

Final Progress Report for Research Projects Funded by Health Research Grants

Instructions: Please complete all of the items as instructed. Do not delete instructions. Do not leave any items blank; responses must be provided for all items. If your response to an item is “None”, please specify “None” as your response. “Not applicable” is not an acceptable response for any of the items. There is no limit to the length of your response to any question. Responses should be single-spaced, no smaller than 12-point type. The report **must be completed using MS Word**. Submitted reports must be Word documents; they should not be converted to pdf format. Questions? Contact Health Research Program staff at 717-783-2548.

1. **Grantee Institution:** The Fox Chase Cancer Center
2. **Reporting Period (start and end date of grant award period):** 1/1/2009-12/31/2011
3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Maria Minko Gill
4. **Grant Contact Person’s Telephone Number:** 215-728-2659
5. **Grant SAP Number:** 4100047634
6. **Project Number and Title of Research Project:** 4 - Anti-Glucose Transporter-1 Antibodies as a Novel Treatment against Human Cancers
7. **Start and End Date of Research Project:** 1/1/2009 - 1/31/2010
8. **Name of Principal Investigator for the Research Project:** George Simon, M.D.
9. **Research Project Expenses.**

9(A) Please provide the amount of health research grant funds spent on this project for the entire duration of the grant, including any interest earned that was spent:

\$561,358.04

9(B) Provide the last names (include first initial if multiple individuals with the same last name are listed) of **all** persons who worked on this research project and were supported with health research funds. Include position titles (Principal Investigator, Graduate Assistant, Post-doctoral Fellow, etc.), percent of effort on project and total health research funds expended for the position. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name	Position Title	% of Effort on Project	Cost
-----------	----------------	------------------------	------

Simon	Principal Investigator	28% YR01-02	\$66,681.56
Banerjee	Postdoctoral Fellow	100% YR01	\$29,775.98
Das	Postdoctoral Fellow	100% YR01-02	\$52,029.51

9(C) Provide the names of **all** persons who worked on this research project, but who *were not* supported with health research funds. Include position titles (Research Assistant, Administrative Assistant, etc.) and percent of effort on project. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name	Position Title	% of Effort on Project

9(D) Provide a list of **all** scientific equipment purchased as part of this research grant, a short description of the value (benefit) derived by the institution from this equipment, and the cost of the equipment. To the best of my knowledge no scientific equipment was purchased with these grant monies.

Type of Scientific Equipment	Value Derived	Cost
MAPI - Automatic filling, sealing and printing machine for CBS™ high security straws	This system allows automated printing of sample identification numbers and codes. It is used by the Institutional Biosample Repository Facility to accurately and permanently label clinical research samples for long-term storage (patient de-identified) and can rapidly and securely identify wide arrays of fresh frozen tissue samples.	\$63,360.61

10. Co-funding of Research Project during Health Research Grant Award Period. Did this research project receive funding from any other source during the project period when it was supported by the health research grant?

Yes _____ No X _____

If yes, please indicate the source and amount of other funds:

11. Leveraging of Additional Funds

11(A) As a result of the health research funds provided for this research project, were you able to apply for and/or obtain funding from other sources to continue or expand the research?

Yes _____ No X _____

If yes, please list the applications submitted (column A), the funding agency (National Institutes of Health—NIH, or other source in column B), the month and year when the application was submitted (column C), and the amount of funds requested (column D). If you have received a notice that the grant will be funded, please indicate the amount of funds to be awarded (column E). If the grant was not funded, insert “not funded” in column E.

Do not include funding from your own institution or from CURE (tobacco settlement funds). Do not include grants submitted prior to the start date of the grant as shown in Question 2. If you list grants submitted within 1-6 months of the start date of this grant, add a statement below the table indicating how the data/results from this project were used to secure that grant.

