

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 717-231-2825.

1. **Grantee Institution:** University of Pittsburgh- of the Commonwealth System of Higher Education
2. **Reporting Period (start and end date of grant award period):** 1/1/2011 - 12/31/2014
3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Margaret C. McDonald, PhD
4. **Grant Contact Person’s Telephone Number:** 412-383-7474
5. **Grant SAP Number:** 4100054875
6. **Project Number and Title of Research Project:** 04 - Prostate Cancer Vaccine Clinical Trials
7. **Start and End Date of Research Project:** 1/1/2011 – 12/31/2012
8. **Name of Principal Investigator for the Research Project:** Leonard J. Appleman, MD
9. **Research Project Expenses.**

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

\$ 186,363.48

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, First Name	Position Title	% of Effort on Project	Cost
Beattie	Clinical Research Coordinator	100% July 2012-December 2012; 75% January 2013	\$29,891.23
Kelley	Research Data Coordinator	100% January 2011-June 2011	\$14,816.53
Long	Clinical Research Coordinator	75% January 2011-December 2012	\$91,696.96
Rowles	Regulatory Specialist	35% September 2012-January 2013	\$7,438.20
Schmotzer	Clinical Research Coordinator	30% January 2011-June 2011	\$8,242.80
Shepherd	Clinical Research Coordinator	30% August 2011-June 2012	\$12,879.36
Taylor	Research Data Coordinator	50% November 2011; 100% December 2011-June 2012	\$21,398.40

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, First Name	Position Title	% of Effort on Project
Appleman, Leonard	Principal Investigator	10%
Chatta, Gurkamal	Former Principal Investigator	10%

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.

Type of Scientific Equipment	Value Derived	Cost
None		

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 awarded:
None	<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:

We plan to apply for grants to support a follow-up, Phase II study.

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

Grant applications and protocols are being developed to support a Phase II study (UPCI 14-109) of the LNCaP dendritic cell vaccine developed in 06-070.

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 _____ No X _____

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

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

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

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

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

Yes _____ No X _____

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

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

Yes X _____ No _____

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

This research enhanced productive translational collaborations between basic immunology

researchers and clinical investigators. In addition, these funds were used to support clinical research coordinators, data coordinators, and a regulatory specialist, which had a direct and positive effect on clinical trial infrastructure at our institution.

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 X

If yes, please describe the collaborations:

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 agreement). Summarize the progress made in achieving these goals, objectives and aims for the period that the project was funded (i.e., from project start date through end date). 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 (□) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

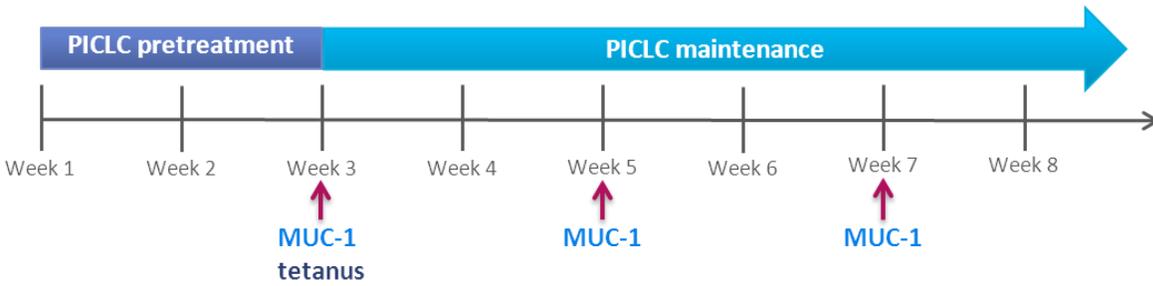
UPCI 05-086:

The goal of this study is to develop a safe and effective peptide-based vaccine for men with advanced prostate cancer, which could potentially prolong survival with minimal side effects. The Phase I portion of this trial was completed. Results were presented at the 2011 American Society of Clinical Oncology (ASCO) meeting in Chicago and are summarized below.

