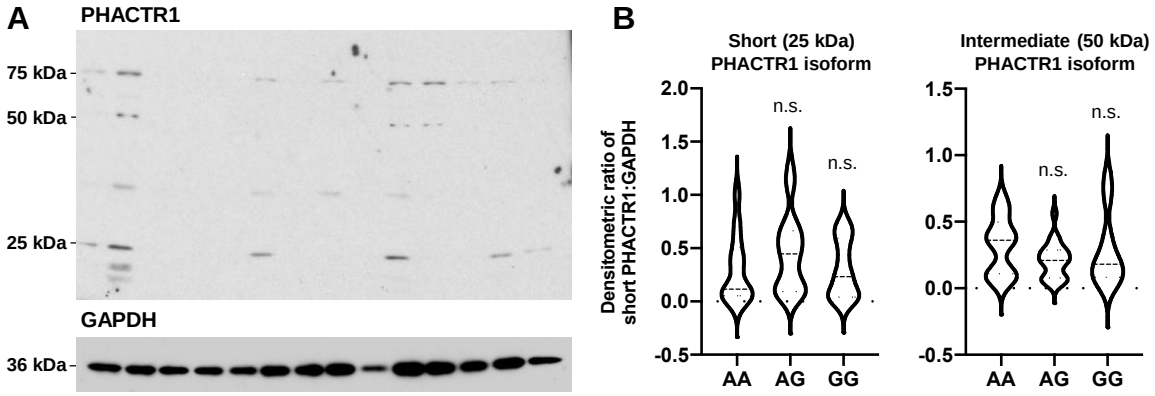
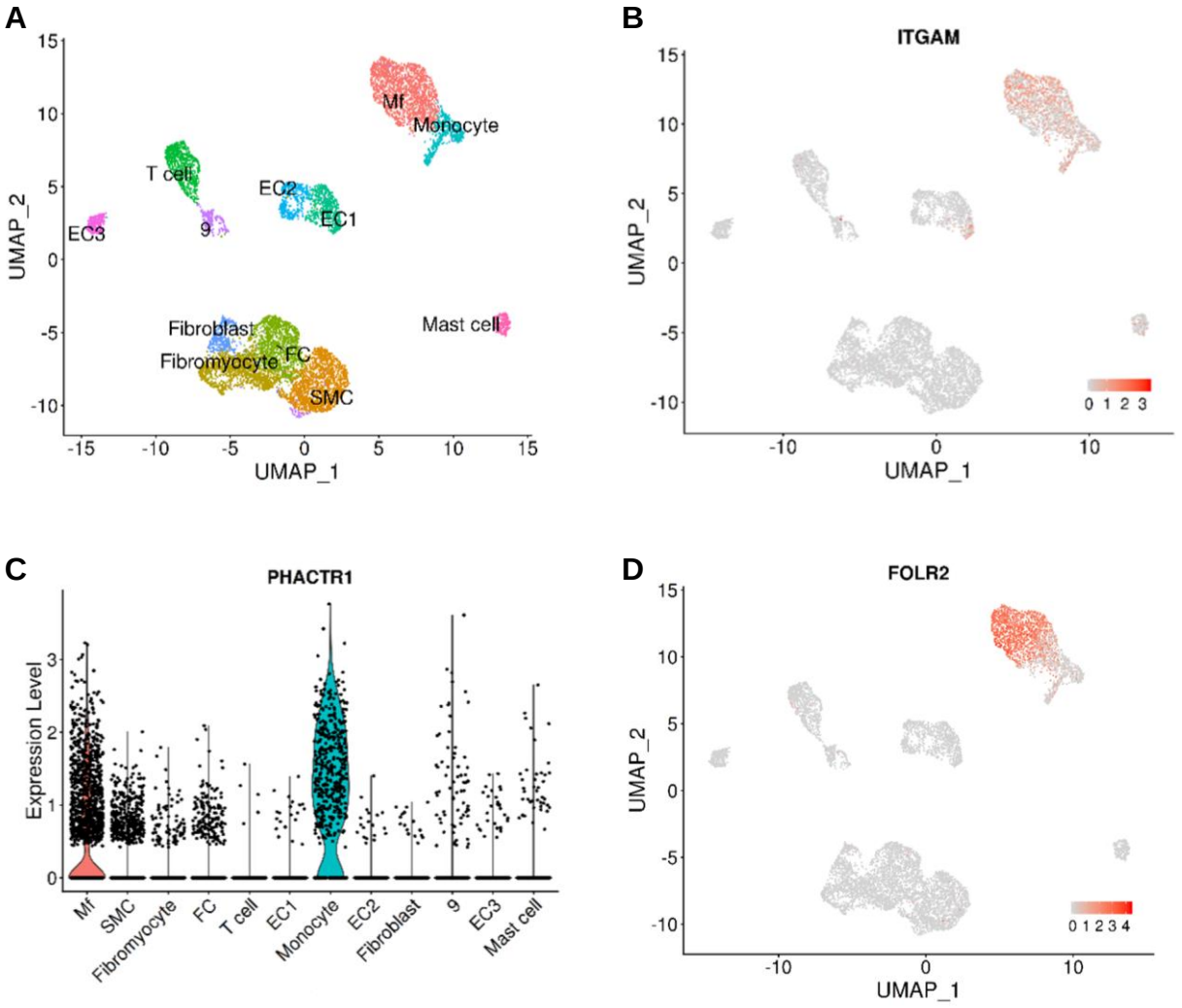
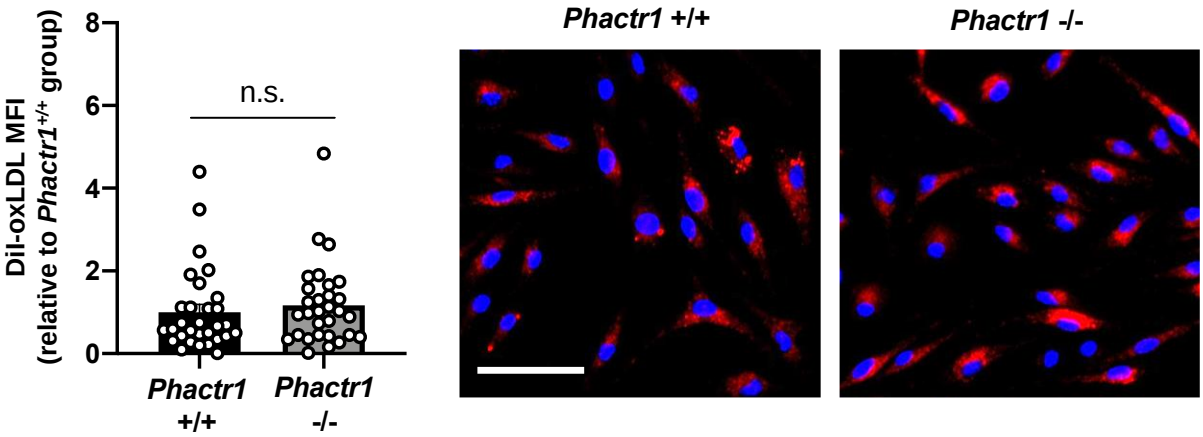


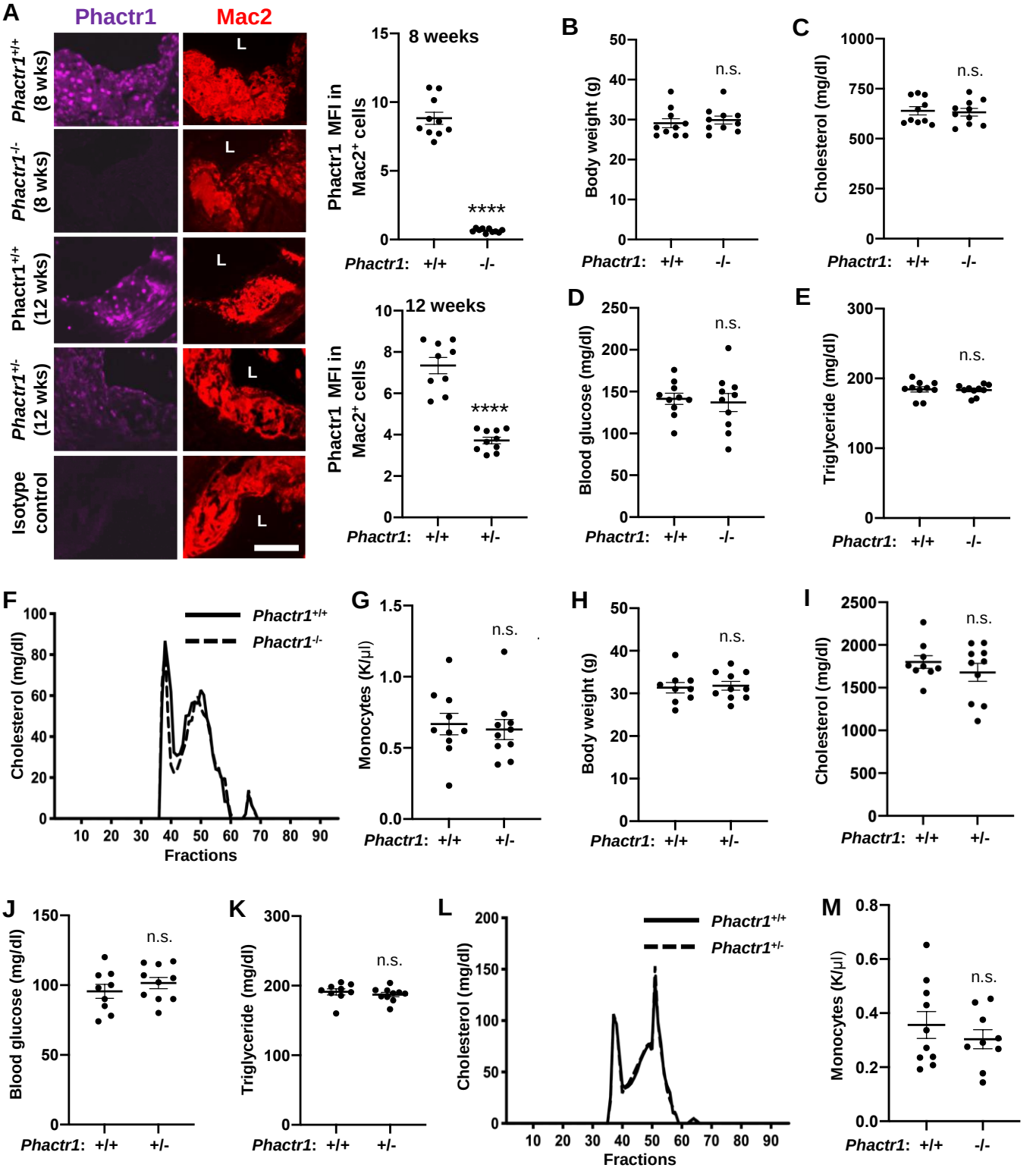
Supplemental Figure 1. HMDMs carrying the rs9349379-G CAD-risk variant do not have a lower expression of the short and intermediate isoforms of PHACTR1. (**A**) Full, unedited immunoblot of PHACTR1 in human monocyte-derived macrophages (HMDMs) genotyped for rs9349379 SNP (n = 48; AA = 14, AG = 24, GG = 10), showing multiple isoforms with different molecular weights. (**B**) The densitometric ratios of the short (25 kDa) and intermediate (50 kDa) PHACTR1 isoforms to GAPDH were plotted relative to the AA-group. Means were compared using one-way ANOVA with Dunnett's multiple comparisons test. n.s., non-significant.



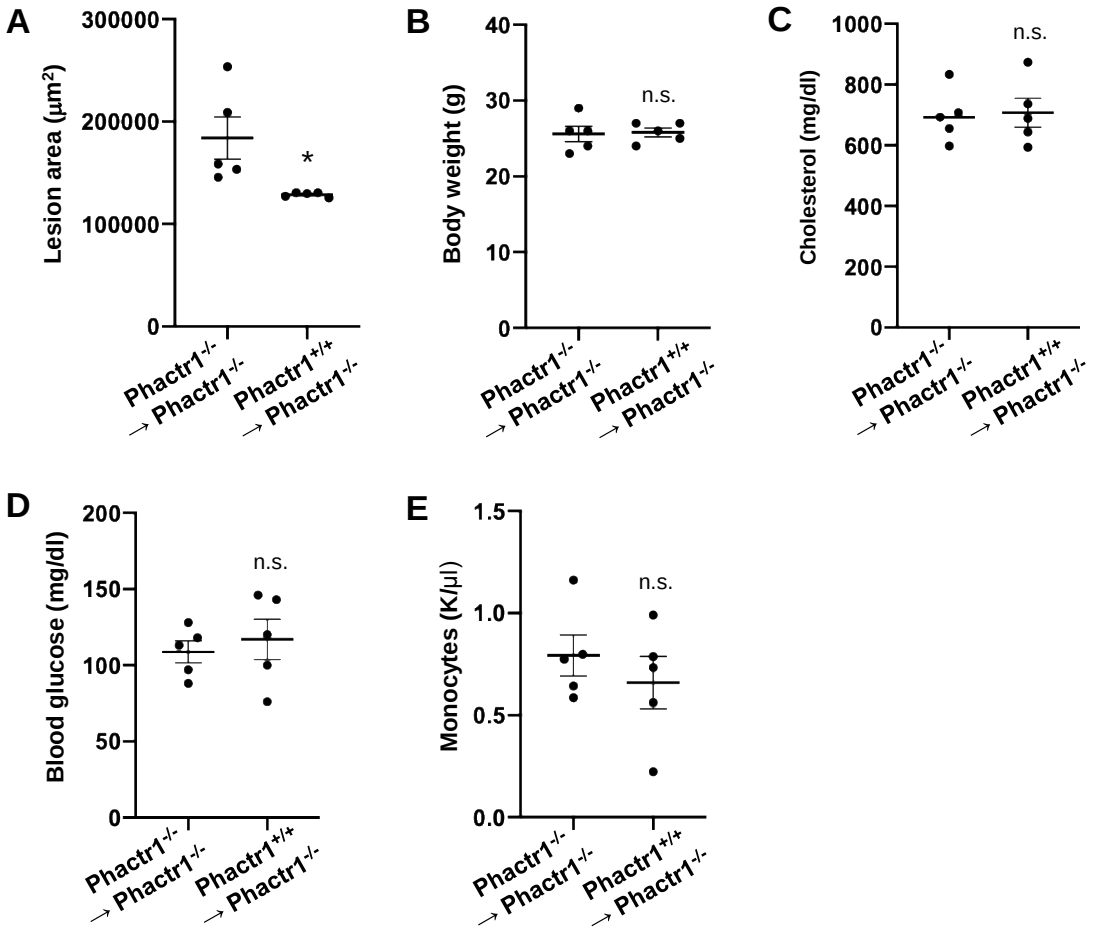
Supplemental Figure 2. Human atherosclerotic carotid artery scRNA-seq reveals that macrophages and monocytes express *PHACTR1*. (**A**) UMAP visualization of cell types identified from atherosclerotic carotid arteries of three