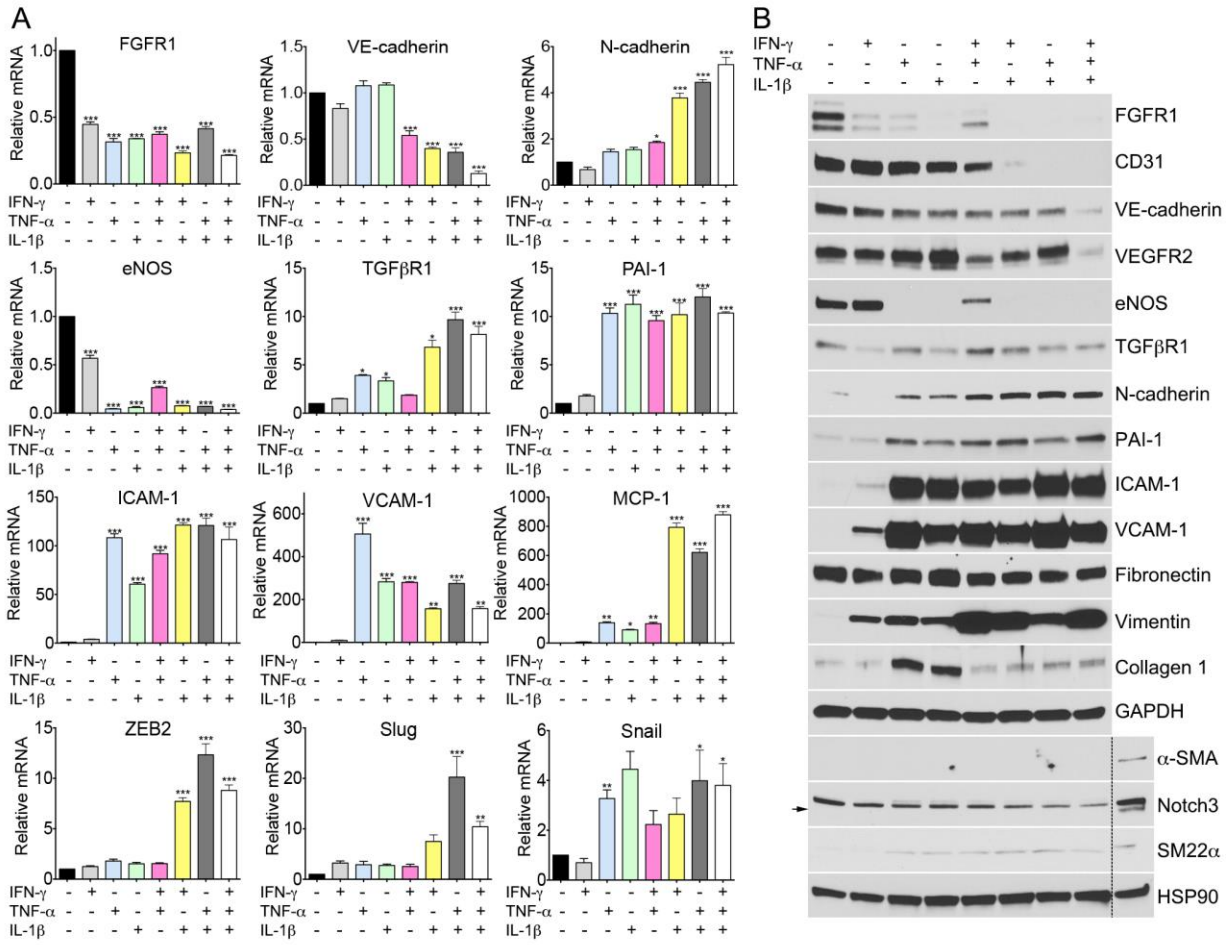


Figure S3. Cytokine treatment downregulates FGFR1 expression and increases endothelial cell inflammation and EndMT.

(A) Quantitative real-time polymerase chain reaction (qRT-PCR) analysis of FGFR1, endothelial cell markers (VE-cadherin, VEGFR2, and eNOS), TGFβ pathway (TGFβR1 and PAI-1), inflammation markers (ICAM-1, VCAM-1, and MCP-1), and EndMT transcription factors (ZEB2, Slug, and Snail) in HUVECs after cytokine stimulation (10 ng/ml). Bar graphs of qRT-PCR results are representative of four independent experiments. (*p<0.05; **p<0.01; ***p<0.001, one-way ANOVA with Newman-Keuls *post hoc* test for multiple comparison correction). (B) Immunoblot analysis of cytokine treated HUVECs. Blots are representative of six independent experiments.

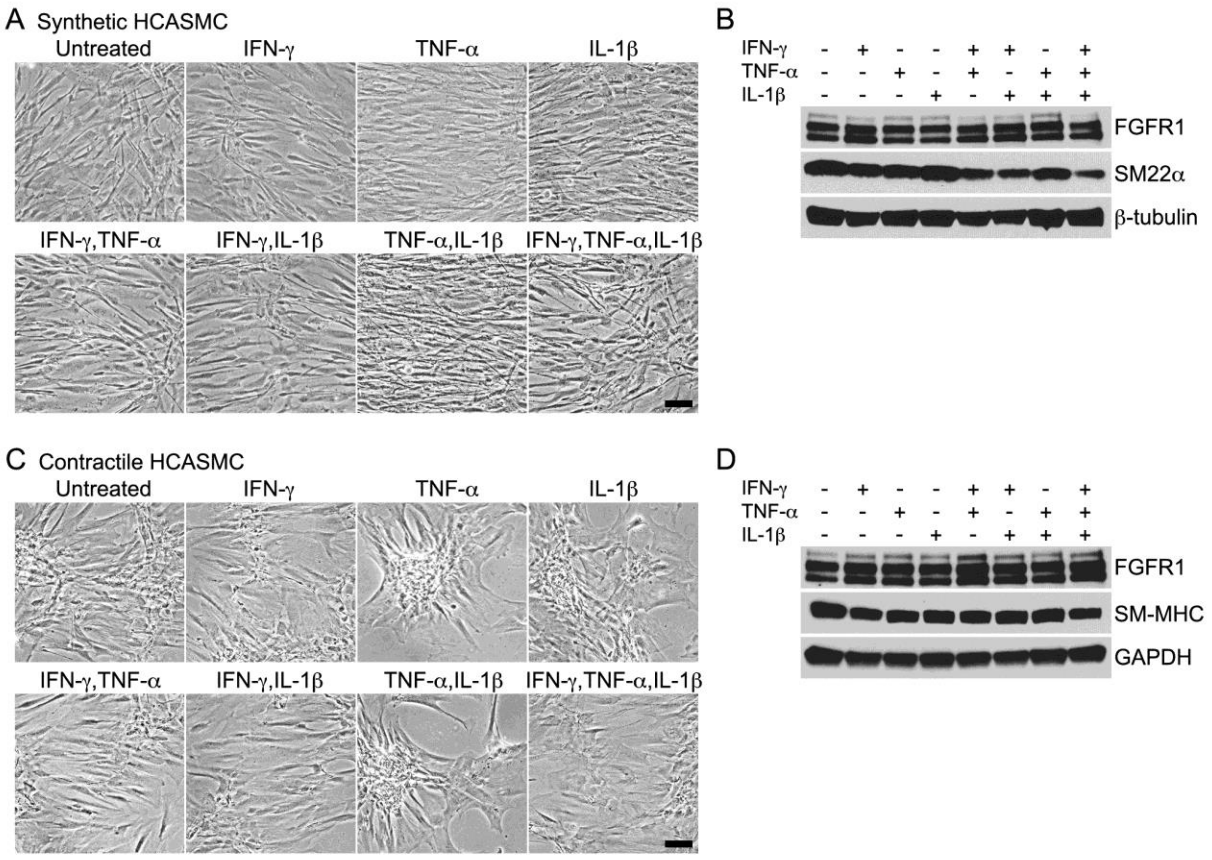


Figure S4. Effect of cytokine treatment on FGFR1 expression in primary human coronary artery smooth muscle cells (HCASMCs).
(A-B) HCASMCs were cultured in the growth medium (M231 + SMGS). (A) Phase-contrast of synthetic HCASMCs after cytokine treatment for 6 days. (B) Immunoblot analysis of cytokine treated synthetic HCASMCs. Blots are representative of three independent experiments. (C-D) HCASMCs were first cultured in the differentiation medium (M231 + SMDS) for 8 days then stimulated with cytokines for 6 days in the differentiation medium (M231 + SMDS). (C) Phase-contrast of contractile HCASMCs after cytokine treatment for 6 days. (D) Immunoblot analysis of cytokine treated contractile HCASMCs. Blots are representative of three independent experiments