A single-arm study was conducted to evaluate the *in vivo* efficacy of immunostimulant poly-ICLC at a dose of 25 μ g/kg. Eligible participants were men with advanced prostate cancer (PCa) and evidence of systemic immunosuppression (defined as less than 30 percent of peripheral T-cells expressing gamma interferon [IFN- γ]).

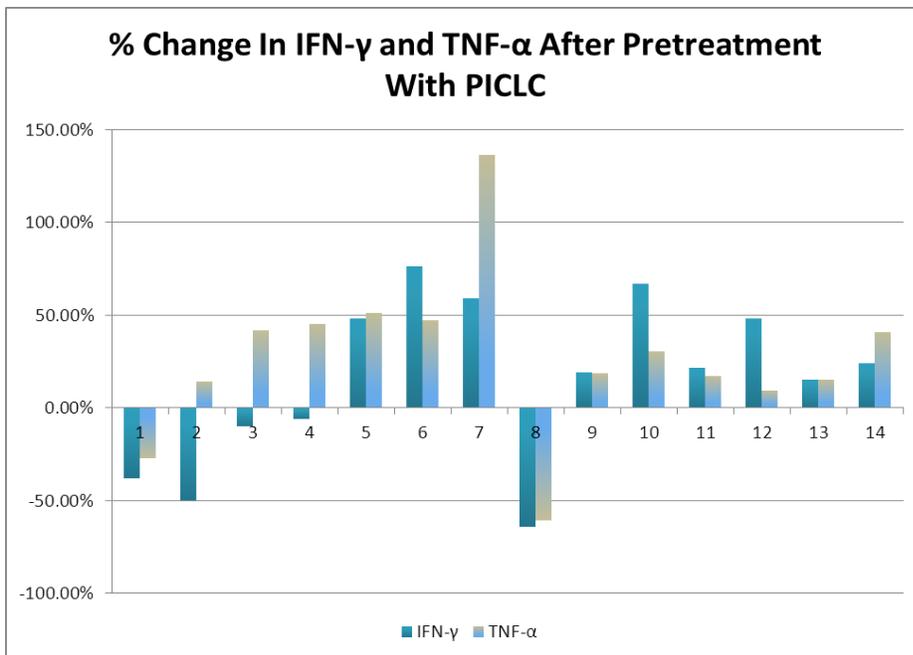
14 participants were recruited, with ages ranging from 51 to 80 years (median 72). Thirteen of those enrolled had castrate-resistant disease, and 12 had evidence of metastatic disease. On study Weeks 1 and 2, participants were pretreated with intramuscular injections of poly-ICLC (25 μ g/kg) three days a week. On Weeks 3, 5, and 7, patients were treated with subcutaneous injections of mucin-1 (MUC-1) vaccine (100 μ g). A dose of tetanus toxoid was administered via intramuscular injection on Week 3. Granulocyte macrophage colony stimulating factor (GM-CSF) (100 μ g) was administered on days 2-4 of the weeks of MUC-1 injection. Participants continued to receive poly-ICLC twice weekly while they remained in the study (Figure 1).

Figure 1. Study Schema.



