Cím:	TRANSIENT RECEPTOR POTENTIAL ANKYRIN 1 (TRPA1) RECEPTOR HAS A PRO INDUCED MOUSE COLITIS
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TRANSIENT RECEPTOR POTENTIAL ANKYRIN 1 (TRPA1) RECEPTOR HAS A PROTECTIVE ROLE IN DEXTRANE-SULFATE INDUCED MOUSE COLITIS

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Transient Receptor Potential Ankyrin 1 (TRPA1) cation channel activation on sensory nerves leads to the release of pro- and anti-inflammatory neuropeptides. Its expression was also described on non-neural (e.g. epithelial, immune) cells, but data on functional significance are contradictory. Therefore, we investigated its role in a colitis mouse model.

Dextrane-sulfate (DSS) was added to the drinking water of male TRPA1 knockout (KO, n=11) and wildtype (WT, n=9) mice for 10 days. Disease activity index (DAI) was calculated from weight loss, stool consistency and blood content. Expression of TRPA1, the pro-inflammatory tachykinins substance P, neurokinin A (NKA), neurokinin B (NKB) and NK1 tachykinin receptor was measured by qPCR, radioimmunassay (RIA) and immunohistochemistry. The levels of interleukin-1 beta (IL-1β), tumor necrosis factor alpha (TNFα), B-lymphocyte chemoattractant (BLC) mRNA and protein were measured by qPCR and Luminex bead-based assay, respectively. TRPA1 activation by the agonist mustard oil (200 µmol) was determined on isolated peritoneal macrophages by fluorescence calcium imaging and on lymph node-derived T cells by flow cytometry.

TRPA1 is present on enteric ganglion cells and macrophages, DSS upregulated its expression 4-fold on day 7 compared to the untreated control. In TRPA1 KO mice, DAI was significantly higher compared to WTs which is supported by the significantly elevated levels of substance P, NKA, NKB, NK1 receptor, IL-1beta, TNFα mRNA and BLC peptide levels in the distal colon. The functionality of TRPA1 ion channel was evidenced by Ca^{2+} influx as a response to mustard oil in WT macrophages and T cells but not in TRPA1 KO cells.

TRPA1 is upregulated in the inflamed colon, macrophages and T cells express functional channels. It exerts a clear protective role in DSS-induced colitis by decreasing tachykinin, NK1 receptor and cytokine /chemokine expressions.

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