

DKK1'S POTENTIAL ROLE AS A BIOMARKER IN PANCREATIC
ADENOCARCINOMA

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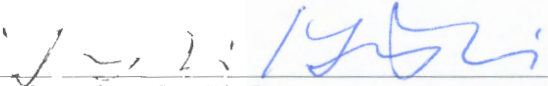
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ABSTRACT

DKK1'S POTENTIAL ROLE AS A BIOMARKER IN PANCREATIC ADENOCARCINOMA

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Under the direction of JINPING LI, M.D., Ph.D.

Dickkopf-1 (Dkk1)'s dysregulation has been implicated in the pathogenesis of a variety of cancers. It is part of the Dkk family of proteins that includes Dkk2, Dkk3 and Dkk4. This family of secreted proteins shares similar conserved cysteine domains and inhibits the Wnt/b-catenin pathway by causing the degradation of beta-catenin, thereby stopping cell proliferation. Dkk1 has also been previously shown to affect the CKAP/Akt pathway to increase Akt phosphorylation and promote cell proliferation. To determine the location and pathway that Dkk1 may regulate in pancreatic cancer cells, we performed immunofluorescence assays on Suit-2 cells. The results showed that Dkk1 is mainly located in the nucleus with a small percentage of the proteins in the cytoplasm. For Dkk1's potential receptors, CKAP4 was found to have a similar staining to Dkk1 while Lrp6 was found to be evenly spread through the nucleus and cytoplasm. Further staining with the Wnt/b-catenin downstream protein, beta-catenin, showed that it was colocalized with Dkk1 in the nucleus indicating that Dkk1's presence did not inhibit its ability to translocate into the nucleus. Further studies into the cause of Dkk1's inability to degrade and stop b-catenin's translocation that causes increased cell proliferation is needed.