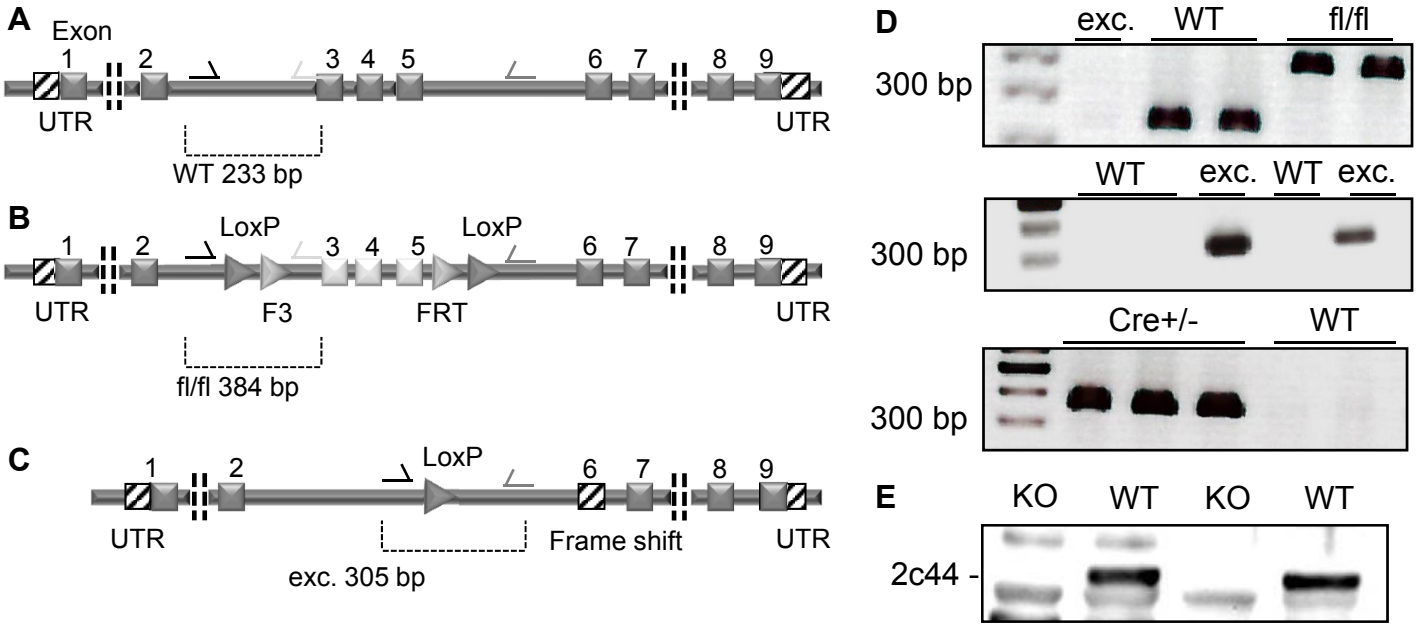
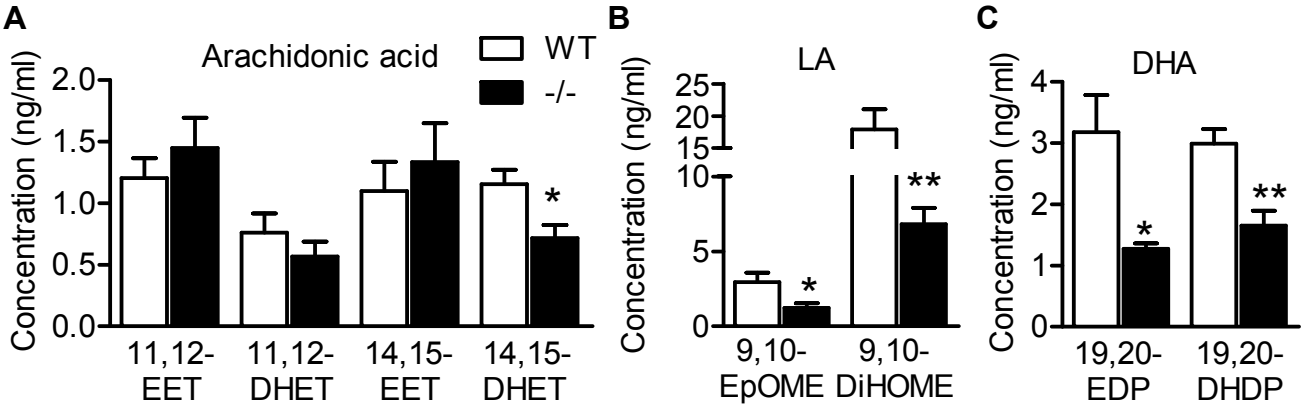
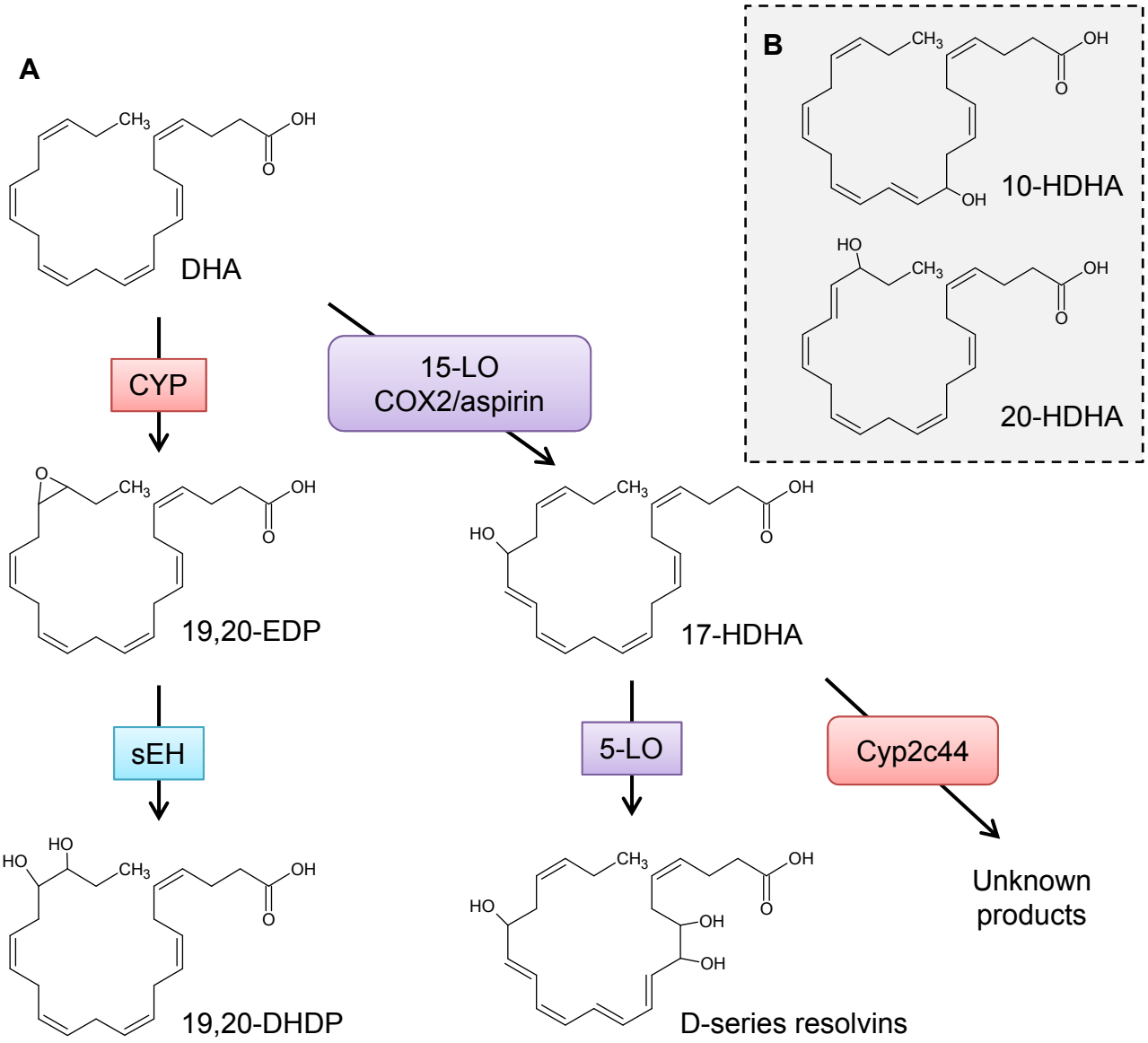


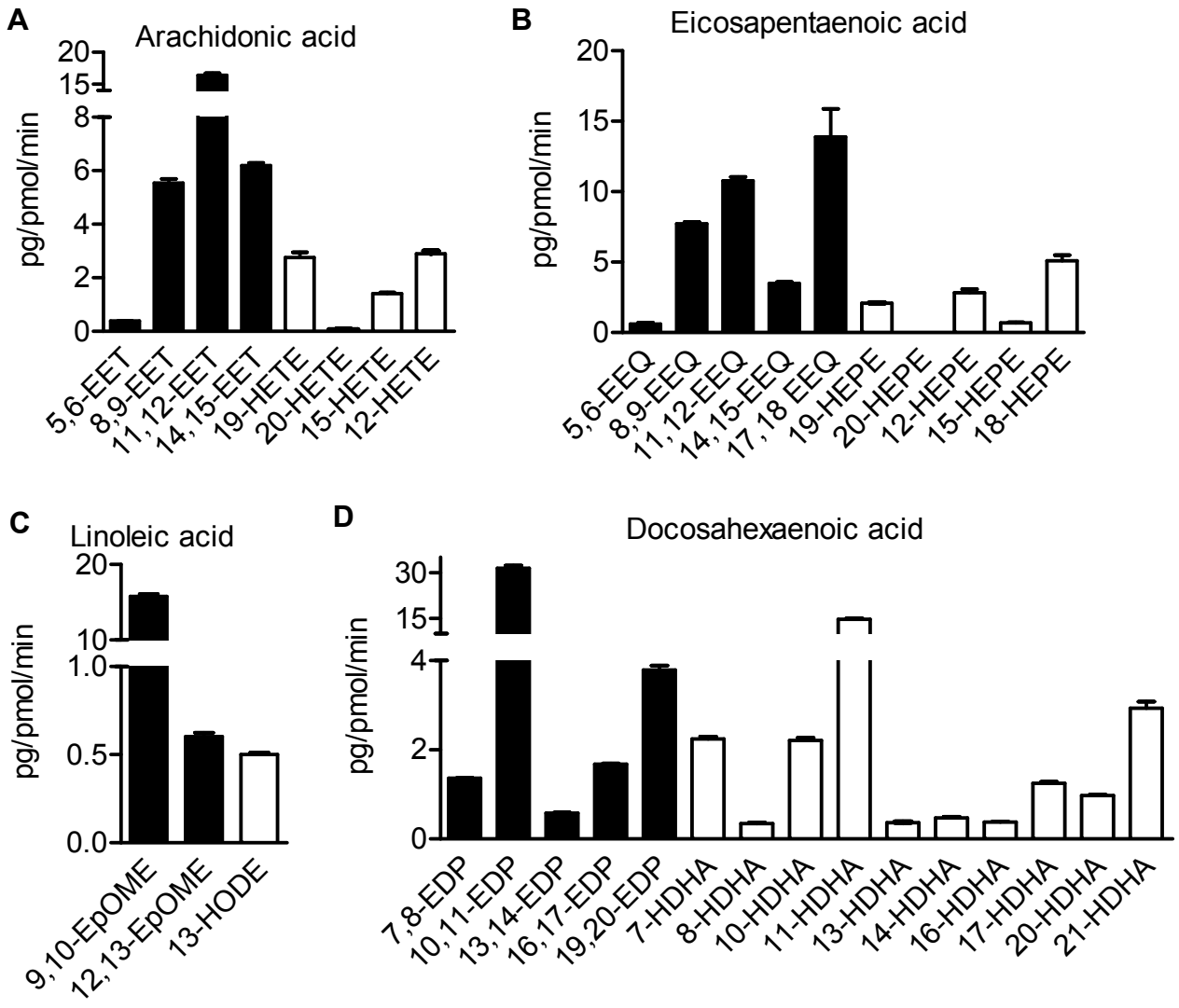
Supplementary Figure 1. **Schematic depiction (not drawn to scale) of a Cre-dependent *Cyp2c44* knock out mouse.** (**A**) *Cyp2c44* wild-type genomic locus. (**B**) Conditional knockout allele after *in vivo* Flp recombination. (**C**) Constitutive knockout allele after Cre recombination. Primer binding sites for genotyping are market with arrows. (**D**) PCR-based detection of the floxed locus (fl/fl), and wild-type (WT) alleles, as well as detection of excision (exc.) after Cre recombination. (**E**) Western blot showing Cyp2c44 expression in livers (microsomal fractions) from wild-type (WT) and Cyp2c44$^{-/-}$ mice.



