



Research

PANCREATIC CANCER ACTION NETWORK

ADVANCE RESEARCH. SUPPORT PATIENTS. CREATE HOPE.

www.pancan.org | 877.272.6226

GRANT SNAPSHOT

2007 Seena Magowitz – Pancreatic Cancer Action Network – AACR Career Development Award

Grantee:	Rebekah White, MD
Institution:	Duke University Medical Center, Durham, NC
Project Title:	<i>Prostate Stem Cell Antigen: A Specific Target for Pancreatic Cancer Therapy</i>
Award Period:	July 1, 2007 – June 30, 2009
Amount:	\$100,000



Biographical Highlights

Dr. White earned her MD and then completed an internship and residency in general surgery at Duke University in North Carolina. After completing a surgical oncology fellowship at Memorial Sloan-Kettering Cancer Center in New York, she returned to Duke as Assistant Professor of Surgery in the School of Medicine. In 2004, Dr. White was inducted into Alpha Omega Alpha Honor Medical Society and received the Hilliard F. Seigler Award for Excellence in Basic Science Research.

Project Description

Prostate Stem Cell Antigen (PSCA) was initially identified as a marker for prostate cancer and has also been identified as one of the most highly over-expressed genes in pancreatic cancer. Recently, nuclease-resistant aptamers (i.e., RNA molecules that bind to specific proteins and other targets) have been used to deliver small interfering RNAs (siRNAs) to prostate cancer cells, resulting in cell death. The funded study examines how aptamers will bind to and impact pancreatic cancer cells that express PSCA. Specific aims of the study are threefold: (1) select a nuclease-resistant RNA aptamer that binds human PSCA protein with high affinity and specificity; (2) characterize aptamer binding in pancreatic cancer cells in vitro (i.e., in the lab); and (3) determine the extent to which aptamer binding to PSCA directly affects pancreatic cancer cell growth and survival in vitro. The effect of treatment with aptamer on cell viability, apoptosis (i.e., cell death), and proliferation will be measured in pancreatic cancer cells that over-express PSCA. If aptamer binding directly induces cell death, not only will this validate PSCA as a therapeutic target but also the aptamer itself may be useful as a therapeutic agent. If its direct effects are limited, plans are to take advantage of the specific binding properties of aptamer to deliver other therapeutic agents, such as siRNAs that inhibit Kras, to pancreatic cancer cells. The future aims of this project will be to translate this PSCA aptamer into a targeted molecular therapy that can ultimately be applied to patients with pancreatic cancer.

Results/Outcomes

Cells were successfully created that artificially express PSCA on their surface and secrete a modified version of PSCA that can be purified. Using these reagents, several rounds have been completed of “selection” in which RNA molecules (from an enormous library of different sequences



Research

PANCREATIC CANCER ACTION NETWORK

ADVANCE RESEARCH. SUPPORT PATIENTS. CREATE HOPE.

www.pancan.org | 877.272.6226

and shapes) that bind PSCA-expressing cells are separated from molecules that bind non-PSCA expressing cells and from molecules that do not bind at all. The enriched pool binds the purified PSCA protein much better than the starting pool, suggesting that the enriched pool does contain high affinity binders for PSCA.

Lessons Learned

Using cells for selection is much trickier than using purified proteins. Very stringent measures are needed to only select out the molecules that bind to the protein of interest rather than other proteins on the cell surface. Alternating rounds of selection using cells with purified protein seems to be useful for clearing the pool of molecules that bind to the “wrong” proteins on the cell surface.

Next Steps

After a few more rounds of selection, an analysis will be conducted of the individual molecules within the pool of RNAs to see whether and how well they bind to PSCA-expressing cells and to purified PSCA protein. These molecules will then be studied in pancreatic cancer cells in vitro.

Follow-Up Funding

Several grant applications are pending.