Apolipoprotein A-IV inhibits acute vascular inflammation both in vivo and in vitro

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**Objective:** Apolipoprotein (apo) A-IV, the third most abundant apolipoprotein in human HDL, has anti-inflammatory properties in experimental colitis and LPS-induced systemic inflammation. This study investigates the ability of apoA-IV to inhibit acute vascular inflammation in the NZW rabbit and in human coronary artery endothelial cells (HCAECs).

**Methods:** Non-occlusive, peri-arterial carotid collars were inserted into NZW rabbits 24 h after the administration of a single iv infusion of apoA-IV (1 mg/kg) or saline. Animals were sacrificed 24 h post-collar insertion. Carotid arteries were analysed immunohistochemically for expression of vascular cell adhesion molecule (VCAM-1), inter-cellular adhesion molecule (ICAM-1) and intima-media neutrophil infiltration (CD18+ cells). HCAECs were pre-incubated (16 h) with discoidal reconstituted HDL (rHDL) containing phosphatidylcholine and apoA-IV (final apoA-IV concentration 10 μM/L), then stimulated with TNF-α (0.2 ng/mL; 5 h). Cell surface VCAM-1 and ICAM-1 levels were measured by flow cytometry. VCAM-1 and ICAM-1 mRNA levels and mRNA levels of the anti-oxidant and anti-apoptotic enzyme 3β-hydroxysteroid-D24 reductase (DHCR24) were quantified by qPCR.

**Results:** Relative to saline-infused animals, a single infusion of apoA-IV decreased collar-induced neutrophil infiltration into the intima/media by 74% (p<0.05) and endothelial ICAM-1 and VCAM-1 by 75% and 68%, respectively (p<0.01). Pre-incubation of TNF-α-stimulated HCAECs with (A-IV)rHDL reduced ICAM-1 protein and mRNA by 34% and 50%, respectively (both p<0.001) and VCAM-1 protein and mRNA by 62% and 55% (both p<0.001). Furthermore, (A-IV)rHDL increased DHCR24 mRNA 2.6-fold (p<0.001).

**Conclusion:** ApoA-IV has potent vascular anti-inflammatory properties both in vivo and in vitro, which may be mediated by stimulation of DHCR24 expression.