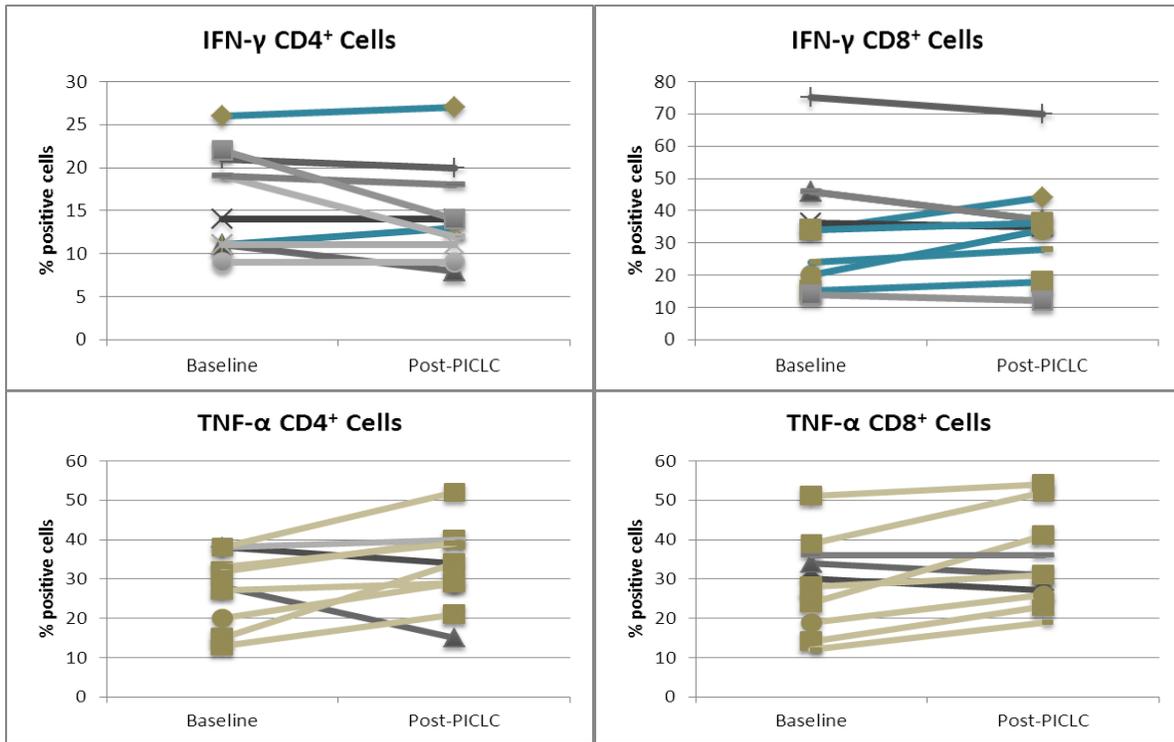
Cytokine levels were measured by Luminex assay prior to pretreatment and again at Week 3 and by ELISPOT prior to pretreatment and again at Week 5. When compared by Luminex assay, nine of 14 participants demonstrated increased IFN- γ production; these increases ranged from 15 percent to 76 percent. Twelve of 14 men showed an increase in tumor necrosis factor alpha (TNF- α) production; these increases ranged from 15 percent to 137 percent. All participants who showed an increase in IFN- γ also showed increases in TNF- α (Figure 2).

Figure 2. Cytokine expression.



Evaluation of T-cell subsets by ELISPOT showed two participants who had increased expression of IFN- γ in CD4⁺ T-cells; five demonstrated increased expression of IFN- γ in CD8⁺ T-cells. Upregulation of TNF- α expression was observed in both CD4⁺ and CD8⁺ T-cells in eight of 14 participants (Figure 3).

Figure 3. T cell subsets



The phenotype of the participants' dendritic cells (DCs) was evaluated by flow cytometry at baseline and at Weeks 3 and 9. Upregulation of CD80, CD86 on DCs was seen only in those patients with a low level of expression at baseline.

Anti-MUC-1 antibody levels were measured at baseline by ELISA and followed on Weeks 3, 5, 7, and 9. Four men achieved at least a 25 percent increase in both anti-MUC-1 immunoglobulin M (IgM) and immunoglobulin G (IgG) levels between Weeks 3 and 9 (Figures 4 and 5). Of these, three participants had demonstrated increases in both TNF- α and IFN- γ production, when measured by Luminex assay, after poly-ICLC pretreatment.

Figure 4.

Anti-MUC-1 IgM titers.

