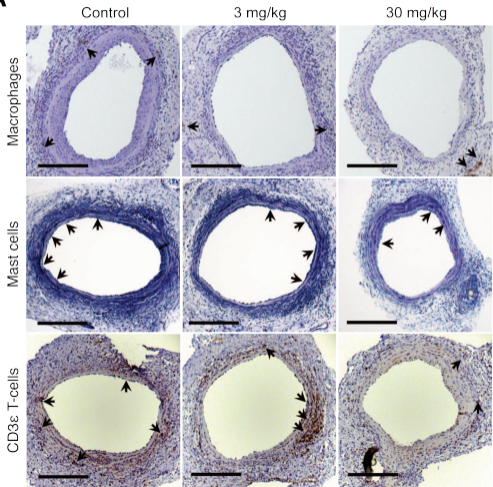


Supplementary Figure 1

A



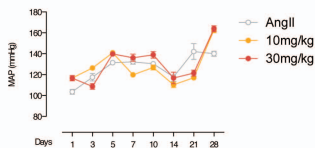
SUPPLEMENTARY FIGURES

Supplementary Figure I

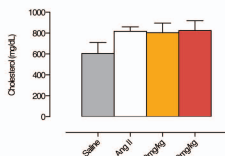
Oral (dietary) inhibition of 5-LO in the elastase perfusion model reduces immune cell infiltration. (A) Representative IHC stains exhibiting macrophage, mast cell and CD3 ϵ T-lymphocyte infiltration in the aorta of elastase perfused mice.

Supplementary Figure II

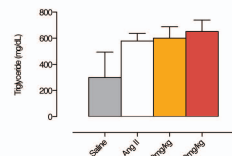
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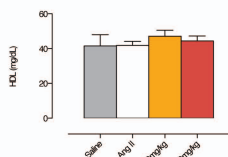
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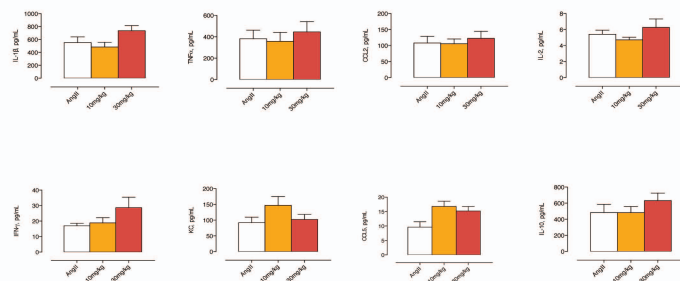
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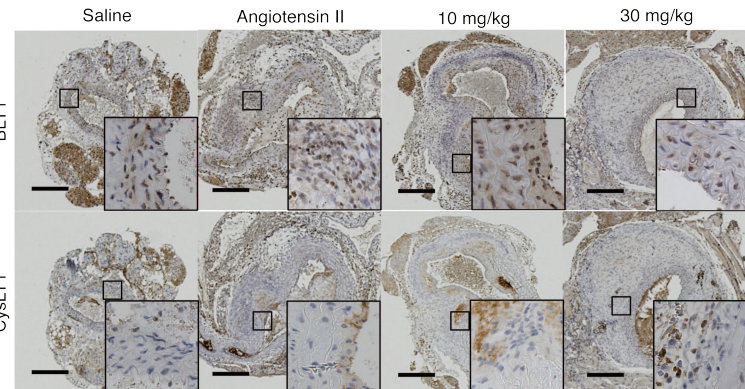
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E



F



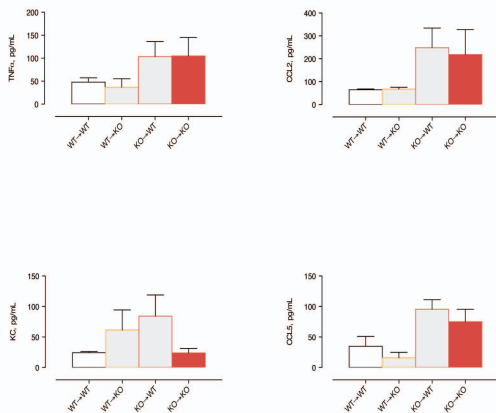
SUPPLEMENTARY FIGURES

Supplementary Figure II

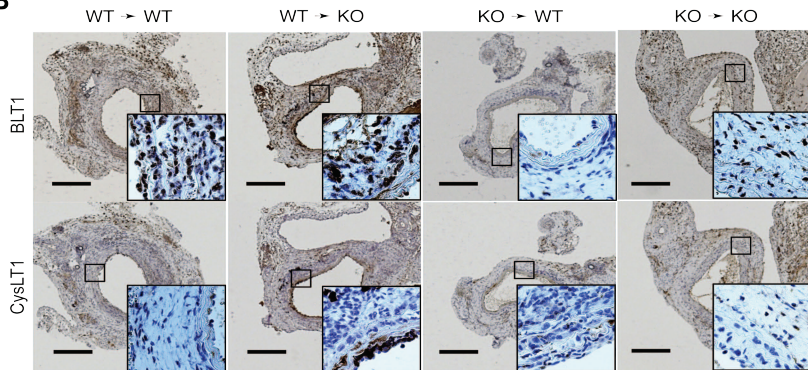
Oral (dietary) inhibition of 5-LO in the Ang II infusion model is blood pressure, plasma lipid and circulating cytokine level independent. (A) Mean arterial blood pressure represented in mmHg measured over time in Ang II infused mice. (B) Plasma cholesterol levels in mg/dL measured in mice at day 28 following continuous Ang II infusion. (C) Plasma triglyceride levels in mg/dL measured in mice at day 28 following continuous Ang II infusion. (D) Plasma high-density lipoprotein levels in mg/dL measured in mice at day 28 following continuous Ang II infusion. (E) Plasma cytokine IL-1 β , TNF α , CCL2, IL-2, IFN- γ , KC, CCL5, and IL-10 levels in pg/mL measured in mice at day 28 following continuous Ang II infusion. (F) Representative IHC stains exhibiting BLT1 and CysLT1 receptor expression in mice at day 28 following continuous Ang II infusion.