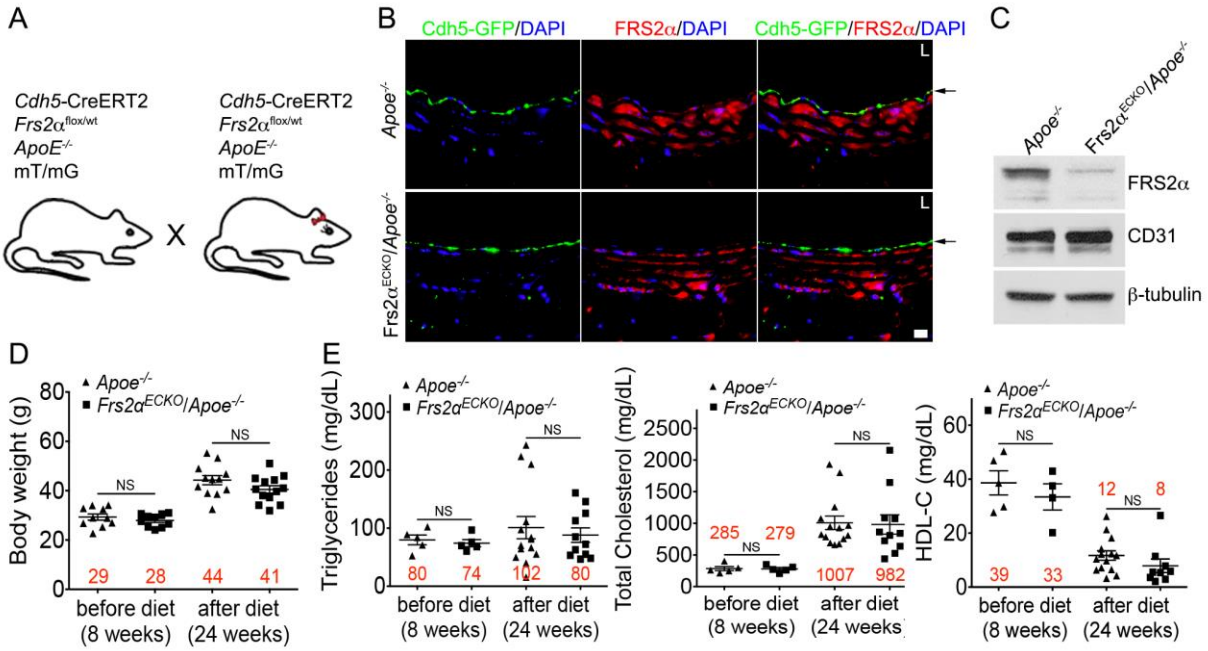


Figure S5. Generation of *Apoe*$^{-/-}$ mice with endothelial-specific *Frs2α* ablation.
(A) Mouse mating strategy to generate *Apoe*$^{-/-}$ and *Frs2*^{ECKO}/*Apoe*$^{-/-}$ mice. (B) Representative images of FRS2α immunofluorescence staining of *Apoe*$^{-/-}$ and *Frs2*^{ECKO}/*Apoe*$^{-/-}$ aorta. Endothelial cells are visualized by GFP fluorescence. Nuclei were stained with DAPI (blue). Black arrows indicate endothelial cells. L: lumen. Images are representative of 3 mice/group. Scale bar: 62 μm. (C) Immunoblot analysis of FRS2α expression in isolated *Apoe*$^{-/-}$ and *Frs2*^{ECKO}/*Apoe*$^{-/-}$ lung endothelial cells. In each group, endothelial cells were isolated and pooled from 3 mice/group. (D) Body weight analysis of *Apoe*$^{-/-}$ and *Frs2*^{ECKO}/*Apoe*$^{-/-}$ mice before and after 16 weeks on a high cholesterol diet. (NS: not significant compared to *Apoe*$^{-/-}$; unpaired two-tailed Student's t test). (E) Serum triglycerides, total cholesterol, and HDL-C levels from *Apoe*$^{-/-}$ and *Frs2*^{ECKO}/*Apoe*$^{-/-}$ mice before and after 16 weeks on a high cholesterol diet. (NS: not significant compared to *Apoe*$^{-/-}$; unpaired two-tailed Student's t test).

