

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

Title of Project : Wnt regulation of cancer cell motility

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Short Description

Noncanonical Wnt signals control morphogenetic movements during cancer metastasis and vertebrate development. Casein kinase I epsilon (CKI ϵ) is a Wnt-regulated kinase that regulates Wnt/ β -catenin signaling and has a β -catenin-independent role(s) in cell fate determination that is poorly understood. We identified a CKI ϵ binding partner, SIPA1L1/E6TP1, a GAP (GTPase activating protein) of the Rap small GTPase family. CKI ϵ phosphorylates SIPA1L1, reducing its stability and hence increasing Rap1 activation. Wnt-8, which activates CKI ϵ , enhances the CKI ϵ -dependent phosphorylation and degradation of SIPA1L1. Inactivation of the Rap1 pathway results in abnormal cell migration in a developmental model. Our data demonstrate a role for CKI ϵ in noncanonical Wnt signaling and indicate that Wnt regulates morphogenesis in part through CKI ϵ -mediated control of Rap1 signaling. Ongoing studies are examining the role of SIPA1L1 and Rap1 in cancer cell metastasis.