EFFECT OF PROTEIN KINASE D FAMILY MEMBERS ON β-CATENIN/T CELL ACTIVITY IN COLON CANCER CELLS

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ABSTRACT

β-catenin is involved in cell adhesion, signal transduction, cellular proliferation, and differentiation. In many colon cancers β-catenin is not degraded properly due to a mutation in the Adenomatous Poli Coli (APC) gene. This leads to β-catenin acting as a co-transcription factor by in the nucleus pushing the cell into a highly proliferating and non-differentiating stage of growth. Protein Kinase D family members (PKD1, 2, 3) are a family of serine kinases involved in modulating many signal transduction pathways. We analyzed the effect of PKD1, 2, and 3 on β-catenin transcription activity in a colon cancer cell line (SW480) with APC mutation. PKD1, 2, 3 and β-catenin were first localized in the SW480 cells by using specific antibodies and confocal microscopy. SW480 cells were then transfected with either an isoform of PKD or just the vector; TOP or FOP, and pRL-tk DNA constructs. Through the use of a dual reporter assay kit we were able to examine the effect of the PKD family members on β-catenin transcription activity. Most notably our results showed that exogenous expression of PKD1 or PKD2 decrease β-catenin/TCF activity. Through an immunohistochemical study down regulation of PKD1 staining was found in colon cancer samples that were moderately and poorly differentiated and had a higher Dukes stage as compared to lower Duke stage colon samples. These results point to a novel regulation pathway in normal cells and point to a possible area of deregulation in colon cancer cells.