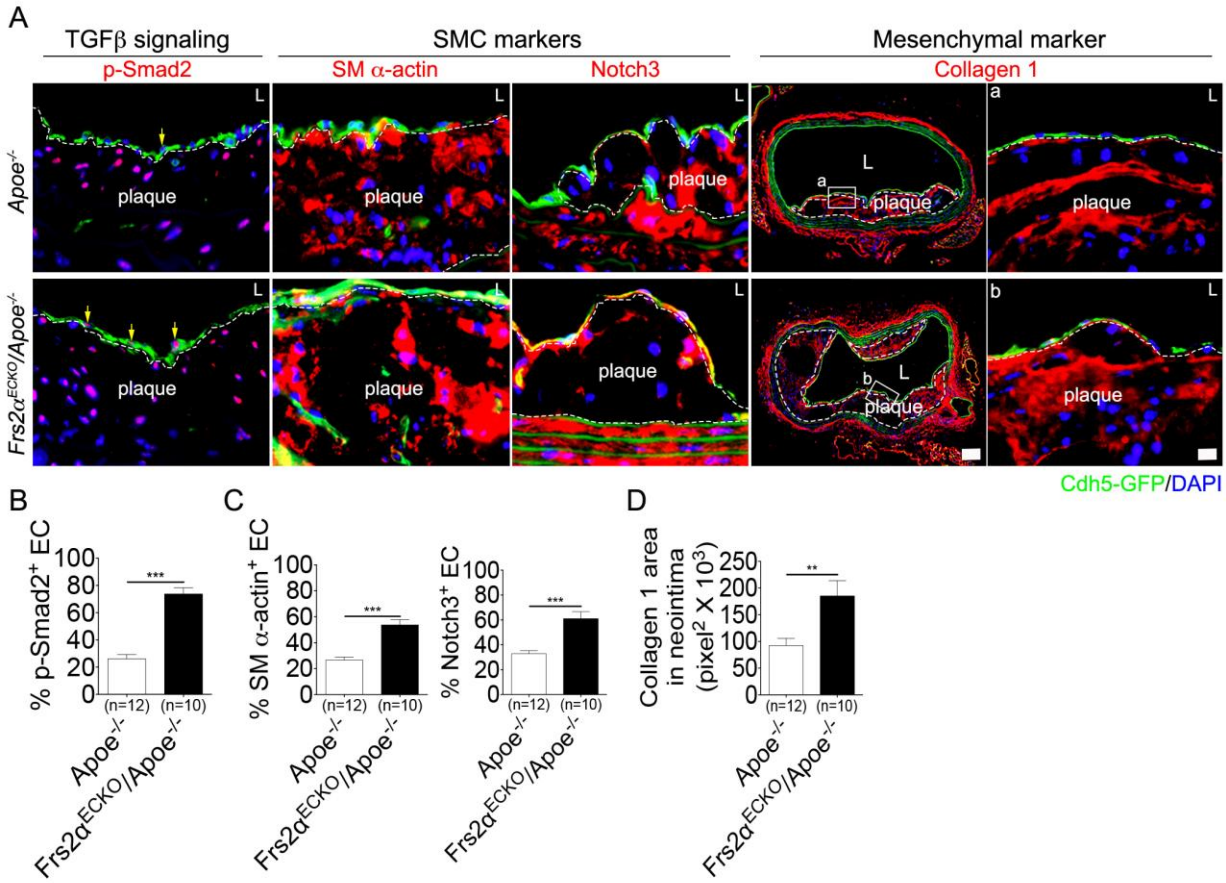


Figure S6. EndMT assessment in *Frs2α*^{ECKO}*/Apoe*$^{-/-}$ after 4 months of high fat diet.
(A) Immunocytochemical analysis of atherosclerotic plaques with anti-p-Smad2, anti-SM α-actin, anti-Notch3, and anti-collagen 1 antibodies. Co-localization (yellow) of Cdh5-GFP^{+} (green) with Notch3 (red) and SM α-actin (red) staining indicates EndMT. Nuclei were counterstained with DAPI (blue). L: lumen. Yellow arrows: endothelial cells expressing p-Smad2. Scale bar: 62 μm for low-magnification images and 10 μm for high-magnification images. *Apoe*$^{-/-}$ mice N=12, *Frs2*^{ECKO}*/Apoe*$^{-/-}$ mice N=10. (B-C) Percentage of Cdh5-GFP-positive cells that have phosphorylated Smad2 (p-Smad2), SM α-actin, or Notch3 staining in the lumen (***p<0.001 compared to *Apoe*$^{-/-}$; unpaired two-tailed Student's t test). (D) Measurement of collagen 1 area (**p<0.01 compared to *Apoe*$^{-/-}$; unpaired two-tailed Student's t test).