A. Title of research project on grant application	B. Funding agency (check those that apply)	C. Month and Year Submitted	D. Amount of funds requested:	E. Amount of funds to be awarded:
	<input type="checkbox"/> NIH <input type="checkbox"/> Other federal (specify: _____) <input type="checkbox"/> Nonfederal source (specify: _____)		\$	\$
	<input type="checkbox"/> NIH <input type="checkbox"/> Other federal (specify: _____) <input type="checkbox"/> Nonfederal source (specify: _____)		\$	\$
	<input type="checkbox"/> NIH		\$	\$

	<input type="checkbox"/> Other federal (specify: _____) _____)		
	<input type="checkbox"/> Nonfederal source (specify: _____) _____)		

11(B) Are you planning to apply for additional funding in the future to continue or expand the research?

Yes X No _____

If yes, please describe your plans:

Based on our work, at the institution that I am moving to I plan to apply for federal funding. Data generated from this project will be instrumental in allowing me to design clinical trials with correlative components which will validate this work in humans, principles that have been laid down in cell line studies and that are to be confirmed in xenograft models.

12. Future of Research Project. What are the future plans for this research project?

Data generated from this project and Dr. Simon’s continued studies at the Medical University of South Carolina will be used for future development of clinical trials.

13. New Investigator Training and Development. Did students participate in project supported internships or graduate or post-graduate training for at least one semester or one summer?

Yes X No _____

If yes, how many students? Please specify in the tables below:

	Undergraduate	Masters	Pre-doc	Post-doc
Male				1
Female				1
Unknown				
Total				2

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic				2
Unknown				
Total				2

	Undergraduate	Masters	Pre-doc	Post-doc
White				
Black				
Asian				2
Other				
Unknown				
Total				2

14. Recruitment of Out-of-State Researchers. Did you bring researchers into Pennsylvania to carry out this research project?

Yes No

If yes, please list the name and degree of each researcher and his/her previous affiliation:

This funding allowed Dr. Simon to recruit two individuals from the H. Lee Moffitt Cancer Center, Tampa, FL, Rajat Das, Ph.D. and Sarmistha Banerjee, Ph.D. both Postdoctoral Fellows.

15. Impact on Research Capacity and Quality. Did the health research project enhance the quality and/or capacity of research at your institution?

Yes No

I have decided to leave the institution and join another institution.

If yes, describe how improvements in infrastructure, the addition of new investigators, and other resources have led to more and better research.

16. Collaboration, business and community involvement.

16(A) Did the health research funds lead to collaboration with research partners outside of your institution (e.g., entire university, entire hospital system)?

Yes No

Through our work, we were able to determine the primary mechanism by which tumoral growth inhibition by anti-Glut-1 antibodies work. We then were able to identify other inhibitors that work with similar mechanisms of action. Work with these inhibitors confirmed our suspicions that generated ideas for clinical trials that are currently under consideration for funding by private agencies.

If yes, please describe the collaborations:

The confidential nature of these collaborations preclude me from revealing this here but are from private agencies

16(B) Did the research project result in commercial development of any research products?

Yes _____ No X

If yes, please describe commercial development activities that resulted from the research project:

16(C) Did the research lead to new involvement with the community?

Yes _____ No X

If yes, please describe involvement with community groups that resulted from the research project:

17. Progress in Achieving Research Goals, Objectives and Aims.

List the project goals, objectives and specific aims (as contained in the grant application’s strategic plan). Summarize the progress made in achieving these goals, objectives and aims for the entire grant award period. Indicate whether or not each goal/objective/aim was achieved; if something was not achieved, note the reasons why. Describe the methods used. If changes were made to the research goals/objectives/aims, methods, design or timeline since the original grant application was submitted, please describe the changes. Provide detailed results of the project. Include evidence of the data that was generated and analyzed, and provide tables, graphs, and figures of the data. List published abstracts, poster presentations and scientific meeting presentations at the end of the summary of progress; peer-reviewed publications should be listed under item 20.

