Abstract: Introduction: The Wnt/β-Catenin signaling pathway regulates multiple cellular processes and therefore its abnormal activation has been observed in various human cancers. We and others have got some evidence that heterotrimeric G-proteins regulate Wnt signaling. Our previous results have shown that activation of Gαq in HEK293T cells increases cellular β-Catenin protein levels. Here we have investigated the biological outcome of Gαq-mediated cellular accumulation of β-Catenin by measuring the expression of several β-Catenin-target genes like cyclin D1, c-myc, and fgf-20.

Methods: HEK-293T cells were grown under standard conditions and then were transfected with the Gαq-encoding plasmid or treated with thrombin and carbachol, two agonists of the Gαq signaling. Cellular β-Catenin protein levels and its intracellular localization were analyzed by western blotting and immunofluorescence microscopy assays. Gene expression was assayed by reverse transcriptase-PCR and (or) real time-PCR.

Results: Thrombin or carbachol treatment of HEK-293T cells led to an approximate two-fold increase in cellular β-Catenin protein levels, although the target gene transcription was not enhanced more than 1.5-fold. Consistently, transfection of cells with low amounts of the Gαq-encoding plasmid led to about 2-fold increase in transcription of the selected target genes. Interestingly, we found out that overactivation of Gαq which normally produces high cellular levels of β-Catenin, has a negative effect on β-Catenin-target gene expression. Our laboratory is currently investigating this issue.

Conclusions: The current results suggest that although upregulation of β-Catenin protein levels by Gαq is biologically relevant, the interaction between these two signaling pathways is tightly regulated.

Keywords: β-Catenin, Gαq, HEK-293T

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