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Expression change of the transient receptor potential ankyrin 1 (TRPA1) receptor in inflammatory bowel disease (IBD) and dextran sulfate-induced colitis in mice

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The transient receptor potential ankyrin 1 (TRPA1) receptor has been implicated in thermo and pain sensation, hyperalgesia and neurogenic inflammation. It is a receptor-ion channel complex functioning as a sensor of noxious stimulus, chemical irritants and cold. Besides sensory nerves it is also localized on non-neural structures such as dermal, epithelial, mucosal cells. TRPA1 occurs in the GI tract and its activation on visceral sensory neurons leads to inflammation. Neural TRPA1 has been shown to induce and maintain colitis. However, the funcion of non-neural TRPA1 in this process has not been elucidated, yet. The aim of the present study was to detect the existence and expression change of non-neural TRPA1 receptors at the protein and mRNA level in human IBD and mouse colitis model.

Human colon biopsies were derived from three groups of patients: 1. patients with non-inflammatory conditions (n=5); 2. patients with colon tumors (n=8); 3. patients with ulcerative colitis or Crohn's disease (n=12). In female mice (C57BL/6 strain, weight: 20-25 g, age: 6-8 weeks), DSS colitis was induced by adding 2% DSS to the drinking water of six animals. Another six mice received only water as a control. Distal third of the colon was taken for further examination. Immunohistochemistry was performed with polyclonal rabbit anti-TRPA1 primary and HRP-conjugated anti-rabbit secondary antibody on paraffin-embedded sections followed by diamino-benzidine (DAB) development. To measure non-neural, i.e. locally synthetized TRPA1 mRNA expression, quantitative real-time PCR was carried out with TaqMan primers and probes on a Roche LightCycler detection system. Transcripts of beta-glucuronidase (GUSB) were determined as internal control.

According to our immunohistochemical evidence TRPA1 receptors are located on the epithelial cells of the colon samples from patients with no inflammation and IBD. A 3.3 fold increase of the TRPA1 mRNA was found in patients with IBD compared to the negative control group and a 2.6 fold increase compared to the tumor patients (ANOVA p=0.0028). In DSS-treated murine samples non-neural TRPA1 receptor gene expression also inreased 8.1 fold (unpaired t-test p=0.0022) compared to the water-treated control group.

The elevation of non-neural TRPA1 receptor mRNA in both human IBD samples and mouse colitis model may suggest a role for the extraneurally localized receptor. Thus the modulatory role of non-neural TRPA1 receptors int the pathomechanism of IBD needs to be further investigated.