

Introduction: A key feature of abdominal aortic aneurysm is the loss of proliferation and paucity of vascular smooth muscle cells, the major cells within the aortic tunica media. It has been suggested that urocortin 2 (UCN2), a selective ligand for corticotrophin releasing factor receptor 2 (CRFR2) may play a beneficial role in various cardiovascular diseases. However, the role of this peptide in abdominal aortic aneurysm has not been studied in detail. Here we assessed the hypothesis that urocortin 2 promotes an aneurysm phenotype in human aortic smooth muscles in vitro via CRFR2.

Experimental Procedure: We assessed the release of UCN2 from explants of human tissue biopsies in vitro (Aortic aneurysm thrombus, n = 14; aortic aneurysm body, n = 11; femoral atheroma control, n = 6) using ELISA. We investigated the effect of incubating human aortic smooth muscle cells with recombinant UCN2 or aneurysm thrombus explants secretions at a UCN2 dose of 0, 10 and 100 nM for 24 and 48 hours (n = 6 per group x 3 experiments). Cell proliferation was determined by the alamarBlue® cell viability reagent. Results were analyzed and presented as mean ± SEM relative to the control. We also investigated the impact of blocking CRFR2 on UCN2 induced changes on these cells.

Results: Secretion of UCN2 was significantly higher from aneurysm thrombus (n = 14, p = 0.0020) and aneurysm body (n = 11, p = 0.0104) compared to femoral atheroma. Human aortic smooth muscle cells proliferation was dose dependently inhibited by recombinant UCN2 (p = 0.0172) and aortic aneurysm thrombus conditioned medium (p = 0.0273) after 24 hours. This effect of recombinant UCN2 was abrogated significantly by prior incubation with the CRFR2 blocker Astressin-2B (p = 0.0043). Similar effects were seen on incubating cells for 48 hours.

Conclusion: UCN2 is released in high concentrations by aortic aneurysm thrombus. UCN2 inhibits aortic vascular smooth muscle cell proliferation in vitro via CRFR2. This effect may be relevant to the pathogenesis of abdominal aortic aneurysm.