**Epithelial TNFR2 signaling in the setting of IBD may be involved in the development of colitis-associated carcinogenesis**

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**Abstract**

We have previously reported that NF-kB activation in association with specific up-regulation of TNFR2 was observed in the intestinal epithelial cells of mice suffering from adenoma associated carcinogenesis (AAC). It has been shown that prolonged inflammatory bowel diseases (IBD) may promote carcinogenesis in the epithelial, but the role of TNFR expression in the setting of AAC has not been elucidated.

**Aim and Methods:**

The aim of this study was to analyze TNFR2 signaling in the colonic epithelial cells in the setting of IBD. A mouse colorectal adenoma model, AAC, was established by the injection of intestinal colon adenoma cells from male mice (RA10) and administration with dextran sodium sulfate (DSS). In this mouse model, AAC was induced by administration with DSS. As previously reported, TNFR2 expression was up-regulated in the epithelial cells of AAC mice with or without TNFR2 expression. Furthermore, TNFR2 expression was up-regulated in the epithelial cells of AAC mice with or without TNFR2 expression. In this mouse model, AAC was induced by administration with DSS. As previously reported, TNFR2 expression was up-regulated in the epithelial cells of AAC mice with or without TNFR2 expression. Furthermore, TNFR2 expression was up-regulated in the epithelial cells of AAC mice with or without TNFR2 expression.

**Results:**

TNFR2 up-regulation is observed in the murine colorectal epithelial cell line, AAC, when stimulated with rIFN-γ and TNF. The expression of MLCK induces the loss of barrier function in the epithelial layer in a TNF-dependent manner. TNFR2-specific siRNA abrogates the expression of MLCK in rIFN-γ and TNF-stimulated AAC cells. The expression of NF-κB induces the loss of barrier function in the epithelial layer in a TNF-dependent manner. TNFR2-specific siRNA abrogates the expression of MLCK in rIFN-γ and TNF-stimulated AAC cells.

**Conclusion:**

The epithelial TNFR2 signaling in the context of IBD may be involved in epithelial permeabilization and pro-tumorigenic cytokine production that result in AAC development. These results suggest that MLCK may be a potential target for the prevention of IBD-associated tumor development in humans.

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