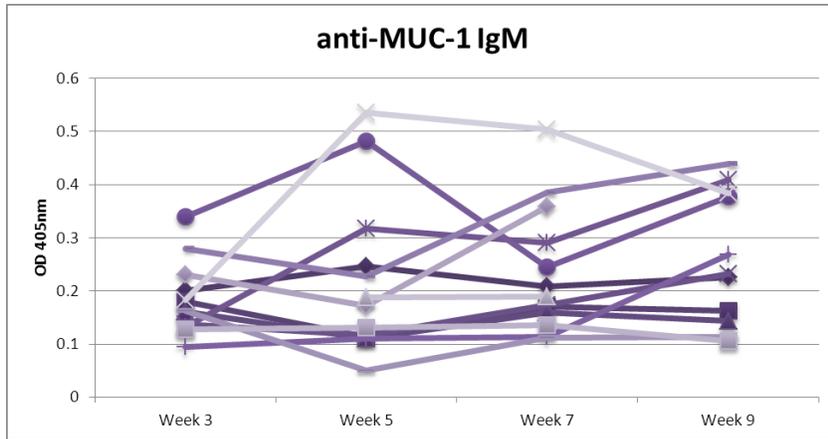
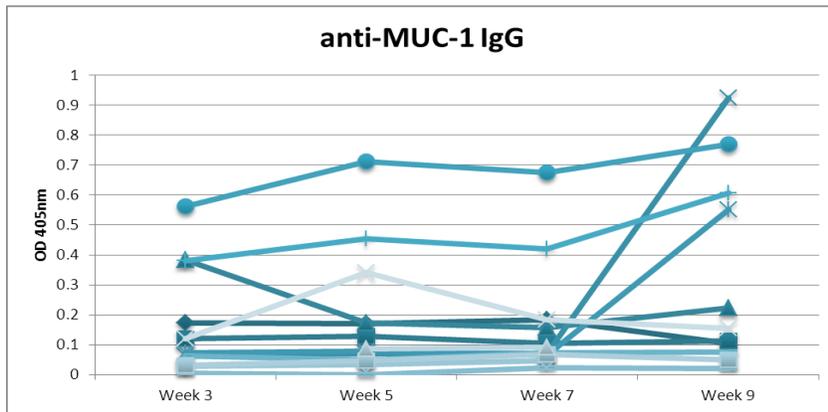


Figure 5. Anti-MUC-1 IgG titers.

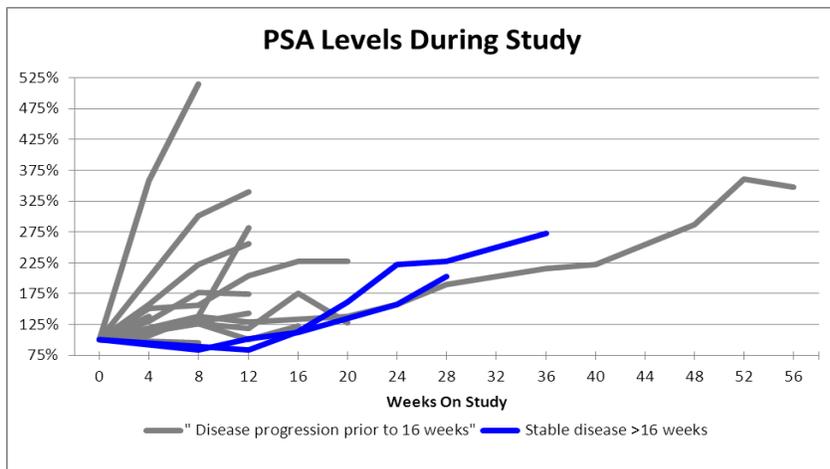


Serum tetanus antitoxin levels were measured at Week 3 and Week 9. One patient showed low anti-tetanus antibody titers post-immunization, which is consistent with anergy. This man had no upregulation of either cytokine production or anti-MUC-1 antibody titers.

Disease progression was defined according to the outcome measures recommended by the Prostate Cancer Clinical Trials Working Group 2 (PCWG2). Prostate specific antigen (PSA) values were measured serially while participants remained on study protocol (Figure 6). Imaging studies were performed as clinically appropriate. Two patients remained free of evidence of disease progression for more than 20 weeks. Both of these men had demonstrated increased levels of IFN- γ and TNF- α after pretreatment with poly-ICLC. Five participants demonstrated evidence of disease progression on either bone scan or computed tomography (CT) scan. One

patient was removed from the protocol after hospitalization with acute kidney injury. However, this condition was believed to be unrelated to our study interventions.

