TRPM8 and experimental colorectal cancer: pharmacological evidence

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Colorectal cancer (CRC) is one of the most common malignancies of the gastrointestinal tract, and the third most devastating cancer worldwide (Siegel et al., 2017). Transient receptor potential (TRP) melastatin 8 (TRPM8) is a calcium-permeable channel which is believed to contribute to the initiation, promotion and progression of carcinogenesis by disturbing Ca2+ homeostasis that, in turn, may lead to an increase in cell proliferation and induction of differentiation and apoptosis (Prevarskaya et al., 2007; Prevarskaya et al., 2011). Here, we evaluated the effect of TRPM8 ligands on the development of experimental colon cancer in vivo.

The effect of the TRPM8 agonist WS12 and of the TRPM8 blocker M8B were evaluated in two different murine models of colon cancer, i.e. the azoxymethane model of colon carcinogenesis and the xenograft model generated by injection of colorectal cancer cells in nude mice (Borrelli et al. 2014).

The TRPM8 agonist WS12 (10 mg/kg, ip), but not the blocker M8B (6 mg/kg, ip), reduced the tumour weight and volume in a xenograft model of colon cancer. Furthermore, the intraperitoneally administration of WS12 attenuated the colonic numbers of polyps as well as the tumours induced by azoxymethane. These preliminary pharmacological data suggest a possible involvement of TRPM8 in colon carcinogenesis. Studies are in progress to assess i) TRPM8 expression (by RT-PCR and western blot) and localization (by immunohistochemistry) and the expression of Bcl2, Ki67, VEGF, factor VIII-related antigen, CD31, and CD34 (by immunohistochemistry) in intestinal tumoural segments and, importantly, ii) the expression (protein and mRNA) and the localization (by immunohistochemistry) of TRPM8 in tumoural and healthy colonic biopsies from patients at various stages (I-IV) of colorectal carcinoma.

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