Supplementary Figure III

A



B



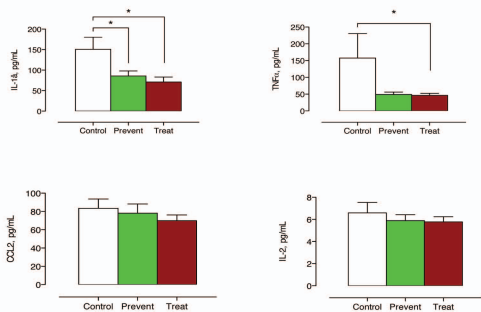
SUPPLEMENTARY FIGURES

Supplementary Figure III

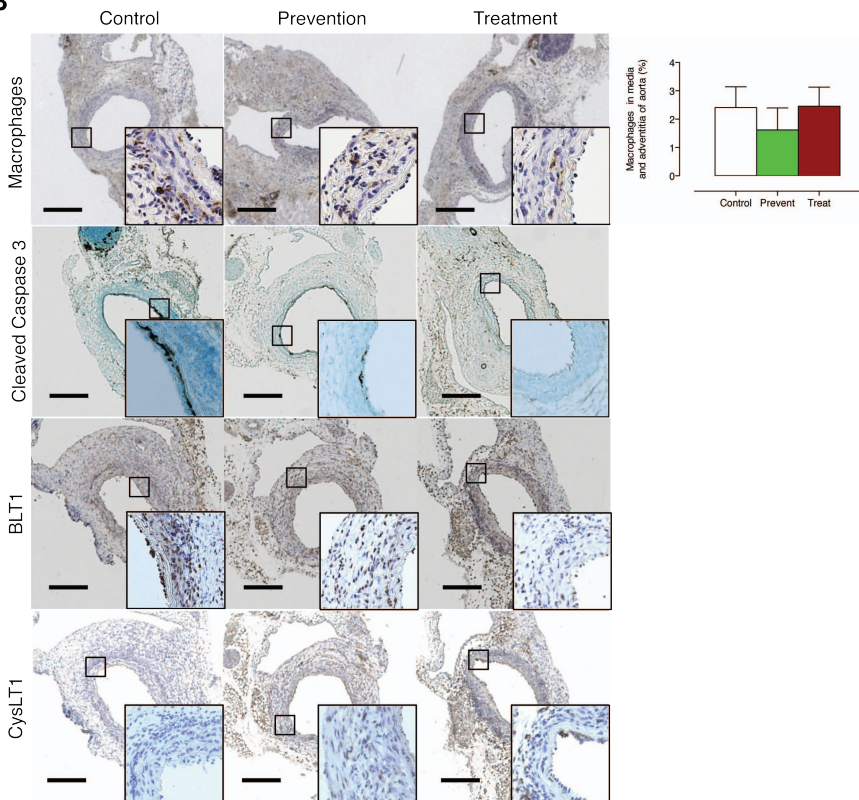
Adoptive transfer of bone marrow derived 5-LO mitigates aneurysm formation. (A) Plasma cytokine TNF α , CCL2, KC, and CCL5 levels in pg/mL measured at day 14 after elastase perfusion. (B) Representative IHC stains exhibiting BLT1 and CysLT1 receptor expression in the aorta of elastase perfused mice.

Supplementary Figure IV

A



B



SUPPLEMENTARY FIGURES

Supplementary Figure IV

Prophylactic and therapeutic oral (dietary) inhibition of 5-LO mitigates aneurysm formation in the elastase perfusion model. (A) Plasma cytokine IL-1 β , TNF α , CCL2, IL-2 levels in pg/mL measured at day 14 after elastase perfusion. * $P < 0.05$ pair-wise comparison versus control. (B) Representative IHC stains and quantification exhibiting macrophage infiltration in the aorta of elastase perfused mice, and representative IHC stains of cleaved caspase-3, BLT1 and CysLT1 receptor expression in the aorta of elastase perfused mice.

Assay

IC₅₀

5-LO, human enzyme

525 nM (n=2)

LTB₄ production, PMNL

9.9 ± 1.2 nM (n=30)

LTB₄ production, human blood

39 ± 2.8 nM (n=30)

cysLT production, human blood

51 nM (n=2)

LTB₄ production, mouse blood

240 nM

15-LO, human enzyme

>10,000 nM

COX-1, human enzyme

>10,000 nM

COX-2, human enzyme

>10,000 nM

PGE₂ production, human blood

>10,000 nM

TXB₂ production, human blood

>10,000 nM

SUPPLEMENTARY TABLES

Supplementary Table I

Specificity of AZD4407 (AstraZeneca PLC, London, UK) in human and mice whole blood, and PMNL samples illustrates significant inhibition of LTB₄ production, and low non-specific activity against other lipoxygenases, and cyclooxygenases from the eicosanoid pathway.