Figure 6. Serum PSA levels.



In conclusion, poly-ICLC at a dose of 25 μ g/kg reversed systemic immunosuppression in nine of 14 participants with advanced Pca, as demonstrated by increased levels of IFN- γ and TNF- α . Coupled with the encouraging immune and clinical responses observed in some patients, this observation warrants further investigation of poly-ICLC as a vaccine adjuvant in advanced PCa.

UPCI 06-070:

This trial was designed to examine alpha type 1 polarized dendritic cell (α DC1)-based vaccines loaded with an allogeneic prostate cell line (LNCaP) in combination with androgen ablation (AA) in patients with recurrent prostate cancer who have failed local therapy and have no measurable metastasis, but have a rising prostate-specific antigen (PSA), with a doubling time of fewer than 12 months. The primary efficacy objective is to evaluate the effect of the α DC1 vaccine on time to PSA progression compared to AA alone.

Under the original study protocol, nine of 16 patients were accrued. In fiscal year 2012, we received approval to transfer leadership of this project because Dr. Gurkamal Chatta had left the University of Pittsburgh Cancer Institute (UPCI). Dr. Leonard Appleman then assumed the role of principal investigator of the 06-070 study at UPCI. While this transition of leadership inevitably caused delays in progress of the 06-070 trial, Dr. Appleman has since worked with clinical research staff and laboratory scientists to complete a comprehensive protocol amendment to update the vaccine procedures to reflect state-of-the-art protocols for dendritic cell isolation and processing. The amendment was approved by the Institutional Review Board (IRB), and enrollment resumed. Two additional participants have been enrolled in the study and have begun study treatment since protocol modification. A number of other patients have been screened for the study. Additional participants are in screening or have been given the informed consent forms to review.

This trial holds the promise of significantly improving outcomes for patients with recurrent prostate cancer. Preliminary data showed that, in the first six patients treated, there was a statistically significant improvement in time to PSA failure for those who received AA+vaccine versus those who received AA alone, with a median response of 6.2 months for AA compared to 7.3 months for AA+vaccine (Figure 7). Interestingly, we see a trend toward prolonged time to PSA progression associated with vaccine—independent of whether the vaccine was included in the first or second course of AA. However, the vaccine-associated advantage was particularly pronounced in two patients who received α DC1s during the second course of AA, providing preliminary indication of a desirable carry-over effect.

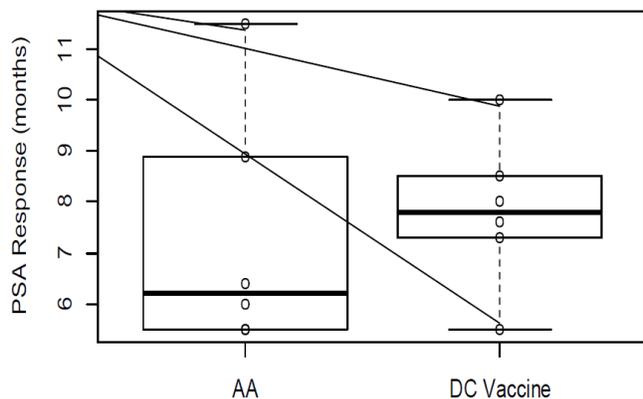


Figure 7. PSA response for six patients from UPCI 06-070 who all received two courses of AA with or without α DC1 vaccine (double cross-over design). Two patients received AA alone followed (upon PSA relapse) by AA+vaccine, while four patients received AA+vaccine, followed by AA alone.

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 (05-086)
 No (06-070 is still underway)

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?

12 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?

