



## **Activated CDC42-Associated Kinase (Ack) as a Therapeutic Target for Ras Induced Cancer** (*Nur-E-Kamal, RWJ 04-49*) Therapeutic Target

### **Background**

Activation of Ras GTPase function has been shown to be associated with various types of cancer identifying Ras as a target for cancer therapeutics. However, Ras GTPase activity is also essential for multiple normal signaling pathways involved in controlling growth and differentiation of mammalian cells. Thus targeting Ras directly may have deleterious effects on non-cancer cells. This invention is based on the discovery that Ras signal for transformation transduces through the activated CDC42-associated kinase (Ack). This invention validates Ack kinase as an attractive therapeutic target for Ras-induced cancer.

### **Description of the Technology**

The present invention discloses the fact that CDC42 and activated CDC42 associated kinase (Ack) act downstream of Ras signaling in cancer cells. To prove this, the expression of Ack was knocked down using siRNA in v-Ha-Ras NIH 3T3 transformed cells. siRNA knocked down the expression of Ack in a dose-dependent manner in v-Ha-Ras transformed NIH 3T3 and parental NIH 3T3 cells. Additionally, Ack-deficiency in the v-Ha-Ras transformed cells was shown to induce apoptosis. Therefore Ras signals transduced through Ack protect v-Ha-Ras transformed cells from apoptosis. PD 158780 tyrosine kinase inhibitor inhibits the kinase activity of Ack *in vitro* and affects the growth of v-Ha-Ras transformed NIH3T3 cells in a dose-dependent manner. Thus Ras-CDC42-Ack signaling pathway is required for survival of Ras-transformed mammalian cells and Ack kinase is an attractive target to develop a chemotherapeutic agent for Ras-induced cancer.

### **Applications**

CDC42-Ack can be used as a target in search of novel therapeutic agents for Ras-induced cancers, i.e. brain tumors, breast and prostate cancers.

### **Patent Status**

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