Involvement of TRPM8 in colorectal cancer cell viability

S. Finizio[1], E. Pagano[1], B. Romano[1], R. Capasso[1]; P. Orlando[2], A.A. Izzo[1], F. Borrelli[1]

[1]Dept. of Pharmacy, University of Naples Federico II, Italy
[2]Institute of Protein Biochemistry, National Research Council, Pozzuoli (NA), Italy

Background: Transient receptor potential (TRP) melastatin 8 (TRPM8) is a cold-sensitive Ca^{2+} channel protein belonging to the TRP superfamily of ion channels (Bautista et al., 2007). TRPM8 is over-expressed in a number of primary tumours including colon, lung, skin, prostate and breast cancers (Tsalaver et al., 2001), but its role in colon carcinogenesis is largely unexplored to date. Here, we investigated the effect of TRPM8 antagonists on the viability of colorectal cancer cells.
Methods: Colorectal cancer (Caco-2) cells and healthy colonic epithelial cells (HCEC) were used**.** TRPM8 channel mRNA expression was assessed by RT-PCR and western blot. Cell viability was evaluated by using the MTT assay; apoptosis was examined by assessing caspase 3/7 activity; CCAAT/Enhancer-binding protein homologous protein (CHOP) mRNA expression was quantified by RT-PCR; small hairpin RNA-vector silencing of TRPM8 was performed by electroporation.
Results: Colorectal cancer cells expressed TRPM8 (mRNA and protein). The TRPM8 channel antagonists, AMTB, cannabigerol (CBG), cannabidivarin (CBDV) inhibited, in a concentration-dependent manner, Caco-2 cells viability. CBG, which was the most potent among the three antagonists, reduced cell viability (in tumoural but not healthy colonic cells), promoted apoptosis and up-regulated CHOP mRNA expression in CaCo-2 cells. The effect of CBG on cell growth and on CHOP mRNA expression was reduced in TRPM8 silenced cells.
Conclusions: TRPM8 is involved in colorectal cancer cell viability. Further *in vivo* studies are needed to fully elucidate the potential of this channel in colon carcinogenesis.

Bautista et al. (2007) *Nature* 448: 204-208
Tsavaler et al. (2001) *Cancer Res*. 61: 3760-9.