26-44 Number of subjects originally targeted to be included in the study (10-28 patients for 05-086, and 16 patients for 06-070)
25 Number of subjects enrolled in the study (14 patients for 05-086, and 11 patients for 06-070 thus far)

Note: Studies that fall dramatically short on recruitment are encouraged to provide the details of their recruitment efforts in Item 17, Progress in Achieving Research Goals, Objectives and Aims. For example, the number of eligible subjects approached, the number that refused to participate and the reasons for refusal. Without this information it is difficult to discern whether eligibility criteria were too restrictive or the study simply did not appeal to subjects.

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

Gender:

25 Males
0 Females
 Unknown

Ethnicity:

0 Latinos or Hispanics
21 Not Latinos or Hispanics
4 Unknown

Race:

 American Indian or Alaska Native
 Asian
1 Blacks or African American
 Native Hawaiian or Other Pacific Islander
24 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.)

Allegheny County

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
 No

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

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 or paper submitted for publication, listed in the table, in a PDF version 5.0.5 (or greater) format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, and an abbreviated title of the publication. For example, if you submit two publications for Smith (PI for Project 01), one publication for Zhang (PI for Project 03), and one publication for Bates (PI for Project 04), the filenames would be:

- Project 01 – Smith – Three cases of isolated
- Project 01 – Smith – Investigation of NEB1 deletions
- Project 03 – Zhang – Molecular profiling of aromatase
- Project 04 – Bates – Neonatal intensive care

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. None				<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 X No _____

If yes, please describe your plans:

A manuscript describing results from the 05-085 trial is currently in preparation and will be submitted to a peer-reviewed journal shortly. Upon completion of the 06-070 study, results will likewise be submitted for publication in a peer-reviewed journal.

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.

None

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.

05-086: Poly-ICLC treatment reversed systemic immunosuppression in nine of 14 patients with advanced prostate cancer, as demonstrated by increased levels of IFN- γ and TNF- α . This finding, coupled with the encouraging immune and clinical responses observed in some patients, indicates that further investigation of poly-ICLC as a vaccine adjuvant in advanced prostate cancer is warranted.

06-070: We have demonstrated the feasibility of vaccination with LNCaP-loaded alpha-1 dendritic cells for the treatment of prostate cancer. Preliminary data showed a statistically

significant improvement in time to PSA failure for those who received androgen ablation (AA) plus vaccine versus those who received AA alone.

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 _____

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 _____
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 _____
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 ___

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 _____

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.

BIOGRAPHICAL SKETCH

NAME Leonard Joseph Appleman		POSITION/TITLE Assistant Professor of Medicine	
NIH eRA Commons Login lappleman01			
EDUCATION/TRAINING			
INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Princeton University, Princeton, NJ	A.B.	1988	Molecular Biology
New York University, New York, NY	M.D., Ph.D.	1995	Cell and Molecular Biology
Beth Israel Hospital, Boston, MA	Residency	1995-1998	Internal Medicine
Dana Farber/Partners CancerCare, Boston, MA	Fellowship	1998-2001	Hematology/Oncology

A. Personal Statement

My research efforts focus on genitourinary oncology and phase I clinical trials. Areas of scientific interest include immunotherapy and targeted therapy for renal cell carcinoma, prostate, and bladder cancer, inhibition of DNA damage repair in combination with cytotoxic chemotherapy, and inhibition of the PI3 kinase pathway. Current phase I trials that I am leading at our institution include a phase I study of cisplatin, gemcitabine and ABT-888 (enrollment completed), a phase I study of the PI3-K inhibitor, BAY 80-6946 (industry-sponsored, enrolling), and a phase I study of tivantinib plus bevacizumab (enrolling). I am currently the chair of ECOG Study 2810, *Randomized, Double-Blind Phase III Study of Pazopanib vs. Placebo in Patients with Metastatic Renal Cell Carcinoma Who Have No Evidence of Disease Following Metastatectomy*. My laboratory background is in tumor immunology and T lymphocyte costimulatory signaling.

B. Positions and Honors

POSITIONS AND EMPLOYMENT

1987-1988 Undergrad Research Student, lab of Dr. Jeffery Stock, Princeton University
 1988-1994 Graduate Student, lab of Dr. Alan Frey, New York University School of Medicine
 1995-1996 Medical Intern, Beth Israel Hospital, Boston
 1995-2001 Clinical Fellow in Medicine, Harvard Medical School
 1996-1997 Medical Junior Assistant Resident, Beth Israel Hospital, Boston
 1997-1998 Medical Senior Assistant Resident, Beth Israel Hospital, Boston
 1998-2001 Clinical Fellow in Medicine, Dana-Faber Cancer Institute
 1998-2001 Clinical Fellow in Medicine, Brigham and Woman's Hospital
 1998-2001 Clinical Fellow in Medicine, Massachusetts General Hospital
 2001-2006 Instructor in Medicine, Dana-Farber Cancer Institute, Brigham & Women's Hospital
 2001-2006 Instructor in Medicine, Harvard Medical School
 2006- Assistant Professor of Medicine, University of Pittsburgh School of Medicine

LICENSURE AND CERTIFICATION

1998-2006 Registered Physician, Commonwealth of Massachusetts
 1998-2008 Diplomat, American Board of Internal Medicine
 2002- ABIM subspecialty Diplomat, Oncology
 2003- ABIM subspecialty Diplomat, Hematology
 2006- Registered physician, Commonwealth of Pennsylvania.

AWARDS AND HONORS

1988 William Pierson, MD Hibben Memorial Scholarship, Princeton University

- 1995 American Federation for Clinical Research, Medical Student Award for Clinical Excellence, New York University School of Medicine
- 1998 Medical Resident Research Award, Beth Israel Hospital, Boston
- 2000 Leukemia Research Foundation, Clinical Scientist Training Award
- 2008 Alan Winkelstein, MD Memorial Fellow Educator of the Year, UPCI
- 2010 Alan Winkelstein, MD Memorial Fellow Educator of the Year, UPCI

MEMBERSHIPS

- 2007- Member, American Society of Clinical Oncology (ASCO)

C. Selected Publications

1. Egorin MJ, Shah DD, Christner SM, Yerk MA, Komazec KA, **Appleman LJ**, Redner RL, Miller BM, Beumer JH. Effect of a proton pump inhibitor on the pharmacokinetics of imatinib. *Br J Clin Pharmacol*. 2009 Sep;68(3):370-4.
2. Eder JP, Shapiro GI, **Appleman LJ**, Zhu AX, Miles D, Keer H, Cancilla B, Chu F, Hitchcock-Bryan S, Sherman L, McCallum S, Heath EI, Boerner SA, LoRusso PM. A phase I study of foretinib, a multi-targeted inhibitor of c-Met and vascular endothelial growth factor receptor 2. *Clin Cancer Res*. 2010 Jul 1;16(13):3507-16.
3. Tolcher AW, **Appleman LJ**, Shapiro GI, Mita AC, Cihon F, Mazzu A, Sundaresan PR. A phase I open-label study evaluating the cardiovascular safety of sorafenib in patients with advanced cancer. *Cancer Chemother Pharmacol*. 2011 Apr;67(4):751-64.
4. Tannir NM, Wong YN, Kollmannsberger CK, Ernstoff MS, Perry DJ, **Appleman LJ**, Posadas EM, Cho D, Choueiri TK, Coates A, Gupta N, Pradhan R, Qian J, Chen J, Scappaticci FA, Ricker JL, Carlson DM, Michaelson MD. Phase 2 trial of linifanib (ABT-869) in patients with advanced renal cell cancer after sunitinib failure. *Eur J Cancer*. 2011 Dec;47(18):2706-14.
5. Argiris A, Feinstein TM, Wang L, Yang T, Agrawal S, **Appleman LJ**, Stoller RG, Grandis JR, Egloff AM. Phase I and pharmacokinetic study of dasatinib and cetuximab in patients with advanced solid malignancies. *Invest New Drugs*. 2012 Aug;30(4):1575-84.
6. Leng S, Nallamotheu BK, Saint S, **Appleman LJ**, Bump GM. Clinical problem-solving. Simple and complex. *N Engl J Med*. 2013 Jan 3;368(1):65-71.
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