Abstract

Colorectal cancer (CRC) is the second most common cause of cancer death. Molecular events in CRC has been extensively studied and several data suggest that Wnt/β-catenin signaling deregulation play a pivotal role in colorectal carcinogenesis. Majority of both familial syndromes (FAP) and sporadic colon cancers, arise from APC or β-catenin genes alterations, leading to Wnt signaling hyperactivation. According to the cancer stem cells (CSCs) theory, some cancer-initiating cells, harboring stem-cell like properties, evade standard chemotherapies, resulting in recurrent and metastatic tumors. Wnt/β-catenin signaling and its deregulation is involved in the recurrence and maintenance of CSCs. In recent years, understanding of molecular mechanisms underlying CSCs biology, led to development of novel strategies to completely eradicate colorectal cancer.

Some evidences suggest a potential crosstalk between the endocannabinoid system and the Wnt pathway, also in cancer stem cells, in several tumor types. This could represent a key mechanism in the control of the anti-cancer activity of cannabinoids, as well as a novel putative site for pharmacological intervention.

Results from this work led to identification of Rimonabant, originally an inverse agonist of CB1 cannabinoids receptor, as modulator of Wnt/β-catenin pathway in CRC, able to control colon cancer stemness, without toxicity toward cells from healty tissue. Moreover, for the first time, we proposed a novel epigenetic mechanism Rimonabant-mediated.