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ANTI-INFLAMMATORY EFFECTS OF ANGIOTENSIN 1-7 IN A CHEMICALLY-INDUCED MODEL OF COLITIS

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Background: Emerging evidences suggest important anti-inflammatory properties for angiotensin (Ang) 1-7 in various models of inflammation. In regard to the gut, enhanced expression of the key enzyme responsible for its production; angiotensin converting enzyme 2 (ACE2) was observed in patients with inflammatory bowel disease (IBD) suggesting a role in the pathogenesis. In this study, we aim to demonstrate the role of this peptide in the pathogenesis of IBD by using the murine dextran sulfate sodium (DSS) colitis model.

Methods: Ang 1-7 was daily administered (by ip injection), or its endogenous levels was depleted (by using MAS1-R antagonist; A779) and colitis severity was determined at gross and histological levels. The colonic expression/activity profile of ACE2, Ang 1-7, MAS1-receptor (MAS1-R), and various signaling molecules (p38 MAPK, ERK1/2, and Akt) were determined by western blot and immunofluorescence. The plasma levels of various cytokines/chemokines were also determined. *In vitro* effect of Ang 1-7 treatment on various immune cell effector functions (apoptosis, chemotaxis and superoxide release) was also examined.

Results: A779 treatment aggravated while Ang 1-7 treatment reduced colitis severity in mice through modulating the expression of the signalling molecules of MAPK family and PI3K and reducing the circulating levels of several cytokines and chemokines, and neutrophil recruitment to the colonic tissue. Enhanced expression of ACE2, Ang1-7 and MAS1-R was also observed post-colitis induction. Ang 1-7 treatment significantly enhanced immune cell apoptosis and reduced neutrophil chemotaxis and superoxide release *in vitro*.

Conclusion: Our results indicate important anti-inflammatory actions of Ang 1-7 in the pathogenesis of IBD through modulating the expression/activity of pro-inflammatory signaling molecules, circulating levels of cytokines/chemokines, and immune cell activity

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