Abstract: Disregulation of the Wnt/β-Catenin signaling pathway often leads to abnormal activation of the proto-oncogene, β-Catenin. β-Catenin is a multi-functional protein that in the cell membrane maintains epithelial tissue integrity and in the nucleus, functions as a transcription modulator to regulate transcription of many genes involved in carcinogenesis. The previous results from our laboratory indicate a positive interaction between the Gq signaling and β-Catenin-target gene expression in HT-29 colon cancer cells.

Methods: Here we have extended those studies by treating HT-29 colon cancer cells with two Gq class of Gαq agonists, thrombin and carbachol.Briefly, HT-29 cells were cultured, treated with the agonists, the cell extracts were isolated, and then cellular β-Catenin expression and function were measured by western blotting, immunofluorescence microscopy, and reverse-transcriptase PCR respectively.

Results: Exposure of HT-29 cells to thrombin and carbachol led to a dramatic increase in the cytoplasmic levels of the β-Catenin protein, levels, its intracellular localization, and the target gene expression were measured by western blotting, immunofluorescence microscopy, and reverse-transcriptase PCR respectively.

Thrombin or carbachol treatment of HT-29 cells also enhanced expression of several β-Catenin-target genes including c-myc, cyclin D1, cox2, and the reporter luciferase gene placed downstream of the Catenin/Tcf binding elements, although this increase was not more than two-fold.

Conclusions: Collectively our results further support the positive role of Gq signaling in the regulation of the Catenin signal transduction occurs in colorectal cancer and some other human malignancies. In these cancers, genetic and epigenetic changes in the components of this signaling pathway often leads to abnormal activation of the proto-oncogene, β-Catenin.