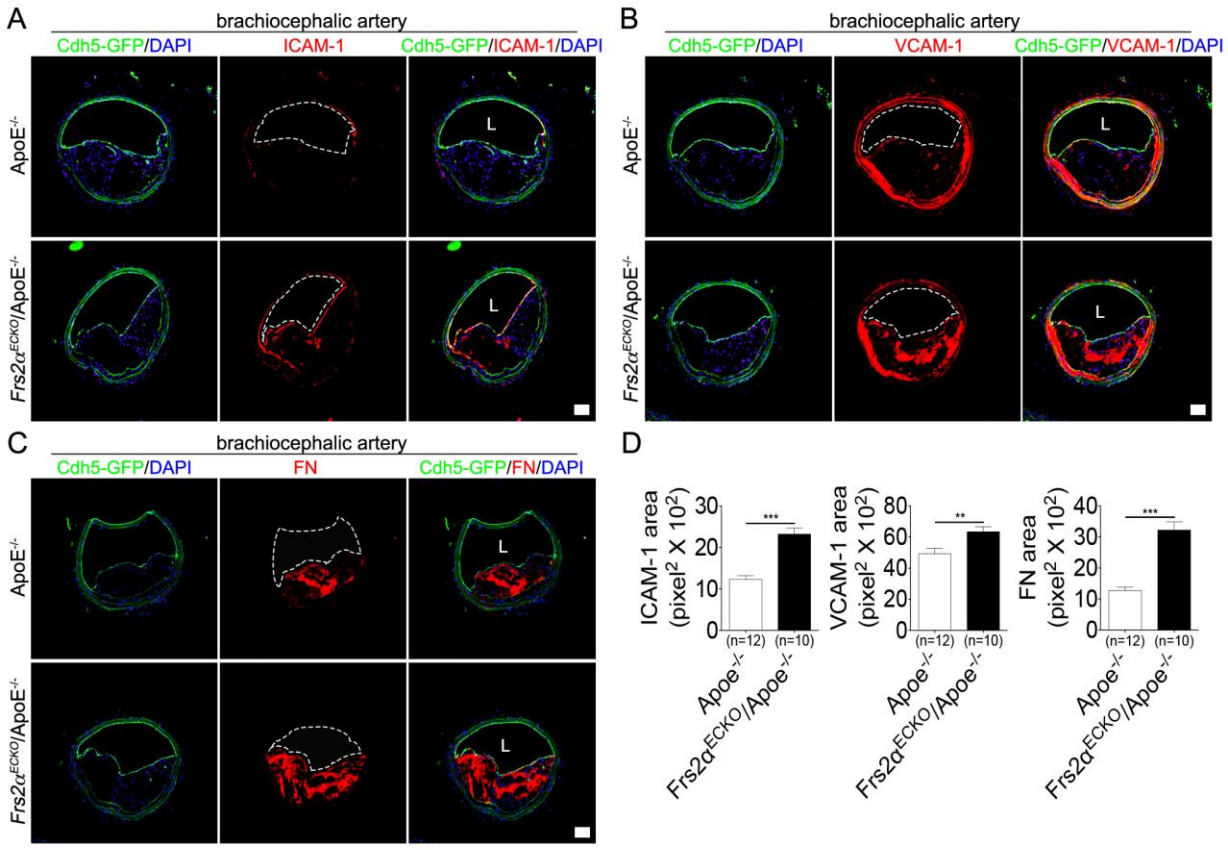


Figure S7. Analysis of brachiocephalic artery atherosclerotic lesions in *Frs2α^{ECKO}/Apoe$^{-/-}$* mice after 4 months of high fat diet.

