NUS Graduate School for Integrative Sciences and Engineering
Research Project Write-up

Title of Project :	Molecular regulation of the Wnt/β-catenin signaling pathway
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Short Description

The Wnt/β-catenin signaling pathway is critical in both cellular proliferation and organismal development. However, how the β-catenin degradation complex is inhibited upon Wnt activation remains unclear. Using a directed RNAi screen we found that protein phosphatase 1 (PP1), a ubiquitous serine/threonine phosphatase, is a novel potent positive physiologic regulator of the Wnt/beta-catenin signaling pathway. Our data suggests that PP1 controls Wnt signaling through interaction with, and regulated dephosphorylation of, axin. Inhibition of PP1 leads to enhanced phosphorylation of specific sites on axin by casein kinase I. Axin phosphorylation markedly enhances the binding of glycogen synthase kinase 3, leading to a more active β-catenin destruction complex. Wnt-regulated changes in axin phosphorylation, mediated by PP1, may therefore determine beta-catenin transcriptional activity. Ongoing studies aim to better understand how PP1 is regulated, and the specific effects of PP1 activity on axin. Specific inhibition of PP1 in this pathway may offer therapeutic approaches to cancer.