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Anti-inflammatory effect of angiotensin 1-7 (Ang 1-7) in the mouse DSS colitis model

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Background: The role of angiotensin II (Ang II) in the pathogenesis of inflammatory bowel disease (IBD) is well documented but little is known of its more recently identified counter-regulatory peptide Ang1-7 and its signaling pathway ACE2/Ang 1-7/ ***mas***. Enhanced ACE2 expression has been observed in patients with IBD suggesting a role in its pathogenesis.

Aim: To determine the role of Ang 1-7 in modulating colitis severity ***in vivo*** using the mouse DSS colitis model, and its effect on immune cell functions ***in vitro***.

Methods: DSS (3.5% w/v) was used to induce colitis in BALB/C mice and its severity was determined by gross and histological assessments, daily weight changes, and differential WBC counts. Plasma levels of several cytokines and chemokines was measured by proteome profiler kit from R&D systems. Colonic protein level for Ang II, ACE2, ***mas*** receptor, P-ERK1/2, P-p38MAPK, and P-Akt was determined by western blotting and immunofluorescence. Immune cell chemotaxis, apoptosis, and superoxide release was determined using the under agarose assay, Annexin-V/7AAD assay, and luminol oxidation kit respectively.

Results: Enhanced AngII, ACE2, and MasR1 expression was observed in the colon of mice after DSS treatment. Daily IP injections with Ang 1-7 (0.01-0.06 mg/kg, at both prophylactic and treatment approaches) significantly reduced colitis severity at gross and histological level, reduced phosphorylated levels of ERK1/2, p38, and Akt in the colon, and significantly reduced plasma levels of various cytokines and chemokines. Also, Ang 1-7 treatment significantly reduced neutrophil chemotaxis and superoxide release in response to WKYMVm (fMLP-peptide) stimulation, and increased neutrophil and mononuclear cell spontaneous apoptosis.

Conclusion: Ang 1-7 is a promising future therapeutic approach to control colitis severity in part through modulating the activity of various inflammatory signaling molecules, levels of various cytokines and chemokines, and immune cell functions which all are important for the inflammatory process.

Biography

Maitham Khajah has completed his BPharm degree from Faculty of Pharmacy, Kuwait University and obtained his PhD degree from the University of Calgary, Canada. He is currently an Assistant Professor in Kuwait University, Faculty of Pharmacy- Department of Pharmacology & Therapeutics since January 2010. His research interest focuses on studying new targets for the treatment of inflammatory bowel disease. He published various abstracts and peer reviewed manuscripts in international journals. He co-supervised many students for the MSc Molecular Biology Program. Since, he joined Kuwait University, he got various grants as PI and Co-I. He was awarded the Best Young Researcher Award by Kuwait University for the year 2013 – 2014.

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