GRANT SNAPSHOT

2007 Laurie and Paul MacCaskill – Pancreatic Cancer Action Network – AACR Career Development Award

Grantee:	Kimberly A. Kelly, PhD
Institution:	University of Virginia, Charlottesville
Project Title:	*Molecular Imaging Agents for Early Detection of Pancreatic Cancer*
Award Period:	July 1, 2007 – June 30, 2009
Amount:	$100,000

Biographical Highlights

Dr. Kelly received her PhD in Oncological Sciences at the Huntsman Cancer Institute at the University of Utah. She then completed postdoctoral training at the Center for Molecular Imaging Research at Massachusetts General Hospital, where her research focused on the development of novel targeted molecular probes utilizing optical and magnetic resonance imaging modalities. Subsequently, she became an Instructor in Radiology, an Assistant in Biochemistry, an Assistant Professor in Radiology, and the Director of the Cell Culture Core at Harvard Medical School. She recently relocated to the University of Virginia, Charlottesville, as an Assistant Professor in the Department of Biomedical Engineering. Dr. Kelly serves as a reviewer for several scientific journals, including *Cancer Detection and Prevention* and *Molecular Imaging*.

Project Description

The overall goal of this study is to develop novel molecular imaging agents for the early diagnosis of pancreatic cancer. Recently developed mouse models will be used that recapitulate the genetics of human disease such as Kras activation and Ink4a deletion, genes that are responsible for 95% of pancreatic cancers. Sophisticated chemical biology approaches will be used to find novel tags that will allow the earliest forms of cancer to be pinpointed where surgical resection becomes curative. The hope is to use these tags in commonly used imaging approaches such as MRI or endoscopic detection.

Results/Outcomes

A phage display approach was used to screen for peptides that specifically bind to cell surface markers on pancreatic ductal adenocarcinoma (PDAC) cells. These screens yielded a tag that distinguishes PDAC cells from normal pancreatic duct cells. As a result of the approach, it was possible to identify a novel biomarker, plectin-1, that may serve as a means for the early detection of pancreatic cancer and confirmation of pancreatic cancer diagnosis. In addition, by decorating nanoparticles capable of being detected via MRI or fluorescence endoscopy with the PDAC targeted tag, small pancreatic cancer was detected non-invasively in mouse models of PDAC. The developed, specific imaging probe along with the discovery of plectin-1 as a novel biomarker, may have clinical utility in the diagnosis and management of PDAC in humans.

Next Steps

To follow-up on the initial observations of plectin-1 as a potential biomarker of pancreatic cancer, additional studies have been performed that demonstrate the utility of plectin-1 as a diagnostic molecule. In addition, further studies have been conducted using the developed imaging probes to optimize the tumor targeting capability of the nanoparticles. Dr. Kelly is in the process of partnering with clinicians to begin a clinical pilot study with the developed imaging probe to determine its utility in patient diagnosis.

Follow-Up Funding

NIH/NCI RO1 Grant (Five Year Grant; Amount: $1,350,000). Development of molecularly targeted imaging agents for the early detection of pancreatic ductal adenocarcinoma.

Publications Related to Funded Project

Kelly KA, Bardeesy N, Anbazhagan R, Gurumurthy S, Berger J, Alencar H, DePinho RA, Mahmood U, Weissleder R. Targeted Nanoparticles for Imaging Incipient Pancreatic Ductal Adenocarcinoma. *PLoS Med,* 2008;5(4):e85. doi:10.1371/journal.pmed.0050085.