TRPV3 in intestinal inflammation and colitis-associated cancer: functional role and pharmacological targeting

The transient receptor potential (TRP) channels belong to a large superfamily of polymodal sensors that convert environmental changes into cellular signalling. TRP channels are classified into seven subfamilies that mediate a wide spectrum of cellular processes (Nilius and Szallasi, 2014). Recently, it has been reported that the TRP vanilloid (TRPV) subfamily clearly displays a differential expression in the ulcerative colitis (UC) patients compared with the controls, suggesting a pivotal role in the pathophysiology of inflammatory bowel diseases (IBDs) (Toledo et al., 2020). Among TRPV channels, we will deeply investigate the functional role of the member 3 (TRPV3), which is activated by innocuous warm temperature (35-39°C) and highly expressed in the intestine (Xu et al., 2002). TRPV3 expression follows a gradient along the gastrointestinal tract, with the highest expression in the distal colon (Bischof et al., 2020). Furthermore, despite one study reports that a synonymous-coding single nucleotide polymorphism (SNP) in TRPV3 may be a risk factor for colorectal cancer (CRC) incidence (Hoeft et al., 2010), its role in gut cancer is completely unknown.

The aim of this project is to explore the functional role of TRPV3 and its therapeutic potential in gastrointestinal diseases driven by inflammation, including IBD and colitis-associated cancer (CAC).

For the achievement of our goals, experiments will be performed in: i) primary intestinal and immune cells, ii) colonic organoids generated from wild-type (WT) and TRPV3- knockout (ko) mice, and iii) human biopsies collected from IBD and CRC patients.

Furthermore, a model of colitis induced by dextran sulfate sodium (DSS) and a model of CAC induced by azoxymethane (AOM) and DSS will be performed by using WT and TRPV3-ko mice.

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