(A-C) Histological analysis of atherosclerotic plaque with anti-ICAM-1, anti-VCAM-1, and anti-FN antibodies. Nuclei were counterstained with DAPI (blue). L: lumen. Scale bar: 16 μm. Panels A-C: *Apoe*$^{-/-}$ mice N=12, *Frs2*^{ECKO}/*Apoe*$^{-/-}$ mice N=10. (D) Measurement of ICAM-1, VCAM-1, and FN area (**p<0.01 compared to *Apoe*$^{-/-}$; ***p<0.001 compared to *Apoe*$^{-/-}$; unpaired two-tailed Student's t test)..

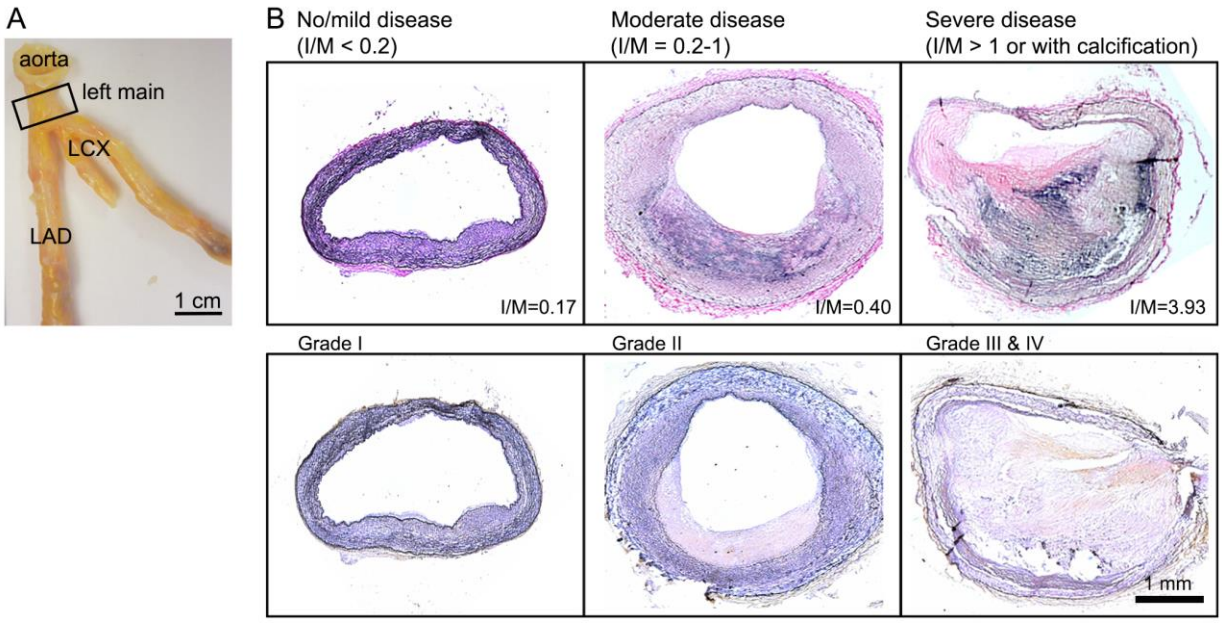
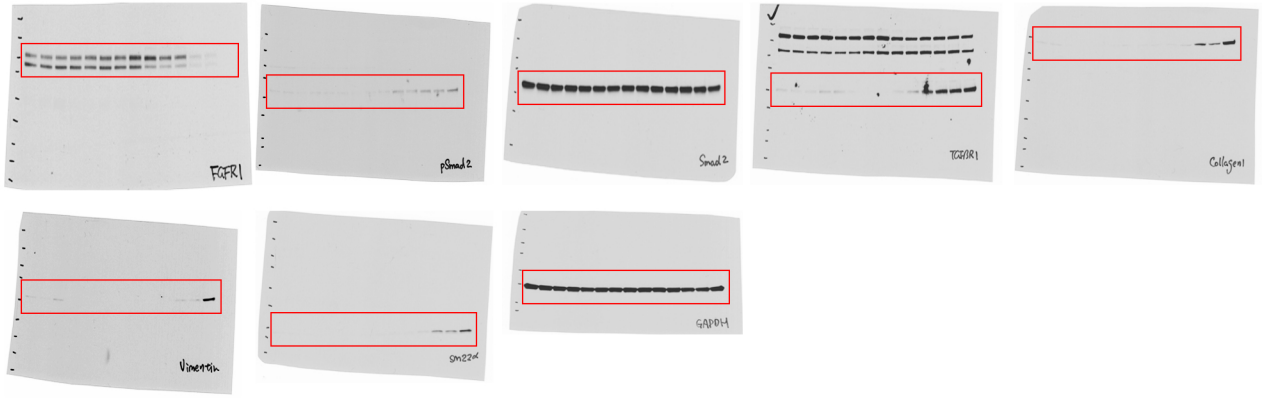
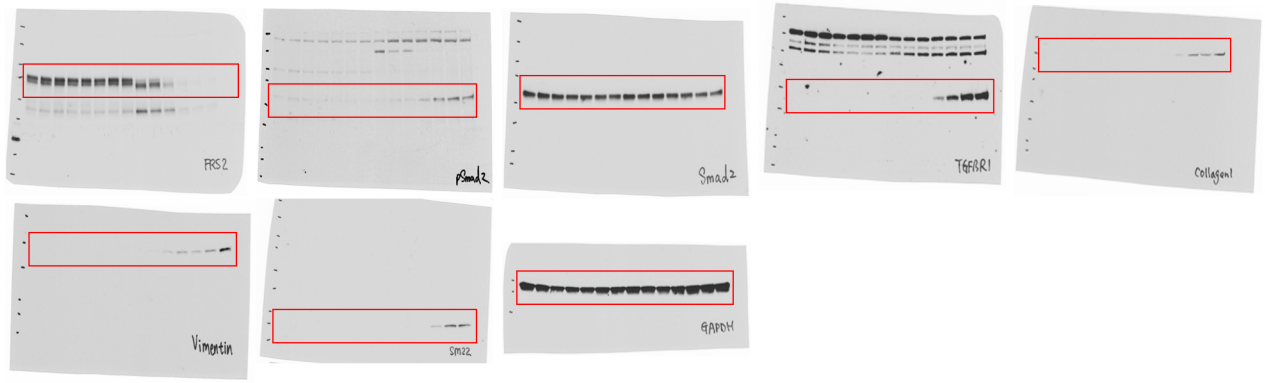


