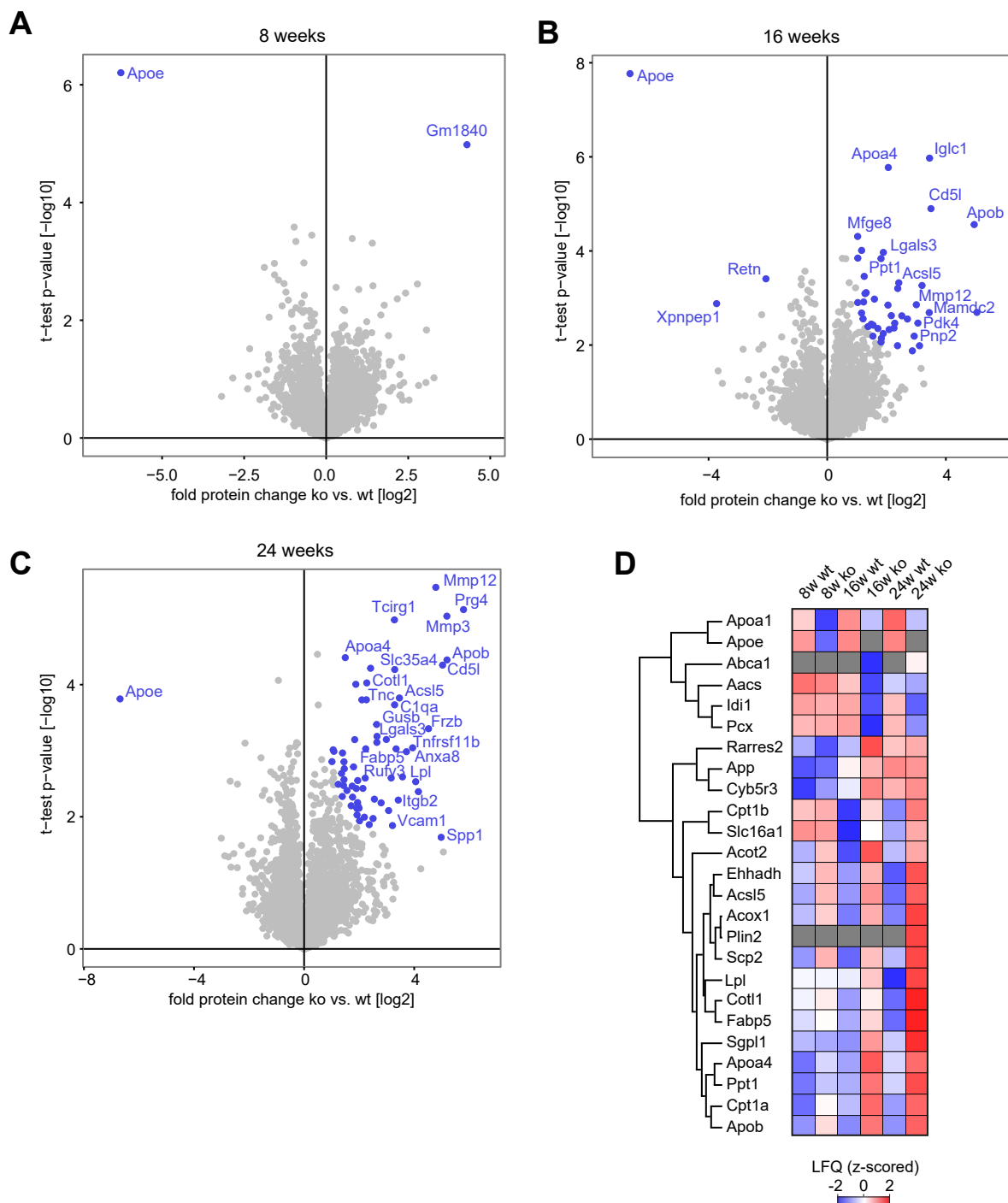
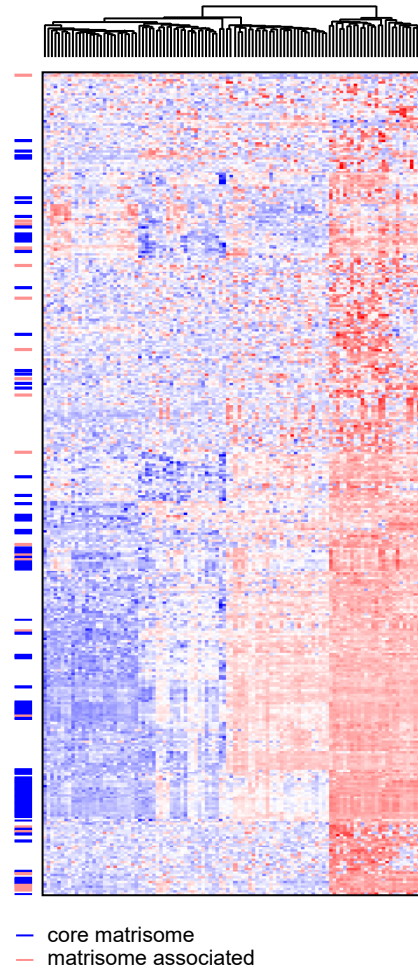


