

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:** Magee-Womens Research Institute and Foundation
2. **Reporting Period (start and end date of grant award period):** 01/01/2010-12/31/2010
3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Cheryl A. Richards, MBA
4. **Grant Contact Person’s Telephone Number:** 412-641-8932
5. **Grant SAP Number:** 4100050901
6. **Project Number and Title of Research Project:** #1 - Refinement of the Appropriate Animal Model for Respiratory Infection with Influenza in Pregnancy
7. **Start and End Date of Research Project:** 01/01/2010-12/31/2010
8. **Name of Principal Investigator for the Research Project:** Richard H. Beigi, MD, MSc.
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:

\$ 39,625.00

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	Position Title	% of Effort on Project	Cost
Beigi	Principal Investigator	2.5%	\$3,107.53

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
Stefano-Cole	Co-Investigator	5%
Reed	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
N/A		

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

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

Department funding of approximately \$5,000

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

Yes No _____

If yes, please describe your plans:

Once we have finalized the proposed experiments with 2009 H1N1 Seronegative ferrets and analyzed the data, we will be putting together another NIH R level grant to permit future investigations. The specific R will depend on extent of pilot data and quality of data/outcomes we obtain from these projects.

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

Having the opportunity to perform the completed and proposed experiments because of the Health Research Grants has provided an excellent foundation to foster our collaboration. As stated we plan to continue to apply for influenza-related research in pregnancy both to external NIH grants but also upcoming internal funding opportunities. In addition, we will also be looking to large grants supporting research into other pathogens of high importance and its effects during pregnancy. We also await correspondence from FDA about our model and their interest in collaborator contract work.

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

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.

The funding in this projects allowed for continuing momentum of our burgeoning collaboration that has to date generated 1 abstract at national meeting (this funding cycle).. In addition, when we receive our 2001 H1N1 seronegative ferrets and perform our second study we will undoubtedly generate more data for future meetings and manuscripts. Even more important is that a solid scientific relationship has been further fostered between the principal investigator and the co-investigators. This has clearly generated ongoing momentum to be gained from a project and scientific relationship standpoint and recognition within the institution from senior leadership. This undoubtedly has many tangible and intangible benefits.

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 X _____ No _____

If yes, please describe the collaborations:

The work presented at national meetings has helped to engage other researchers across the country and opened a productive dialogue between our University of Pittsburgh group and the NIH-NIAID/NICHD. In addition, the FDA has expressed interest in our projects and collaborator team and this will likely lead to contract-level work.

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.

We proposed the following plans at the outset of this grant period:

1. Further develop and refine a model of collaboration and infrastructure that will allow for ongoing investigation of susceptibility, immunological response and countermeasures to emerging and threatening infectious diseases among pregnant animals.
2. To demonstrate and compare the disease course of aerosolized novel 2009 H1N1 in both a late gestation pregnant and non-pregnant ferret model of influenza infection.
3. To evaluate and compare the pathogenesis and immune response elicited by aerosolized novel 2009 H1N1 in both late gestation pregnant and non-pregnant ferrets.

With regard to the 1st specific aim:

We have undoubtedly achieved our first specific aim above. Significant strides have been made in terms of further developing and refining our collaborative model for aerosol challenge studies of pregnant animals. Funds from the project have further supported investigator effort, actual aerosol challenge studies of our new animal model for influenza in pregnancy, the ferret. In doing this, we have attracted attention at the FDA and within NIAID for our work. After completion and analysis of our work, abstracts, manuscripts and competitive grant applications will be prepared. This will continue to assist in solidifying our now established scientific collaborator model, infrastructure, and ability to study infectious disease pathogens in pregnancy.

With regard to the 2nd specific aim:

This is what we proposed to do in the original grant:

To begin the experiments by examining aerosol characteristics of novel 2009 H1N1 influenza at 3 dilutions in an empty aerosol chamber starting at @ 10^8 /ml and decreasing ten-fold. Four aerosols per dilution (12 aerosols) will be used in a whole-body exposure box and will then be repeated once for validation. Subsequent determinations of viral concentration in the nebulizer and aerosol by Tissue Culture ID50 (TCID50) will be undertaken. This was performed.

