Role of pH receptors for intestinal inflammation

Summary / Zusammenfassung
Tissue pH is normally maintained in a narrow range around pH 7.4 mainly through regulation of respiration and renal acid extrusion. During inflammation a decrease of the tissue pH frequently occurs. The molecular mechanisms responsible for pH homeostasis are not completely understood, however, recently it has been shown that the three g-protein coupled receptors OGR1 (GPR68), GPR4 and GPR65 (TDAG8) act as proton-sensing receptors stimulating either inositol phosphate or cAMP formation. These receptors are fully activated at pH 6.8 via the extracellular domain. OGR1 expression is very prominent in the small intestine, as well as in leukocytes. Ligation of GPR4 and OGR1 reduced the organ injury caused by LPS in the rat and had potent anti-inflammatory effects.

Acidosis occurs in the gastrointestinal tract as a result of inflammation or ischemia. Acidosis may especially impair epithelial barrier function which has been found to be crucial for the pathogenesis of IBD. The contribution of the pH sensing g-protein coupled receptor to inflammation and the therapeutic potential of ligation or blockade of those receptors has not been studied in detail so far.

Therefore, we hypothesize that 1) G-protein coupled proton sensing receptors are essential for the maintenance of tissue pH in the normal non-inflamed esophagus, stomach and the small and large intestine 2) during inflammation with decreased tissue pH G-protein coupled proton sensing receptors are involved in the regulation of inflammation.

Weitere Informationen unter http://www.zihp.uzh.ch/1610.php

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