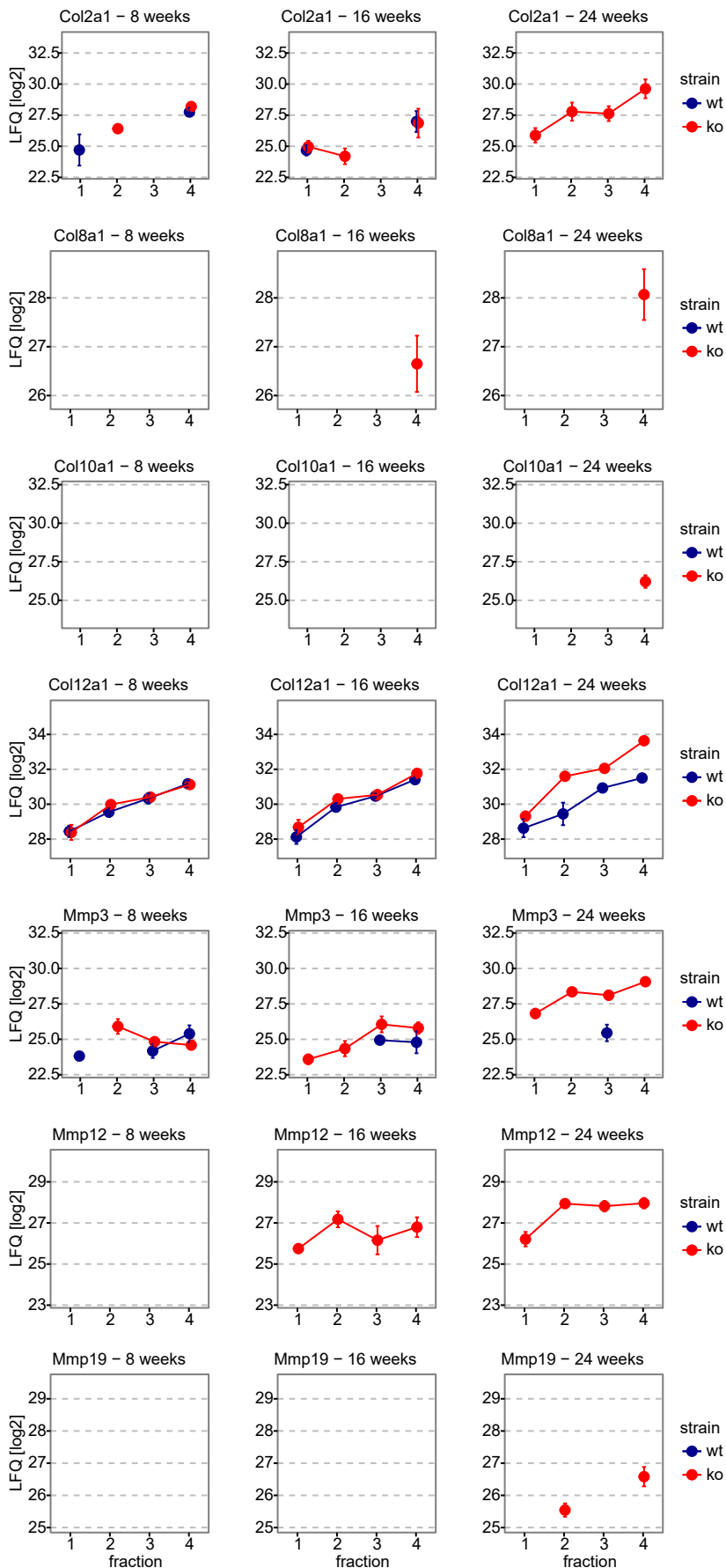
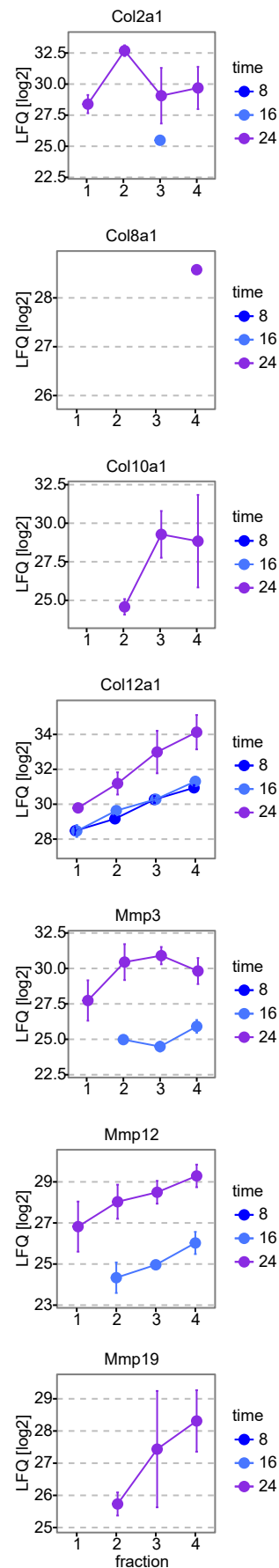
**Supplementary Figure S1:** Proteomic measurement of mouse aortas with high reproducibility. **(A)** Haematoxylin and Eosin stainings of longitudinal sections of the aorta and nuclei counts per plaque section at Brachiocephalic artery (BCA) lesions (mice  $n = 2$  for each group, 7-9 sections per aorta) revealed different developmental stages of atherosclerotic plaques in 16 week and 24 week old mice **(B)** Number of quantified proteins per mouse aorta by single-run, high-resolution mass spectrometry (MS)-based proteomics. ko = ApoE<sup>-/-</sup> **(C)** Correlation matrix of full aorta proteomes reveals low variability. **(D)** QDPS profiles for selected proteins in cohort #2. Data points are filtered for the presence of at least two valid values and are averages. Error bars represent SEM.



**Supplementary Figure S2: (A-C)** Student t-test comparisons of ApoE  $-/-$  vs. wt mice at different timepoints. Blue proteins: permutation based FDR < 0.1,  $s_0 = 0.2$  **(D)** Regulation of proteins related to lipid metabolism and transport in the course of atherogenesis. Unsupervised hierarchical clustering of z-scored MaxLFQ value of significantly (ANOVA, FDR < 0.05) regulated proteins related to lipid metabolism and transport based on GO term annotations and manual database search.



**Supplementary Figure S3:** ECM associated proteins in mouse aorta. (Unsupervised hierarchical clustering of protein expression values (MaxLFQ, z-scored) of ECM-associated proteins as defined by their solubility profiles.

**A****B**

**Supplementary Figure S4:** Upregulation of collagen subtypes and matrix metalloproteases during atherosclerotic plaque formation. **(A,B)** QDPS profiles of significantly upregulated collagens and MMPs in cohort #1 (A) and cohort #2 (B). Data points are filtered for the presence of at least two valid values and are averages.