Our next step that was proposed:

After these quality and quantity control measures challenge experiments will then be undertaken. Ferrets obtained from Marshall Pet Products will be used for the experiments. In order to determine the Infective Dose of 2009 H1N1 that establishes infection in 50% of ferrets (IC_{50}), aerosol challenges with 3 doses in a whole-body chamber at doses expected to bracket the IC_{50} will be performed upon 3 groups of four. Fifty percent of ferrets will be

pregnant and 50% non-pregnant. Challenges will be performed on or about day 33 of a 42 day gestation, approximating 3rd trimester exposure. All ferrets will be followed for 10-14 days after exposure to document clinical disease course quantify upper respiratory tract viral load (PCR). Ferrets that become moribund will be promptly euthanized and necropsied; blood and tissue samples will be taken for analysis.

This was performed, however, with fewer ferrets given increased costs of the pregnant ferrets and increased infrastructure costs. We used 4 groups of 3 ferrets each (6 pregnant and 6 non-pregnant, at two different doses). In addition, we sham exposed 2 pregnant ferrets in order to have a non-infected pregnant control population to compare pregnancy-specific outcomes.

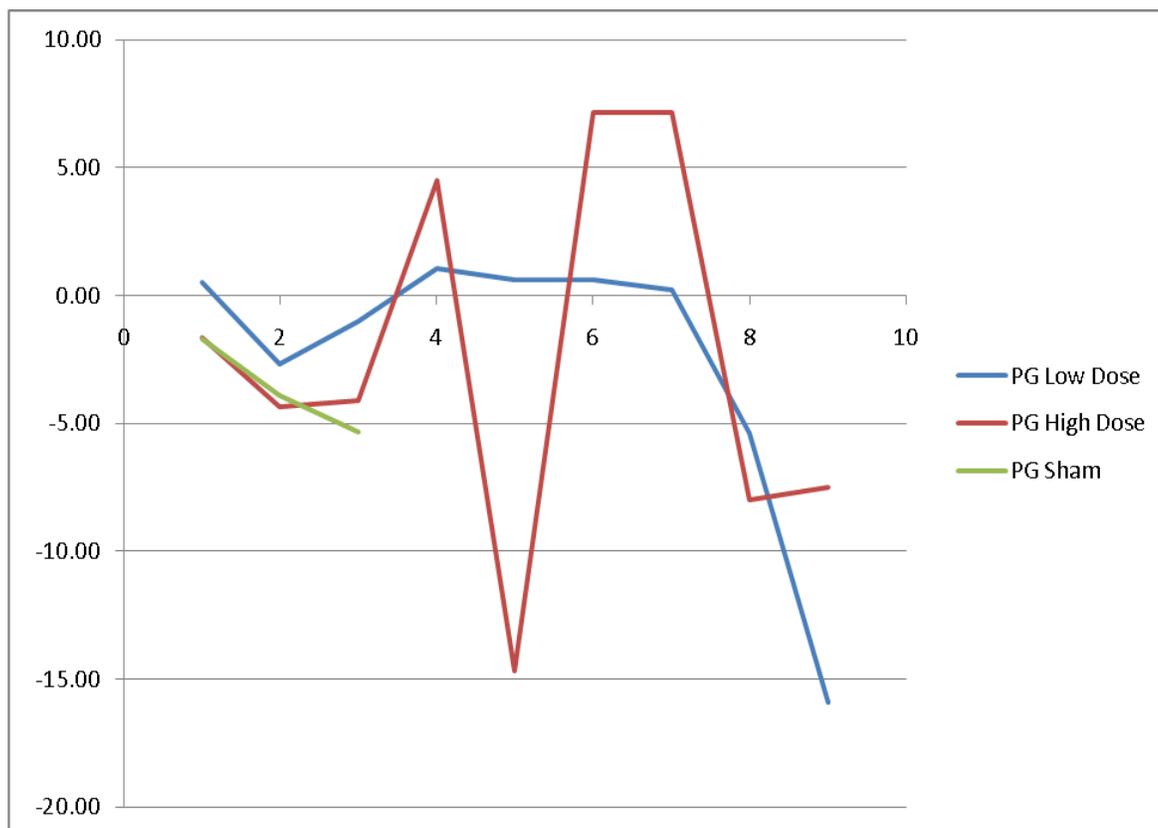
The outcome data is represented below:

The first measured endpoint was % weight change from baseline pre-challenge as a measure of overall health after challenge. This is an accepted endpoint for such aerosol challenges.

The first graph represents the pregnant ferrets % weight change after challenge and graphically displayed up until delivery. It is important to remember that pregnant ferrets are supposed to gain weight due to the gestation. Unfortunately, the 2 sham exposed ferrets required euthanasia due to non-influenza related illness and therefore can't be used for comparison. This was likely due to travel and acclimatization issues.

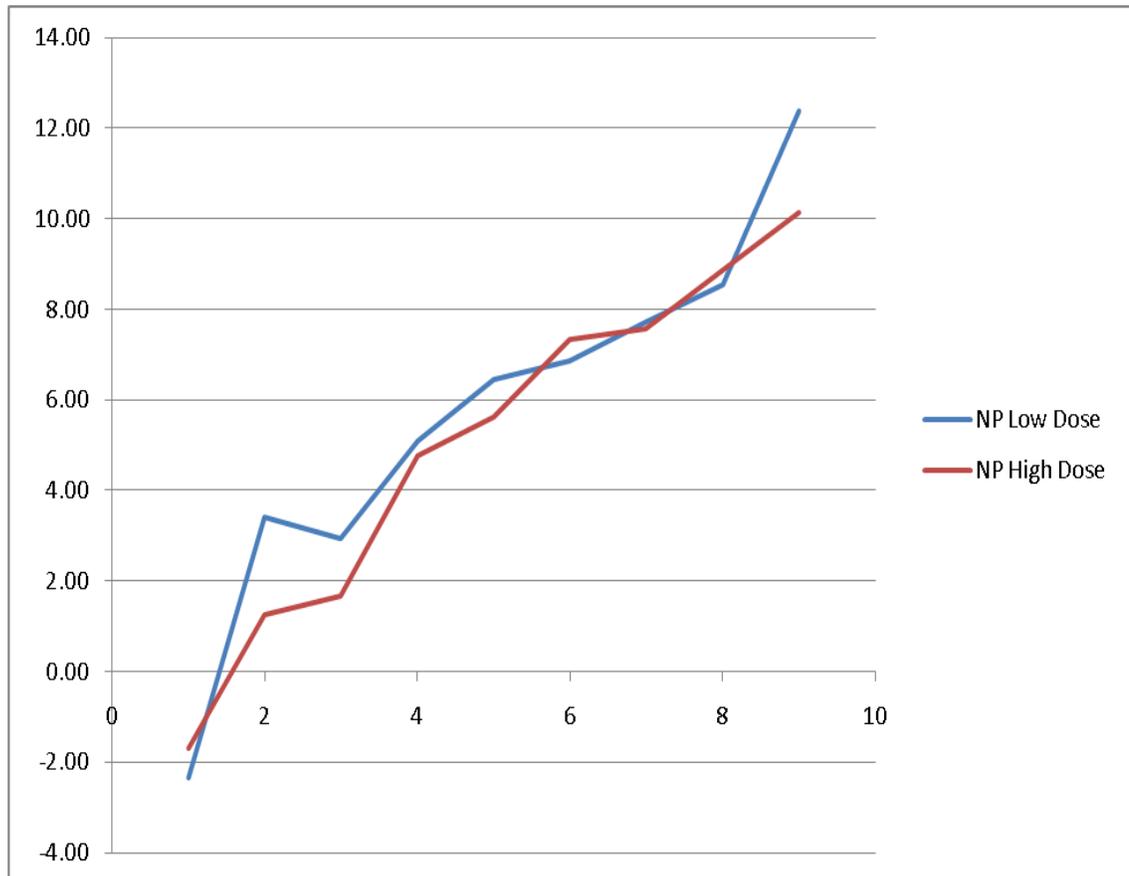
Overall, it is clear from this small experiment that the exposed pregnant ferrets lost weight. The data is not shown but these ferrets also demonstrated a febrile response and had clear influenza clinical illness that manifested as profuse nasal congestion/copious mucus production. In comparison, the non-pregnant ferrets did have a mild febrile response, but did not demonstrate other clear signs of influenza illness such as nasal congestion or respiratory illness. In addition, one high-dose pregnant ferret required early euthanasia due to severe respiratory distress and lethargy.

