

Potential Anti-Colon Cancer Effect of LTC₄ through the Induction of 15-PGDH

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Colorectal cancer is one of the leading causes of cancer-related deaths worldwide. Cyclooxygenase-2, having a key role in the biosynthesis of prostaglandin E₂ (PGE₂), is often up-regulated in CRC. PGE₂ induces angiogenesis and tumor cell survival, proliferation and migration. The tumor suppressor 15-hydroxyprostaglandin dehydrogenase (15-PGDH) is a key enzyme in PGE₂ catabolism, converting it into its inactive metabolite 15-keto-PGE₂ and is often down-regulated in cancer. Interestingly enough, CRC patients expressing high levels of Cysteinyl leukotriene receptor 2 (CysLTR2) have good prognosis and therefore, we investigated a potential link between CysLTR2-signaling and the tumor suppressor 15-PGDH in colon cancer cells.

We observed a significant up-regulation of 15-PGDH after LTC₄ treatment, the ligand for CysLTR2, in colon cancer cells, on both mRNA and protein levels, which could be reduced by a CysLTR2 antagonist or a JNK inhibitor. LTC₄ induced 15-PGDH promoter activity via JNK/AP-1 phosphorylation. Furthermore, we also observed that LTC₄ via CysLTR2/JNK-signaling pathway increased the expression of the differentiation markers sucrose isomaltase and mucin-2 in colon cancer cells.

Restoration of 15-PGDH expression through CysLTR2-signaling promotes differentiation of colon cancer cells, indicating an anti-tumor effect of CysLTR2-signaling.

Biography:

Dr. Shakti Ranjan Satapathy is a postdoctoral researcher at Department of Translational Medicine, Lund University, Sweden where he studies the role of Cysteinyl leukotriene receptors in metastasis of colon cancer. He started his postdoctoral research at Purdue University, USA where he studied the role of novel kinases as potential therapeutic targets for prostate cancer and Alzheimer's disease. He had received his PhD in Cancer nanotechnology in 2015 from KIIT University, India. Apart from his curiosity in life sciences, he is very fond of physics and world history. Dr. Shakti is committed to advance the understanding about cancer and making the world a better place.