patients. Mf, macrophage; EC, endothelial; SMC, smooth muscle cell; FC, fibrochondrocyte. The number "9" represents an unidentified cell type. (**B**) Normalized expression of ITGAM (**B**) visualized on UMAP. Raw gene counts were normalized by the library size of each cell, multiplied by 10,000, and then log-transformed with the addition of a pseudo-count of 1. (**C**) Distribution of normalized gene expression of PHACTR1 in each cell type with higher expression in macrophages and monocytes. (**D**) Normalized expression of FOLR2 visualized on UMAP (see panel B).



Supplemental Figure 3. PHACTR1 deficiency does not affect oxLDL uptake by BMDMs. Bone marrow-derived macrophages (BMDMs) from *Phactr1*$^{+/+}$ and *Phactr1*$^{-/-}$ mice were incubated with fluorescently-labeled oxidized LDL (Dil-oxLDL) for 4 hours, after which the cells were fixed and the mean fluorescent intensity (MFI) of DiI within macrophages was quantified and expressed relative to the value in the *Phactr1*$^{+/+}$ group. Representative images from both groups of cells are shown. Values are mean ± SEM including individual datapoints, with n > 25 macrophages quantified for each group. n.s., non-significant, according to the Student's unpaired t-test. Scale bar: 50 μm.



Supplemental Figure 4. PHACTR1 lesional macrophage staining and systemic parameters of Western diet-fed *Ldlr*$^{-/-}$ mice lacking hematopoietic PHACTR1. (**A**) Irradiated *Ldlr*$^{-/-}$ mice were transplanted with bone marrow from *Phactr1*$^{+/+}$, *Phactr1*$^{+/-}$, or *Phactr1*$^{-/-}$ mice. After 4 weeks, the mice were fed a high-fat Western-type diet (WD) for 8 weeks (for the *Phactr1*$^{-/-}$ study) or 12 weeks (for the *Phactr1*$^{+/-}$ study). Aortic root lesional cross-sections were co-stained for PHACTR1 and Mac2. Illustrative images are shown along with MFI of PHACTR1 Mac2+ areas (L, lumen). Scale bar: 100 μm. (**B-G**). Metabolic endpoints (i.e., body weight, total plasma cholesterol, blood glucose, triglyceride, lipid profiles) and monocyte numbers in blood were quantified for the 8-week *Phactr1*$^{+/+}$ and *Phactr1*$^{-/-}$ cohorts. (**H-M**) As in panels B-G, but for the 12-week *Phactr1*$^{+/+}$ and *Phactr1*$^{+/-}$ cohorts. For all panels, results are shown as individual datapoints with lines indicating mean ± SEM; $^{****}P <$ 0.0001, according to Students unpaired t-test and Mann-Whitney test, respectively; n.s., non-significant.



Supplemental Figure 5. Atherosclerotic lesion area and systemic parameters of *Phactr1*$^{-/-}$ *Ldlr*$^{-/-}$ mice with or without hematopoietic PHACTR1. Irradiated *Phactr1*$^{-/-}$ *Ldlr*$^{-/-}$ mice were transplanted with bone marrow from *Phactr1*$^{-/-}$ or *Phactr1*$^{+/+}$ mice. After 4 weeks, the mice were fed a high-fat Western-type diet (WD) for 8 weeks, and then aortic root lesional cross-sections were analyzed. (**A**) Total lesion area in the aortic root was analyzed using H&E stained slides. (**B-E**) Body weight, total plasma cholesterol, blood glucose, and blood monocyte numbers were quantified for both groups of mice. For all panels, results are shown as individual datapoints with lines indicating mean ± SEM; *P < 0.05 according to Student's unpaired t-test; n.s., non-significant.