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Catestatin Regulates Epithelial cells dynamic to Improve Intestinal Inflammation

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Background:

Ulcerative colitis (UC) is characterized by aberrant regulation of tight junctions (TJ), signal transducer and activator of transcription 3 (STAT3) and interleukin (IL)-8/18 which lead to intestinal barrier defects. Catestatin (CST), an enterochromaffin-derived peptide, regulates immune communication and STAT-3 in the inflamed intestine

Objective:

To investigate the effect of CST on the functions IEC during the development of colitis

Methods:

The expression of *CST* and its correlation with mRNA levels of TJ proteins (Claudin-1 [*CLDN1*], zonula occludens-1 [*ZO1*], occludin [*OCLN*]), epithelial associated cytokines (*IL8, IL18*), and *STAT3* were determined in patients with UC. Acute colitis (5 % DSS, 5 days) was induced in C57BL/6mice. Disease activity index (DAI), TJ proteins, and *Il-18* were determined. Caco-2 epithelial cells were treated with CST (100 ng/ml) for 24h in presence or absence of STAT3-inhibitor (STATTIC) then exposed for LPS (1mg/ml) or 5 % DSS for additional 24 h. Proliferation, viability, and migration of Caco-2 cells were quantified using proliferation, MTT and wound healing assay. Levels of phopho-STAT3 (p-STAT3), TJ proteins, IL-8, and IL-18 in LPS- & DSS-stimulated epithelial cells were quantified

Results:

In UC patients, *CST* correlated positively with TJ proteins and STAT3. Experimentally, CST reduced the severity of colitis and IL-18 release through maintaining the expression of TJ proteins.CST significantly increased the proliferation, viability, and migration of epithelial cells in naïve conditions and in response to LPS-&DSS-induced epithelial injury. CST enhanced the release of phospho-STAT3, restrained the release of IL-8 and IL-18, and maintained the expression of TJ proteins in response to LPS- and DSS-stimulated epithelial cells. In the presence of the STATTIC (STAT3 blocker), the beneficial effect of CST treatment on epithelial cytokine release and the expression of TJ proteins was abolished

Conclusion:

CST could regulate intestinal mucosal dynamic via a potential STAT3-dependent pathway. Targeting CST should be a promising therapeutic approach in UC patients