Figure S8. Morphological assessment and classification disease severity in human left main coronary arteries.
(A) Vessel segment dissected from the human heart. Left anterior descending (LAD) and left circumflex (LCX) branches are indicated. Scale bar: 1 cm. (B) Hematoxylin and eosin (H&E) (upper panels) and Movat staining (lower panels) of human left main coronary arteries with various degrees of atherosclerosis. Scale bar: 1 mm.

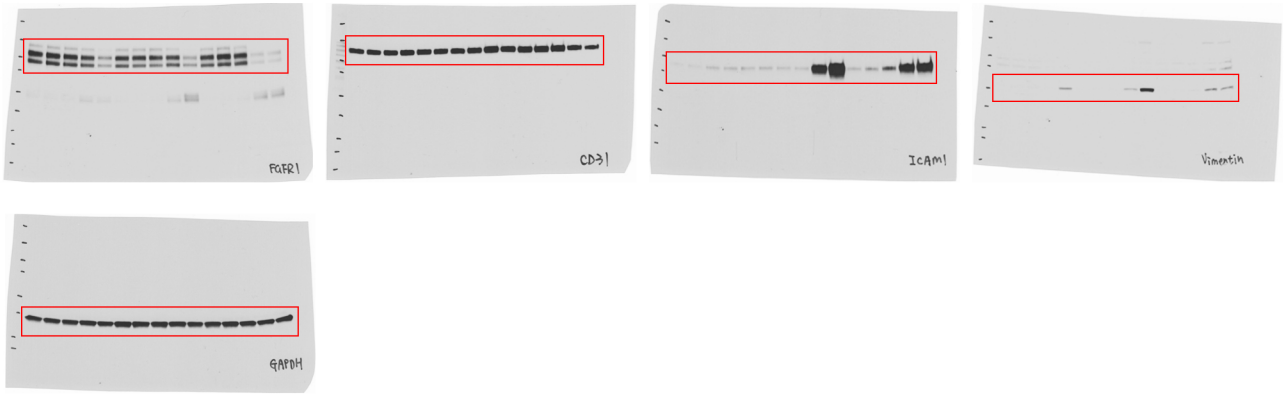
Full unedited gel for Figure S1A



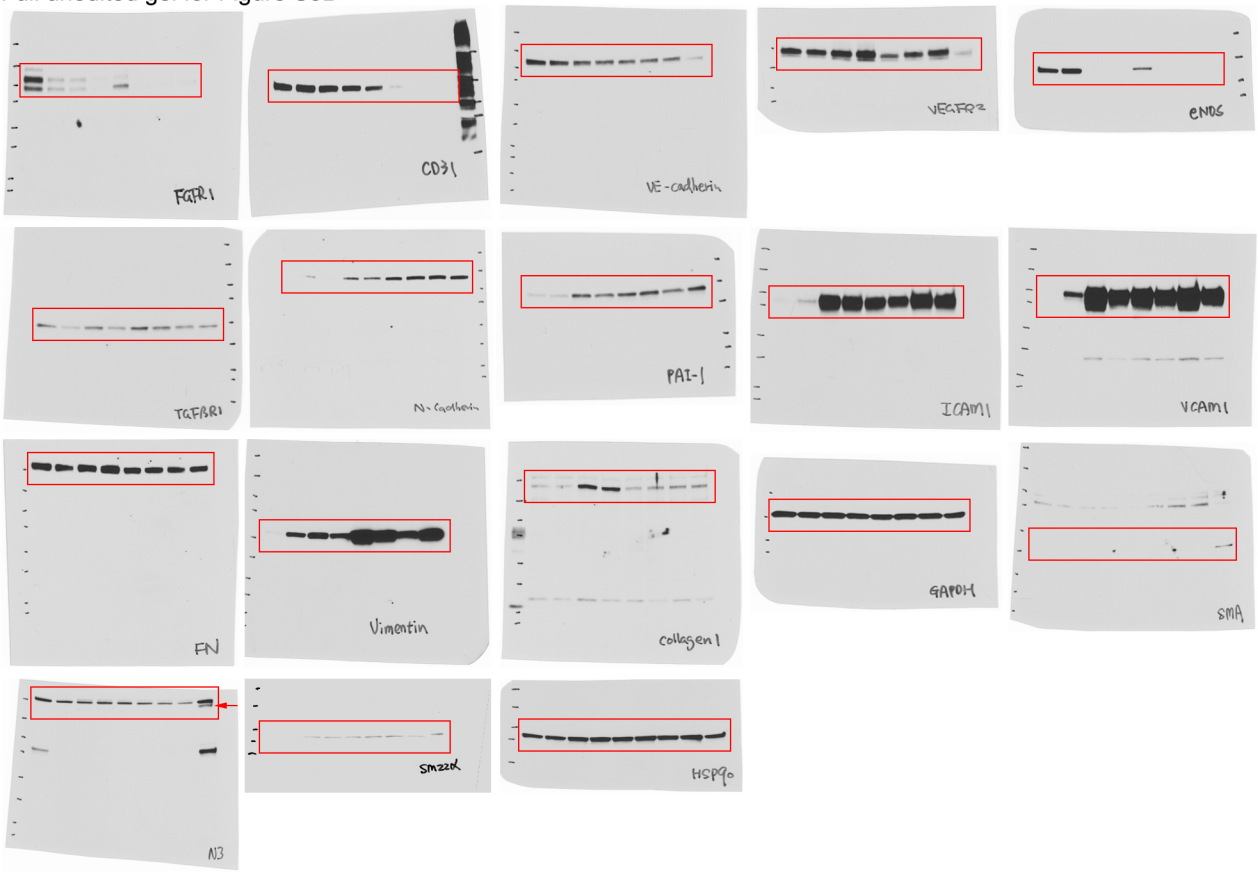
Full unedited gel for Figure S1B



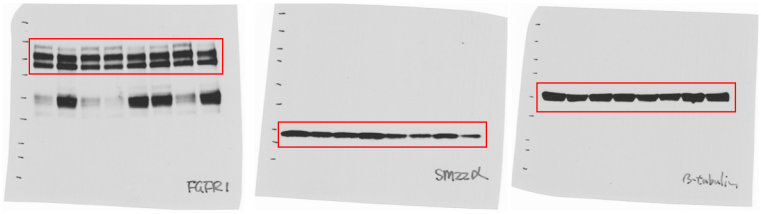
Full unedited gel for Figure S2



Full unedited gel for Figure S3B



Full unedited gel for Figure S4B



Full unedited gel for Figure S4D

Full unedited gel for Figure S5C