

MODULATION OF β -CATENIN SIGNALING BY PROTEIN KINASE D1 IN PROSTATE CANCER CELLS

Katrina Dunham, Joshua E. Hughes, Subhash C. Chauhan and Meena Jaggi
Cancer Biology Research Center
Sanford Research/USD
Department of OBGYN and Basic Biomedical Science
Sanford School of Medicine
The University of South Dakota
Sioux Falls, SD

ABSTRACT

Protein Kinase D1 (PKD1) is a serine kinase involved in modulation of several signal transduction pathways in benign and malignant human diseases. β -catenin is a cell adhesion molecule involved in signal transduction and cellular proliferation and differentiation. We examined the effect of PKD1 on β -catenin/T cell factor (TCF) transcription activity using transiently transfected reporter constructs (TCF and pRL-TK constructs) and cell cycle progression using flow Cytometry in prostate cancer C4-2 cells stably transfected with green fluorescent protein (GFP) or PKD1 fused GFP. The luciferase activities were assayed using Dual Glo reporter assay with a luminometer. Specificity of PKD1 mediated alteration of subcellular distribution of β -catenin was confirmed by silencing PKD1 expression using small interfering RNA (RNAi) in C4-2-GFP-PKD1 cells. Increased PKD1 expression in C4-2-GFP-PKD1 cells lead to two-fold reduction in β -catenin mediated transcriptional activity while decreased PKD1 expression by RNAi resulted in a significant increase in β -catenin mediated transcription activity. C4-2-GFP and C4-2-GFP-PKD1 cells were labeled using Telford method for flow cytometry measurement. As a consequence of PKD1 expression, the percentage of cells in the S and G2/M phases of the cell cycle declined, whereas the number of cells arrested in G1 phase increased.