Title: Chronic inflammation and the development of malignancy in the GI tract

Stefan M. Brunner

Department of Surgery, University Medical Center Regensburg, Regensburg, Germany

Colorectal cancer (CRC) is associated with loss of epithelial barrier integrity, which facilitates the interaction of the immunological microenvironment with the luminal microbiome, eliciting tumor-supportive inflammation. An important regulator of intestinal inflammatory responses is IRAK-M, a negative regulator of TLR signaling. Here we investigate the compartment-specific impact of IRAK-M on colorectal carcinogenesis using a mouse model. We demonstrate that IRAK-M is expressed in tumor cells due to combined TLR and Wnt activation. Tumor cell-intrinsic IRAK-M is responsible for regulation of microbial colonization of tumors and STAT3 protein stability in tumor cells, leading to tumor cell proliferation. IRAK-M expression in human CRCs is associated with poor prognosis. These results suggest that IRAK-M may be a potential therapeutic target for CRC treatment.