

## GSI Symposium 2015 Abstract

### **DISSECTING THE SMAD4 METASTASIS SUPPRESSOR TO IDENTIFY NOVEL PROGNOSTIC BIOMARKERS AND THERAPEUTIC TARGETS IN COLON CANCER**

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Colon cancer is the second most lethal cancer in men and women in the United States and metastasis is the primary cause of mortality. Hence, there is an urgent need to elucidate the molecular mechanisms underlying metastasis in order to develop prognostic markers and identify novel druggable targets. In colon cancer, *SMAD4* is mutated frequently (10-20%) and its low expression level is associated with poor prognosis, presence of metastases, and chemoresistance. We have shown that loss of SMAD4 in colon cancer is associated with increased cell migration and resistance to 5'-fluorouracil, the common chemotherapeutic agent. Based on these studies, we hypothesize that SMAD4 forms a metastasis suppressor complex to inhibit colon cancer progression. We have generated colon cancer cell lines overexpressing FLAG-tagged SMAD4 proteins and identified the components in the SMAD4 metastasis suppressor complex using co-immunoprecipitation and mass spectrometry. The functional roles of these SMAD4 interacting partners in regulating metastasis will be characterized in experimental models of cancer progression and their contribution to human colon cancer assessed through *in silico* analysis of gene expression profiles and examination of clinical specimens at different stages of disease progression. We suggest that these genes may serve as biomarkers in predicting disease progression and therapeutic targets to treat metastatic colon cancer.