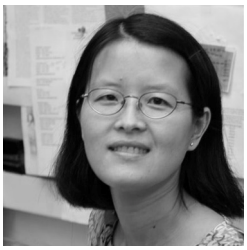
GRANT SNAPSHOT

2006 Pancreatic Cancer Action Network – AACR Career Development Award

Grantee:	Ru Chen, PhD
Institution:	University of Washington School of Medicine, Seattle
Project Title:	*Protein Biomarkers for Detection of Pancreatic Cancer*
Award Period:	July 1, 2006 – June 30, 2008
Amount:	$100,000



Biographical Highlights

After receiving her PhD in Pathology from the University of Washington, Dr. Chen pursued her postdoctoral studies there in gastroenterology and is currently a research assistant professor in the Department of Medicine. Her research interests focus on the discovery of protein biomarkers for early detection of pancreatic cancer and the molecular mechanisms that underlie pancreatic tumorigenesis.

Project Description

The funded project aims to develop early biomarkers of pancreatic cancer to improve early detection when the cancer is still curable. Pancreatic cancer is an almost uniformly lethal disease because the cancer can not be diagnosed at an early, curable stage. Moreover, once the cancer has formed, chemotherapy offers only minimal improvement in survival. What is needed is a better understanding of how pancreatic cancer forms, and to exploit that knowledge to improve early diagnosis. The study proposes to use proteomics technology to identify the proteins that are specific to pancreatic cancer. The protein candidates identified through this study will provide the basis for further serum biomarker development for early detection of pancreatic cancer.

Results/Outcomes

Quantitative proteomics was used to identify dysregulated proteins from pancreatic cancer and PanIN 2-3 compared to normal. Over 150 candidate biomarkers were identified in pancreatic cancer and precancerous specimens including pancreatic tissue and juice. Careful triage assessment of these proteins has prioritized candidate proteins for further ELISA development. Of the two ELISA tests developed so far, candidates IGFBP-2 and MIF had sensitivities of 95% and 100%, respectively, for detecting pancreatic cancer while providing 100% specificity for normal controls. The most common source of false positive findings for all of the tests was pancreatitis (both acute and chronic) and liver disease. IGFBP-2 and MIF had sensitivities of 30% and 41%, respectively, for pancreatic cancer while providing 90% specificity for normal controls and other disease controls.

Lessons Learned

Because patients with pancreatitis (chronic pancreatitis CP and acute pancreatitis AP) or liver disease (such as HCV) may cause a high rate of false-positive for biomarkers detecting pancreatic cancer, biomarker candidates identified through pancreatic cancer need to be tested and evaluated in these "other disease" samples for potential false positive testing. In the funded project, many biomarker candidates performed well in distinguishing pancreatic cancer patients and normal control subjects. However, if the "other disease" category including pancreatitis and HCV is included in the testing, the specificity can be significantly reduced.

Next Steps

Efforts will continue to discover and characterize biomarker candidates. Several strategies will be implemented to increase biomarker sensitivity and specificity, including (a) combination of multiple biomarkers as a biomarker panel; (2) new biomarker candidates from the on-going biomarker discovery project; and (3) addition of biomarker candidates targeted for pancreatitis.

Follow-Up Funding

National Cancer Institute K07 (7/1/06 - 6/30/11; Amount: $568,000).

Publications Related to Funded Project

Chen R, Pan S, Cooke K, White KN, Bronner MP, Goodlett DR, Aebersold R, Brentnall TA. Comparison of pancreas juice proteins from cancer versus pancreatitis using quantitative proteomic analysis. *Pancreas,* 2007;34(1):70-79. http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedid=17198186.

Chen R, Brentnall TA, Pan S, Cook K, Moyes KW, Crispin DA, Goodlett DR, Aebersold R, Bronner MP. Quantitative proteomic analysis reveals that proteins differentially expressed in chronic pancreatitis are also frequently involved in pancreatic cancer. *Mol.Cell Proteomics*, 2007;6(8):1331-42. http://www.mcponline.org/cgi/content/full/6/8/1331.

Chen R, Pan S, Aebersold R, Brentnall TA. Proteomic studies of pancreatic cancer. *Proteomics-Clinical Application*, 2007;1(12):1582-1591. http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedid=18633454.

Chen R, Brentnall TA, Aebersold R. Applications of stable isotope tagging based quantitative proteomics in cancer research. In *Clinical Proteomics*. Jennifer E. Van Eyk and Mike Dunn (eds). Wiley-VCH. 2008.