

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

Title of Project : Small Molecule Inhibitors of the Wnt signaling pathway

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Short Description

The connection between Wnt/ β -catenin or “canonical” Wnt signaling and cancer is well appreciated. Some cancers, such as colon cancer, have mutations in components of the signaling pathway (i.e. adenomatous polyposis coli protein, “APC”, axin, and β -catenin). In breast cancer and leukemias, cancer stem cell maintenance has been shown to depend on Wnt signaling. Both β -catenin dependent and independent signaling pathways are implicated in stem cell maintenance. In the more overtly Wnt dependent cancers, it is clear that intervention at multiple points in the signaling pathway(s) is required for effective treatment of a broad range of cancers. We have developed and validated a cell based screen for inhibitors of Wnt signaling and have identified lead compound inhibitors throughout the entire pathway including secretion from Wnt expressing cells. We have also characterized a series of secondary assays that place the function of each inhibitor within one of six defined portions or compartments of the signaling pathway. These lead compounds have low toxicity and significant efficacy on Wnt-stimulated signaling. Further development may lead to useful cancer chemotherapeutics.