# GRANT SNAPSHOT

## 2007 Pancreatic Cancer Action Network Pilot Grant

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| Grantee: | Gloria Huei-Ting Su, PhD |
| Institution: | Columbia University College of Physicians and Surgeons, New York |
| Project Title: | *Activin Signaling in the Development of Pancreatic Cancer Precursor Lesions* |
| Award Period: | July 1, 2007 – June 30, 2008 |
| Amount: | $60,000 |

## Biographical Highlights

After receiving her PhD in Immunology from University of Chicago, Dr. Su relocated to Johns Hopkins University where she first completed a postdoctoral fellowship in Cancer Genetics/Pancreatic Cancer, then became an Instructor in the Department of Pathology and was promoted to Assistant Professor. In 2003, she joined Columbia University as an Assistant Professor in the Departments of Otolaryngology/Head & Neck Surgery, and Pathology. Her research interests include genetic profiling and mouse modeling for pancreatic cancer.

## Project Description

Previous research has shown that the activin signaling pathway is important for human pancreatic tumorigenesis, although it has not been studied in vivo (i.e., using whole organisms). Genetic engineered mice have been effective tools for cancer modeling and cell pathway studies. In the funded project, genetic engineered mice are used to study the activin signaling pathway and its role in pancreatic cancer. Preliminary data show that the inactivation of the activin pathway in combination with the activation of Kras can lead to the development of mucinous cystic lesions in the pancreases of the mice. Plans are to use the mice to examine tumorigenesis from non-invasive mucinous cystic precursor lesions to invasive cancer in human pancreases. The results are expected to further our understanding of the three common precursor lesions: PanIN (pancreatic intraepithelial neoplasias), IPMN (intraductal papillary mucinous neoplasms), and MCN (mucinous cystic neoplasm), at the onset of pancreatic tumorigenesis.

## Results/Outcomes

Following are key results of the study: (a) the mouse model used in the study simulated human IPMN; (b) IPMN-like lesions in the mice were found to be able to progress to invasive cancer and metastasis; (c) the time line and survival curve that correlate with disease progression in the model were determined; and (d) the inactivation of activin signaling pathway was found to favor IPMN over PanIN development in vivo, which is interesting because the inactivation of SMAD4, a downstream target of both activin and TGFbeta signaling pathways, has been shown previously to favor the development of mucinous cystic lesions as well. The evidence suggests the potential importance of both activin and TGFbeta signaling pathways in the development of IPMN and MCN in humans.

## Lessons Learned

Inactivation of a tumor-suppressor gene alone is insufficient to induce tumorigenesis in vivo. An oncogenic initiation, such as by mutant Kras, is essential. Good pathology support and good antibodies are very critical in mouse modeling projects. A shared database of workable antibodies for both human and mouse research would benefit the research community and reduce wasted efforts and resources.

## Next Steps

A trove of tumor blocks and cell lines have been generated from the mouse model used in this study which will allow further study of any alterations (genetically and epigenetically) that may have occurred in activin signaling pathways as well in known oncogenic and tumor-suppressive pathways important to pancreatic tumorigenesis.

## Follow-Up Funding

NIH/NCI R21 Grant (Start Date: 7/1/08). For continued study of the mouse model.