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INTESTINAL TISSUE KALLIKREIN: KININ SYSTEM IN INFLAMMATORY BOWEL DISEASE

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Introduction & Aim: Kallikreins cleave kininogens to release kinins. Kinins exert their biological effect by activating constitutive bradykinin receptor -2 (BR2), which are rapidly desensitized, and inducible by inflammatory cytokines bradykinin receptor -1 (BR1), resistant to desensitization. Intestinal tissue kallikrein (ITK) may hydrolyze growth factors and peptides whereas kinins increase capillary permeability, evoke pain, stimulate synthesis of nitric oxide and cytokines and promote adhesion molecule – neutrophil cascade. Thus activation of intestinal kallikrein – kinin system may have relevance to idiopathic inflammatory bowel disease (IBD).

Materials & Methods: The distribution and significance of the ITK – kinin components has been investigated in experimental and human IBD.

Results: Our and other results have demonstrated that ITK is localized in intestinal goblet cells, and it is released into interstitial space during inflammation. Kallistatin, an inhibitor of tissue kallikrein, has been shown in epithelial and goblet cells, and was decreased in inflamed intestine as well as in plasma compared with noninflammatory controls. Alterations in both the distribution and levels of kinin receptors in intestinal tissue of IBD patients were demonstrated. B1R was upregulated in inflamed intestine, and has been found to be expressed in a basal part of normal intestine but in the apical portion of enterocytes in the inflamed tissue. In addition ITK and B1R (but not B2R) were visualized in macrophages forming granuloma in Crohn's disease. In animal studies B2R blockade decreased intestinal contraction, however had limited effect on inflammatory lesions. Recent results documented B1R upregulation, in part dependent of TNF-α, in experimental enterocolitis, and demonstrated that selective, nonpeptide B1R receptor antagonist decreased morphological and biochemical features of intestinal inflammation. In addition both B1R and B2R have been indicated to mediate epithelial ion transport that leads to secretory diarrhea.

Conclusions: Taken together it seems that upregulation of B1R in human and animal intestinal inflammation provides a structural basis for the kinins function, and selective B1R antagonist may have potential in therapeutic trial of IBD patients.

Biography

Dr. Antoni worked in Thrombosis Research Center, Temple University Medical School, Philadelphia, USA, having faculty position, investigated a role of plasma and intestinal tissue kallikrein kinin system in experimental IBD, in collaboration with Prof. Dr. RB Sartor, NC, and Chapel Hill, US. Currently working as Professor, Silesian Medical University doing research, medical practice, and teaching students. He has supervised two large research projects founded by Polish Ministry of Sciences related to pathogenesis and treatment of human IBD. He also continued IBD coagulation study to evaluate link of coagulation-inflammation in joints and gut diseases, and anti - platelets agents (Clopidogrel) interactions with proton pump inhibitors. My recent projects were also related to the tissue kallikrein kinin system, and kinin receptors in colorectal polyps, and colorectal cancer as well as a significance of angiogenesis related to kinins and grow factors in ulcerative colitis.

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