This response should be a DETAILED report of the methods and findings. It is not sufficient to state that the work was completed. Insufficient information may result in an unfavorable performance review, which may jeopardize future funding. If research findings are pending publication you must still include enough detail for the expert peer reviewers to evaluate the progress during the course of the project.

Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project’s strategic plan. After the final performance review of each project is complete, approximately 12-16 months after the end of the grant, this Final Progress Report, as well as the Final Performance Review Report containing the comments of the expert review panel, and the grantee’s written response to the Final Performance Review Report, will be posted on the CURE Web site.

There is no limit to the length of your response. Responses must be single-spaced below, no smaller than 12-point type. If you cut and paste text from a publication, be sure symbols print properly, e.g., the Greek symbol for alpha (α) and beta (β) should not print as boxes (\square) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

Specific aims:

Aim 1: In primary human non-small cell lung cancer (NSCLC) specimens, correlate Glut-1 expression with overall survival (OS) and disease free survival (DFS). We will also correlate Glut-1 expression with pAKT and pAMPK expression.

Aim 2: Generate fully human IgG1 antibodies against the large extracellular loop adjacent to the N-terminus of the Glut-1 transporter protein. We hypothesize that binding of antibodies to this domain will effectively inhibit glucose transport, starving the cancer cells and providing a therapeutic effect. To validate our human IgG1 antibodies we will compare their efficacy with that of the commercially available mouse monoclonal antibody (MAB1418 generated from clone# 202915) against human cancer cell lines.

Progress:

Our research consists of the following components; validating the association between Glut-1 expression levels in lung tumors, correlating survival with the associations between Glut-1, AMPK and pAKT, and associating the expression of these proteins with each other and overall survival.

Several factors have resulted in lack of significant progress toward our goals. Firstly, during the previous reporting period, the experimental work was disrupted with the departure of both postdoctoral associates working on the project. Secondly, the PI has refocused his career toward clinical care with a concomitant closure of his research laboratory. However, key conceptual aspects for addressing Specific Aim 2 were clarified during the final months of this project.

When the results of a series of repeated experiments with commercial antibodies obtained from multiple companies failing to induce cell kill reliably, the focus of the project was switched to laboratory production of antibody, thereby negating the reliance on commercially available antibody.

A rationale for inhibiting Glut-1 with an antibody versus a small molecule was based on the fact that Glut-1 is universally expressed on RBCs (Red Blood Corpuscles). We attempted to determine whether the commercially available antibodies both of the MAB1418 clone and the anti-Glut-1 antibody generated against an unspecified epitope against the Glut-1 transporter protein made by the R and D systems would bind to the Glut-1 transporter protein found on the surface of RBCs. Both of the antibodies were able to bind to the Glut-1 on the surface of the RBCs. This raised the question of whether all of the administered antibody would bind to the RBCs, leaving very little antibody to attack to the tumor.

To circumvent this problem, we calculated how much antibody would be needed to saturate the Glut-1 antibodies on the surface of the RBCs while leaving unbound antibody to float freely in

the serum to bind to the tumor. A preliminary analysis revealed that micromolar concentrations per kg body wt would suffice to saturate the antibodies on the surface of the RBCs and leave enough antibodies to bind to the tumor to generate its effect.

An alternative option was to generate the new antibody against an epitope that is unique to tumoral Glut-1 rather than to RBC Glut-1. This would require sequencing the Glut-1 on the RBCs versus the tumors and identifying an extracellular epitope whose sequence was unique to tumoral Glut-1. The sequence of RBC Glut-1 was available from public databases. However, the Glut-1 on lung cancer lines was not available for comparison from RBC Glut-1 sequence. This approach was not pursued due to lack of laboratory personnel.

As detailed by our previous report, we have worked out the mechanism by which the Glut-1 antibody induces cell kill. Two key proteins in the cell signaling pathway are affected. An oncogenic protein is turned off and another protein with tumor suppressor properties is turned on. This prompted us to explore other molecules that have demonstrated similar effects both in our laboratory, as well as in others. This work on other molecules will continue and in the short run is more likely to yield a therapeutic modality of interest. Several such compounds have been identified and combination studies with these easily available compounds are also planned.

