

University of Pennsylvania

Annual Progress Report: 2009 Nonformula Grant

Reporting Period

June 1, 2010 – June 30, 2010

Formula Grant Overview

The University of Pennsylvania received \$4,620,420 in nonformula funds for the grant award period June 1, 2010 through May 31, 2014. Accomplishments for the reporting period are described below.

Research Project: Project Title and Purpose

Novel Adjuvants for Cancer Vaccine Immunotherapy - The purpose is to conduct a series of thematically related projects to test new cancer vaccine approaches. The projects will include a clinical trial in patients with lung and ovarian cancer, and basic, translational and pre-clinical investigation at three institutions to encourage collaboration. A programmatic effort to promote technology transfer in cancer vaccine research in Pennsylvania is included. Finally, there will be an innovative program to develop a pipeline of new scientists and clinicians trained in cancer research in the Commonwealth which will involve outreach in Philadelphia and Lincoln University.

Anticipated Duration of Project

6/1/2010 - 5/31/2014

Project Overview

The overall research objectives of this program are:

1. To prolong survival and reduce mortality of patients with ovarian and lung cancer by enhancing T cell activation in the tumor microenvironment.
2. To support cancer vaccine research and training throughout eastern Pennsylvania.
3. To provide a training and mentoring program in translational cancer research for underrepresented minorities.
4. To promote technology transfer and the potential for job growth within the Commonwealth in the biotechnology of cancer vaccines.

We propose the following specific research aims to accomplish the general objectives of this program:

1. Establish the safety, antitumor activity and optimum biologic dose of a bispecific antibody that targets CD326 (epithelial cell adhesion molecule (EpCAM)) with the first arm and anti-CD3 (MT110) with the second arm in a phase I/II clinical trial.

2. Determine whether or not the inclusion of specificities for costimulatory molecules or antagonists of inhibitory receptors will enhance the activity of the bispecific T cell engager platform.
3. Explore the role of tumor endothelial marker-1 (TEM1) vaccination targeting the tumor microvasculature with combination therapies that antagonize vascular endothelial growth factor (VEGF).
4. Determine whether or not the inclusion of adjuvants that augment the Th17 arm of the cellular immune system enhances antitumor effects.
5. Establish an educational program for undergraduate and graduate level training in translational cancer research.

Principal Investigator

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Other Participating Researchers

Robert H. Vonderheide, MD, DPhil, Michael Kalos, PhD, George Coukos, MD, PhD, Andrea Facciabene, PhD, Yangbing Zhao, MD, PhD, Nicole Aqui, MD, Richard G. Carroll, PhD, Elizabeth Veloso, RN, JD – employed by University of Pennsylvania
Hossein Borghaei, DO, Gregory P. Adams, PhD, Matthew K. Robinson, PhD – employed by Fox Chase Cancer Center
John O. Chikwem, PhD – employed by Lincoln University

Expected Research Outcomes and Benefits

This program in cancer vaccines will produce both short term and long term benefits. In the near term, the program will enable the conduct of a promising clinical trial for patients with lung and ovarian cancer, thereby providing scientific information on the ability of CD326 to serve as a vaccine target using bispecific T cell engager antibody technology. As a result of the inter-institutional collaborative research efforts, long term benefits will continue to accrue for patients in eastern Pennsylvania who will benefit by improved access to state of the art trials in cancer vaccine research. At the same time, the development of new approaches to harness the power of the immune system to attack tumor cells and the tumor microenvironment will be pursued in the laboratory. A world-class group of clinicians and scientists has been assembled to address this vital problem and will synergize to develop new cancer therapies. In summary, this Program will allow outstanding scientists, educators and clinicians to leverage the power and potential of the immune system to develop new cancer vaccines with improved efficacy and reduced toxicity.

In addition to research outcomes for cancer therapy, this project contains a significant focus on teaching and education in order to produce a durable result for years to come. We will reach out

to the City of Philadelphia, and to college students at Lincoln University to enhance the pipeline of new investigators trained in this promising scientific field, while providing role models and unparalleled opportunities for aspiring under-represented minority students.

Summary of Research Completed

This project began on June 1, 2010, and this report summarizes only one month of research progress. In general, fund accounts have been set up for each of the Projects and Cores at the three collaborating institutions and PIs have started to implement strategies for progression of each project to include the ordering of reagents and molecular biology tools such as plasmid constructs, and to begin project staffing. An official grant initiation meeting was held with PIs from all projects/cores in attendance on June 30 2010. At this meeting, each PI presented their clinical/research plans for the upcoming year and the milestones they intend to meet. Grant progress highlights from the past month are described below.

Project 1, designed to test the clinical and immunological capability of novel bispecific T cell engaging reagents to redirect the force of polyclonal T cell populations against tumor cells in patients with advanced lung, ovarian, and breast cancer has made significant progress during this reporting period. Drs. Vonderheide and Borghaei along with Dr. Michael Kalos have worked to develop the details of the clinical protocol including eligibility criteria, treatment schema, and endpoint analysis. They have also started thinking about the best regulatory path forward for the clinical protocol.

In addition, the Minority Training Program (Core B) has had a strong start because of our established relationship with the Penn CTSA program. As stated in our application, the goals of this core are: 1.) to provide undergraduate and graduate students with the basic tools necessary to pursue careers in translational research and 2.) to provide intensive, supervised research experiences with mentors in translational research at the undergraduate and graduate level. Our first undergraduate trainee, Bianca Montalmont, started in June. She is a rising senior at Lincoln and is spending the summer in the laboratory of Dr. Nicole Aqui, where she is studying T cell immunotherapy for the treatment of cancer. In addition, she is participating in the Clinical and Translation Science Award (CTSA) seminar series at University of Pennsylvania, which consists of lectures and workshops on a variety of topics. A sampling of titles includes “Translational Research: Innovations in Training and Practice,” “Tick Tock, the Molecular Clock,” “Institutional Review Boards,” and “PhD Admissions.” At the end of the 8 week program, Bianca will participate in a research symposium with other undergraduate students, where she will give an oral presentation summarizing her work.