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Symposium

Involvement of transient receptor potential vanilloid 4 (TRPV4) in the regulation of murine colitis and colitis-associated cancer

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TRPV4 is a nonselective cation channel and involved in physical sensing in various types of tissues. The present study investigated the roles of TRPV4 in the pathogenesis of colitis and colitis-associated cancer in mice. The severity of colitis induced by daily treatment with dextran sulfate sodium (DSS) was significantly attenuated in TRPV4-deficient mice when compared with wild-type (WT) mice. The up-regulation of endothelial TRPV4 in colitis models suggests that this channel plays a crucial role in intestinal inflammation via increasing vascular permeability. TRPV4 activation decreased the major endothelial adhesion molecule VE-cadherin in the mouse colon and mouse aortic endothelial cells. The formation of colonic cancer induced by azoxymethane injection following DSS-treatment was also significantly attenuated in TRPV4-deficient mice. TRPV4 was co-localized with f angiogenesis marker and macrophages marker. Azoxymethane/DSS-treatment upregulated the expression of CD105 and VEGFR2 as well as TRPV4 in WT, but these responses were significantly attenuated in TRPV4-deficient mice. Activation of TRPV4 increased TNF- α and CXCL2 expression in peritoneal macrophages. These results suggest that TRPV4 expressed in vascular endothelia and macrophages contribute to progression of colitis and colitis associated cancer.