This project was halted prior to its anticipated end date due to the closure of the PIs laboratory and subsequent relocation of the PI to another institution. Dr. Simon planned to execute this work using other funds at the Medical University of South Carolina where the PI has taken a faculty position.

18. Extent of Clinical Activities Initiated and Completed. Items 18(A) and 18(B) should be completed for all research projects. If the project was restricted to secondary analysis of clinical data or data analysis of clinical research, then responses to 18(A) and 18(B) should be “No.”

18(A) Did you initiate a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

Yes
 No

18(B) Did you complete a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

Yes
 No

If “Yes” to either 18(A) or 18(B), items 18(C) – (F) must also be completed. (Do NOT complete 18(C-F) if 18(A) and 18(B) are both “No.”)

18(C) How many hospital and health care professionals were involved in the research project?

_____ Number of hospital and health care professionals involved in the research project

18(D) How many subjects were included in the study compared to targeted goals?

_____ Number of subjects originally targeted to be included in the study

_____ Number of subjects enrolled in the study

18(E) How many subjects were enrolled in the study by gender, ethnicity and race?

Gender:

_____ Males

_____ Females

_____ Unknown

Ethnicity:

_____ Latinos or Hispanics

_____ Not Latinos or Hispanics

_____ Unknown

Race:

_____ American Indian or Alaska Native

_____ Asian

_____ Blacks or African American

_____ Native Hawaiian or Other Pacific Islander

_____ White

_____ Other, specify: _____

_____ Unknown

18(F) Where was the research study conducted? (List the county where the research study was conducted. If the treatment, prevention and diagnostic tests were offered in more than one county, list all of the counties where the research study was conducted.)

19. Human Embryonic Stem Cell Research. Item 19(A) should be completed for all research projects. If the research project involved human embryonic stem cells, items 19(B) and 19(C) must also be completed.

19(A) Did this project involve, in any capacity, human embryonic stem cells?

_____ Yes

___X___ No

19(B) Were these stem cell lines NIH-approved lines that were derived outside of Pennsylvania?

_____ Yes

_____ No

19(C) Please describe how this project involved human embryonic stem cells:

20. Articles Submitted to Peer-Reviewed Publications.

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication, listed in the table, in a PDF version 5.0.5 format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, the number of the publication and an abbreviated research project title. For example, if you submit two publications for PI Smith for the “Cognition and MRI in Older Adults” research project (Project 1), and two publications for PI Zhang for the “Lung Cancer” research project (Project 3), the filenames should be:

- Project 1 – Smith – Publication 1 – Cognition and MRI
- Project 1 – Smith – Publication 2 – Cognition and MRI
- Project 3 – Zhang – Publication 1 – Lung Cancer
- Project 3 – Zhang – Publication 2 – Lung Cancer

If the publication is not available electronically, provide 5 paper copies of the publication.

Note: The grant agreement requires that recipients acknowledge the Pennsylvania Department of Health funding in all publications. Please ensure that all publications listed acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

Title of Journal Article:	Authors:	Name of Peer-reviewed Publication:	Month and Year Submitted:	Publication Status (check appropriate box below):
1.				<input type="checkbox"/> Submitted <input type="checkbox"/> Accepted <input type="checkbox"/> Published
2.				<input type="checkbox"/> Submitted <input type="checkbox"/> Accepted <input type="checkbox"/> Published
3.				<input type="checkbox"/> Submitted <input type="checkbox"/> Accepted <input type="checkbox"/> Published

20(B) Based on this project, are you planning to submit articles to peer-reviewed publications in the future?

Yes _____ No X

If yes, please describe your plans: Not in the near future. Some of the work outlined in the work will have to be rigorously confirmed before they can be published.

