

International Conference on
GASTROINTESTINAL CANCER AND THERAPEUTICS

4th World Congress on
DIGESTIVE & METABOLIC DISEASES

26th Annual Congress on
CANCER SCIENCE AND TARGETED THERAPIES

October 29-30, 2018 | San Francisco, USA

Regulation of calcium-sensing receptor expression by vitamin D and proinflammatory cytokines in colorectal cancer

Irfete S Fetahu

Brigham and Women's Hospital, USA

Anti-proliferative effects of calcium in the colon are partially mediated by the calcium-sensing receptor (*CaSR*). The *CaSR* gene is located in the chromosomal region 3q13.3-21 and is constituted of 2 non-coding and 6 coding exons. The transcription of *CaSR* is under the control of promoters 1 and 2, which yield different transcripts containing either of the untranslated exons 1A or 1B. The expression of *CaSR* decreases during colorectal tumorigenesis and the underlying mechanisms regulating its expression are poorly understood. The *CaSR* promoters 1 and 2 harbor vitamin D elements responsive to 1,25-dihydroxyvitamin D3 (1,25-D3) and NF- κ B, STAT, and SP1 binding sites accounting for responsiveness to proinflammatory cytokines. Vitamin D is known for its pro-apoptotic and anti-inflammatory effects in CRC. We have previously shown that high dietary doses of vitamin D prevented the formation of chemically-induced preneoplastic lesions in a mouse model. On contrary, increased production of proinflammatory cytokines, including TNF α and IL-6 has been reported in inflammatory bowel disease and CRC patients. The impact of 1,25-D3 and proinflammatory cytokines (IL-6, TNF α) on *CaSR* expression in colon cancer cells is not well known. This led us to hypothesize that they might regulate the expression of the *CaSR*. We performed a study where we analyzed the role of 1,25-D3, TNF α , and IL-6 on *CaSR* expression in Caco2/AQ, a well differentiated and Coga1A, a moderately differentiated colorectal cancer cell line. Over the time course of 48 hours, we observed upregulation of the *CaSR* expression in both cell lines. The well-differentiated Caco2/AQ cells responded with higher induction of the *CaSR* expression than Coga1A cell line. Moreover, we observed a reduction in the expression of the proliferation markers cyclin D1, minichromosome maintenance 2&7 (MCM2 and MCM7) in Caco2/AQ cells. These studies suggested that in addition to the direct role of vitamin D in chemoprevention, it can also upregulate the expression of the *CaSR*, thereby linking together the chemopreventive actions of vitamin D and calcium in colorectal tumors. In the less differentiated cell line Coga1A, TNF α had a pronounced effect in increasing the expression of the *CaSR*, indicating that *CaSR* might serve as a defense mechanism towards inflammatory stimuli. Additionally, in both cell lines, IL6 induced the expression of the *CaSR*. Interestingly, in the well-differentiated Caco2/AQ cells treated with 1,25-D3 counteracted the effects of IL6 and TNF α . This could be attributed probably to the anti-inflammatory role of the 1,25-D3. This study provides further evidence towards the protective role of the *CaSR* in colon cells against inflammation.

Biography

Irfete S Fetahu received her PhD at the Medical University of Vienna (Austria) under the supervision of Prof Enikő Kallay as a Marie Curie Early Stage Researcher. During this time she was the recipient of several national and international awards, including fellowships from the European Association for Cancer Research and the Federation of European Biochemical Societies. She was a board member of the Young Scientist Association of the Medical University of Vienna. Following her PhD graduation, she started her postdoctoral fellowship at the Harvard Medical School (USA), where she is currently working in uncovering the aberrancies in the epigenomes of Alzheimer's disease and melanoma. She is also a board member of the Harvard Medical Postdoc Association. She currently serves as an Ambassador of the European Association for Cancer Research.

ifetahu@bwh.harvard.edu

Notes: