

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.

1. **Grantee Institution:** Drexel University
2. **Reporting Period (start and end date of grant award period):** 1/1/2010-12/31/2013
3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Anne Martella
4. **Grant Contact Person’s Telephone Number:** (215) 895-6471
5. **Grant SAP Number:** 4100050893
6. **Project Number and Title of Research Project:** 1 - *Effect of Antiretroviral Therapy on Surrogate Markers of Cardiovascular Disease and Inflammation in HIV-infected Patients*
7. **Start and End Date of Research Project:** 1/1/2010-12/31/2013
8. **Name of Principal Investigator for the Research Project:** Christopher Bruno, 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:

\$ 42,139.00

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
Christopher Bruno	Principle Investigator	22.86%	\$32,689.80

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
Margaret Cauterucci	Nutritionist	5
Sharon Lewis	Research Coordinator	5
David Downie	Research Nurse/Coordinator	10
Christine Randazzo	Research Nurse/Coordinator	10
Robert Foley	Echocardiography Technologist	10
Jeffrey Jacobson	Co-Investigator	5
Howard Eisen	Co-Investigator	5
Michele Kutzler	Co-Investigator	5

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 to be 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 _____ No X _____

If yes, please describe your plans:

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

We are planning to evaluate the cytokine profiles from the serum samples that were obtained.

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				
Female				1
Unknown				
Total				1

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic				1
Unknown				
Total				1

	Undergraduate	Masters	Pre-doc	Post-doc
White				
Black				
Asian				1
Other				
Unknown				
Total				1

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 project brought together a multi-disciplinary team that would not have collaborated together without the CURE funds.

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 (\square) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

The goal of the research funded by this grant was to generate pilot data investigating the relationship between HIV infection, antiretroviral therapy, cardiovascular disease and serum markers of inflammation. Our objective was to enroll 10 subjects in a prospective observational cohort study focusing on 3 groups: HIV infected subjects who initiate ART, HIV infected subjects who do not initiate ART, and HIV negative subjects with the following specific objectives: 1) To compare mean change at one year in carotid artery intima-media thickness (IMT) between the three study groups. 2) To compare changes in inflammatory markers, cardiac ejection fraction and pulmonary artery pressure at one year between the three study groups. 3) To assess for correlation between changes in serum markers of inflammation, status of HIV disease (as measured by CD4 and viral load), endothelial activation, physiologic surrogates of CVD such as IMT and cardiac function.

During this funding period, we enrolled 10 patients. Subjects were enrolled from one of 2 sites: the Drexel University College of Medicine Partnership Comprehensive Care Practice for HIV positive subjects, and the General Medicine Clinic at 1427 Vine Street for HIV uninfected subjects. Study related tests were conducted at the Partnership or Hahnemann University Hospital, both located in center city Philadelphia.

Inclusion Criteria: HIV Positive Subjects

Patients were eligible for enrollment in this study if they: 1) Have HIV infection as documented by a clinically licensed ELISA test and confirmed by Western Blot testing 2) Are eighteen years or older 3) Are not currently on ART and have not been on ART within the last one year and 4) are free of exclusion criteria as listed below.

Inclusion Criteria: HIV Negative Subjects

Patients from the general medical clinic were eligible for enrollment if they were 1) Eighteen years or older and 2) Are documented to be HIV negative by a clinically licensed ELISA test 3) are free from the exclusion criteria as listed below.

Exclusion Criteria: Both HIV Positive and HIV Negative Subjects

Patients were ineligible to participate in the study if they met any of the following criteria: History of coronary artery disease including: prior history of myocardial infarction, coronary artery bypass surgery, angioplasty or angina pectoris with a stress test or coronary angiography indicating coronary artery disease. History of stroke, transient ischemic attack, or documented carotid atherosclerosis; use of lipid lowering medications within six months prior to study entry. Pregnant at time of screening or plans to become pregnant during the study period. Any diagnosis of diabetes mellitus, with the exception of a previous history of gestational or steroid-induced diabetes mellitus within 12 weeks prior to study entry. Current use of immunosuppressive medications including current use of systemic steroids (IV or PO), immunosuppressive regimens for solid organ or stem cell transplantation, TNF-alpha antagonists, or monoclonal antibody therapy. Chronic active hepatitis B or C infection. History of chemotherapy within the six months prior to study enrollment. History of active autoimmune disease including SLE, rheumatoid arthritis, sarcoidosis, multiple sclerosis, myasthenia gravis. Diagnosis of active tuberculosis or currently undergoing treatment for active tuberculosis. Active drug or alcohol use or dependence that, in the opinion of the site investigator, would interfere with adherence to study requirements. Impaired mental status that in the opinion of the

site investigator precludes the possibility of informed consent.

Subjects were identified by their provider or by self referral from posted advertising in participating clinics. Patients interested in participating in the study were scheduled to meet with a member of the study team for a screening visit. At this visit the subject was provided with more information about the details of study requirements and was consented for study participation. Subjects in the treatment group initiated ART within one month of their screening visit.

Accrual and follow-up for the study has been completed with 11 subjects enrolled. Accrual goal of enrolling 10 patients was met, however not all subjects completed all 48 weeks of follow-up assessments as defined in the study protocol (see table 1 below).

Table 1: Enrolled subjects and completed study assessments

Subject #	1	2	3	4	5	6	7	8	9	10	11
Baseline											
Anthropometric data	X	X	X	X	X	X	X	X	X	X	X
HIV lab studies (CD4/VL)	X	X	X	X	X	X	X	X	X	X	X
Serum for immune activation	X	X	X	X	X	X	X		X	X	X
Carotid IMT ultrasound	X	X	X	X	X	X			X	X	X
Trans-Thoracic Echo	X	X	X	X	X	X			X	X	X
4 week											
HIV lab studies (CD4/VL)		X	X	X		X			X	X	X
Serum for immune activation		X	X	X		X			X	X	X
Trans-Thoracic Echo		X	X	X		X			X	X	X
12 week											
HIV lab studies (CD4/VL)		X	X	X		X			X		
24 week											
Anthropometric data		X				X					
HIV lab studies (CD4/VL)		X				X					
Carotid IMT ultrasound		X				X					
Trans-Thoracic Echo		X				X					
48 week											
Anthropometric data		X				X					
HIV lab studies (CD4/VL)		X				X					
Serum for immune activation		X				X					
Carotid IMT ultrasound		X				X					
Trans-Thoracic Echo		X				X					

There were several challenges to maintaining long term follow-up in this underserved patient population including unstable housing and incarceration. Additionally, enrolling HIV positive subjects who were not on antiretroviral therapy became increasingly challenging as national HIV treatment guidelines were revised during the study period with recommendations for initiating antiretroviral therapy at higher CD4 cell counts, resulting in fewer patients that did not meet criteria for initiation of therapy. This limited enrollment for this arm of the study.

Trans-thoracic echocardiograms were completed and interpreted with left ventricular ejection fraction and pulmonary artery pressure measured for each subject as specified by the study protocol. Carotid artery ultrasound was performed for each subject as specified by the study protocol with images stored. Changes in available personnel at our institution with expertise in vascular ultrasound resulted in the need to postpone carotid intima-media thickness measurements.

Serum samples were processed and stored. Cytokine profiling will be performed on samples.

Table 2: Baseline characteristics of enrolled subjects

	Mean (range)
Age (y)	32 (21-51)
Body Mass Index	27.5 (21.8-37.7)
CD4+ T-cells (number/microL)	519 (320-840)
HIV-1 Viral load (copies/mL)	35010 (440-67800)
LDL cholesterol (mg/dL)	88.5 (65-172)
Left ventricular ejection fraction (%)	60 (55-65)

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?

6 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?

10 Number of subjects originally targeted to be included in the study
11 Number of subjects enrolled in the study

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:

7 Males
4 Females
 Unknown

Ethnicity:

1 Latinos or Hispanics
10 Not Latinos or Hispanics
 Unknown

Race:

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

Philadelphia 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
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 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 _____ No X

If yes, please describe your plans:

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.

None

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 _____ **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.*

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Christopher J. Bruno, MD	POSITION TITLE Assistant Professor of Medicine-Division of Infectious Diseases		
eRA COMMONS USER NAME (credential, e.g., agency login)			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
University of Michigan, Ann Arbor, MI	BA	06/94	History
Columbia University, New York, NY	MD	06/01	Medicine

A. Positions and Honors

Positions and Employment

- 2001-2004 Hospital of the University of Pennsylvania Philadelphia, PA Internal Medicine Residency
- 2005-2007 Hospital of the University of Pennsylvania, Philadelphia, PA, Fellow Infectious Diseases
- 2004-2005 Lankenau Hospital, Wynnewood, PA, Chief Resident/Hospitalist
- 2007-present Drexel University—College of Medicine, Philadelphia, PA, Assistant Professor Division of Inf. Dis. and HIV Med.

Other Experience

- Aug 2008-present Chair, Hahnemann University Hospital Antibiotic Subcommittee
- Aug 2008-present Medical Director, Hahnemann University Hospital Antimicrobial Management Program
- Aug 2008-present Member Hahnemann University Hospital Pharmacy and Therapeutics Committee

Honors

- 2007 Infectious Disease Society of America Travel Grant
- 2007 Outstanding Research Award, College of Physicians of Philadelphia, Section on Public Health

B. Selected peer-reviewed publications

- Amorosa, V, **Bruno C**, LoRe V, et al. The Influence of Abacavir and Other Antiretroviral Agents on Virologic Response to Hepatitis C Virus Therapy Among Antiretroviral-Treated HIV-Infected Patients. Antiviral Therapy