21. Changes in Outcome, Impact and Effectiveness Attributable to the Research Project.

Describe the outcome, impact, and effectiveness of the research project by summarizing its impact on the incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of outcome, impact or effectiveness of the research project. If there were no changes, insert “None”; do not use “Not applicable.” Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

This work is in it very preliminary stages. However when more confirmatory work has been completed, this work will lead to the development of an entirely new class of agents that will attack tumoral addiction to glucose as a therapeutic modality.

22. Major Discoveries, New Drugs, and New Approaches for Prevention Diagnosis and Treatment.

Describe major discoveries, new drugs, and new approaches for prevention, diagnosis and treatment that are attributable to the completed research project. If there were no major discoveries, drugs or approaches, insert “None”; do not use “Not applicable.” Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

None to report. However once the confirmatory work has been completed, we will find new ways to use old drugs or the development of newer therapeutic modalities.

23. Inventions, Patents and Commercial Development Opportunities.

23(A) Were any inventions, which may be patentable or otherwise protectable under Title 35 of the United States Code, conceived or first actually reduced to practice in the performance of work under this health research grant? Yes _____ No X

If “Yes” to 23(A), complete items a – g below for each invention. (Do NOT complete items a - g if 23(A) is “No.”)

a. Title of Invention:

b. Name of Inventor(s):

c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention):

d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?

Yes _____ No X _____

If yes, indicate date patent was filed:

e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?

Yes _____ No X _____

If yes, indicate number of patent, title and date issued:

Patent number:

Title of patent:

Date issued:

f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes _____ No X _____

If yes, how many licenses were granted? _____

g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes ___ No X _____

If yes, describe the commercial development activities:

23(B) Based on the results of this project, are you planning to file for any licenses or patents, or undertake any commercial development opportunities in the future?

Yes _____ No X _____

If yes, please describe your plans:

24. Key Investigator Qualifications. Briefly describe the education, research interests and experience and professional commitments of the Principal Investigator and all other key investigators. In place of narrative you may insert the NIH biosketch form here; however, please limit each biosketch to 1-2 pages. *For Nonformula grants only – include information for only those key investigators whose biosketches were not included in the original grant application.*

George R. Simon, MD was the Director of the Thoracic Oncology Program and Member, Department of Medical Oncology at Fox Chase Cancer Center in Philadelphia, Pennsylvania until June 23, 2010. Currently, he is the Director of the Tobacco-related Malignancies Program

at the Medical University of South Carolina, Charleston, South Carolina. He is also the Burtschy family endowed Chair of Cancer Research at the Medical University of South Carolina.

After earning his medical degree from the Christian Medical College and Hospital, Ludhiana in Punjab, India, Dr. Simon completed residencies in internal medicine at the Christina Medical College and Hospital, Ludhiana and St. Joseph's Hospital in Denver, Colorado, and a fellowship in medical oncology and hematology at the University of Colorado Health Sciences Center in Denver. Previously, Dr. Simon has served as the director of the mesothelioma research program at the H Lee Moffitt Cancer Center, Tampa, Florida. Prior to joining the H Lee Moffitt Cancer Center, Dr. Simon served as the Director of Clinical Investigation in the Division of Hematology and Oncology at the Denver Health Medical Center.

Dr. Simon is a member of the NCCN Non-Small Cell Lung Cancer Panel and the Thoracic Core Committee of the Eastern Cooperative Oncology Group. He has previously served on the American College of Chest Physician, Lung Cancer Guidelines committee and in the thoracic core committee of the South West Oncology Group.

Dr. Simon is an Ad Hoc reviewer for several panels of the National Institutes of Health, National Cancer Institute, and Department of Defense and also a reviewer for several journals including, *Cancer Research*, *Clinical Cancer Research*, *Chest*, *Cancer*, *Journal of Clinical Oncology*, *Journal of Thoracic Oncology*, and *Indian Journal of Cancer*. He is author or co-author of over 50 peer-reviewed research publications, 13 book chapters and over 60 abstracts.