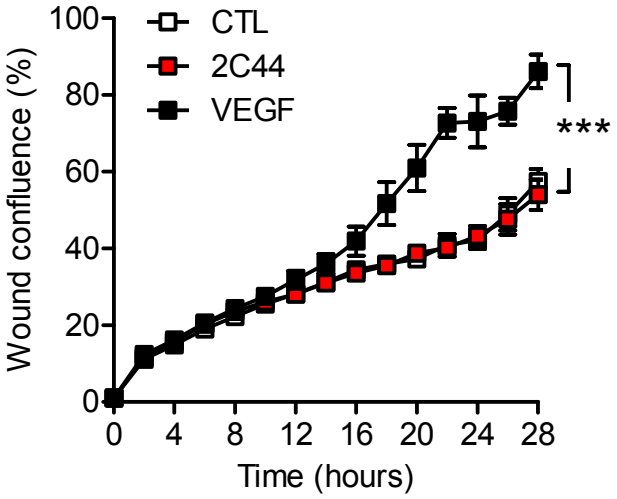
Supplementary Figure 2. PUFA metabolite profile in the blood plasma of the adult mice. Fatty acids from adult wild-type (WT) and Cyp2c44$^{-/-}$ (-/-) mice were extracted from blood plasma and determined by LC-MS/MS. (**A**) Arachidonic acid derived 11,12- and 14,15-epoxyeicosatrienoic acid (EET) and 11,12- and 14,15- dihydroxyeicosatrienoic acid (DHET). (**B**) Linoleic acid (LA)-derived 9,10-epoxyoctadecenoic acid (EpOME) and 9,10- dihydroxyoctadecenoic acid (DiHOME). (**C**) Docosahexenoic acid (DHA)-derived 19,20-epoxydocosapentaenoic acid (19,20-EDP) and 19,20-dihydroxydocosapentaenoic acid (DHDP). The graphs summarize data from 6-9 animals in each group; *P<0.05 **P<0.01)



Supplementary Figure 3. The biosynthesis and chemical structure of HDHAs. (**A**) Docosahexaenoic acid (DHA) is converted by CYP epoxygenases (CYP) for example to the epoxide 19,20-epoxydocosapentaenoic acid (EDP), which is subsequently metabolised to 19,20dihydroxydocosapentaenoic acid (DHDP) by the soluble epoxide hydrolase (sEH). DHA can also be transformed by 15-lipoxygenase (15-LO) or acetylated COX-2 to 17-hydroxydocosahexaenoic acid (17-HDHA). The further processing of 17-HDHA by 5-lipoxygenase (5-LO) leads to the D-series resolvins which are differ in their stereochmistry at the 17 carbon position. In this manuscript, we proposed that the 17-HDHA is metabolised by Cyp2c44 and to as yet unidentified products. (B) The chemical structure of 10-HDHA and 20-HDHA.



Supplementary Figure 4. Products generated by Cyp2c44 *in vitro*. Enzyme activity assays were performed with microsomes (50 pmol) isolated from SF9 cells overexpressing Cyp2c44 and human oxidoreductase and supplemented with (**A**) arachidonic acid, (**B**), eicosapentaenoic acid, (**C**) linoleic acid, and (**D**) docosahexenoic acid (each 10 µmol/L). The CYP products were measured by LC-MS/MS; the black bars indicate epoxides, the white bars the hydroxylated products. The graphs summarize the data from 3 independent experiments.



Supplementary Figure 5. Consequence of Cyp2c44 overexpression on endothelial cell migration. Human endothelial cells were transiently transfected with either a control plasmid or a Cyp2c44 overexpression plasmid. Endothelial cell migration was studied in a scratch wound assay and the time course of wound closure (%) assessed over 28 hours using an automated microscope system. The graph summarises data from 6 independent experiments, each using a different batch of endothelial cells; *** $P<0.001$.