% Weight Change (Pregnant)



Below are the % weight gain/loss data for the non-pregnant ferrets. These data demonstrate clearly that the non-pregnant ferrets did not lose weight, and in fact gained weight. In addition, the overall lack of clinical disease among non-pregnant ferrets compared to pregnant ferrets was striking.

% Weight Change (Non-pregnant)



In terms of births, the average number of kits per mother ferret (N=7 for both groups) was not different between the low and high dose ferrets. In addition, the average weight of the litters and the survival of kits also were not different between the 2 dose groups. Due to the lack of sham infected mothers surviving beyond 2 days, it is difficult to draw any meaningful conclusions about kit size, weight or survival.

Summary From Specific Aim #2:

These data, while limited by the lack of pregnant control (sham exposed) data, strongly suggest that the pregnant ferrets contracted influenza at less of a challenge dose and manifested clearly worse signs of disease compared to the non-pregnant ferrets. This is an

excellent foundation in which to expand our investigations because this is a model that appears to mimic what is seen in human pregnancy.

The data generated from this aim will be presented in March, 2011 at the Society of Gynecologic Investigation:

Beigi RH, Trichel A, Dunsmoore T, Reed DS, Stefano Cole K. Aerosolized Influenza Infection During Late Gestation Ferret Pregnancy. Poster presentation at the Society for Gynecologic Investigation Annual Meeting, Miami, FL, March, 2011.

With regard to specific Aim #3:

We had planned the following:

Using the challenge doses obtained from the above aim we were going to perform more challenges among a second group of ferrets with four in each group (½ preg, ½ non-preg). The first group was to undergo a sham challenge for control purposes. The next 3 groups were to be challenged and then euthanized at day 2, day 4 and then day 7. Pre-euthanization analysis will include: Hemagglutinin antibody titers, viral load, and potentially microarray technologies pending funding specifics. Post-euthanization analysis was to include: pathologic and viral load quantification of tissue specimens including the fetal compartment.

We proceeded with ordering the timed pregnant ferrets (as well as non-pregnant ferrets) to perform this planned experiment from the vendor in November, 2010, after the first experiment was completed. Given ongoing concurrent investigations using ferrets at our institution by other investigators, we consulted with those that had received ferrets at similar times as our second order about the issue of seronegativity to H1N1 among their ferrets. We learned that many of the ferrets that had been obtained from the same vendors for our colleagues respective challenge studies were Seropositive for 2009 H1N1 (previously infected, and thus not usable for challenge pathogenesis studies).

In light of these findings, we queried the vendor about the ferrets (both pregnant and non-pregnant) that we had already ordered for the 2nd experiment (and paid for) and learned after testing that our ferrets were also seropositive for 2009 H1N1. Thus, we canceled the order given the lack of suitability for the pathological challenge studies that we proposed herein. We have received a refund on that order and have obtained a contract with an alternative vendor using these funds.

Currently, we are in the process of working collaboratively with the new vendor to test the new ferrets for seropositivity to 2009 H1N1 prior to obtaining the new batch of ferrets to perform our studies. Once we confirm seronegativity to 2009 H1N1, we will receive the shipment and perform the proposed challenges and pathological investigations. This is projected to take place in the spring of 2011.

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
 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 X No _____

If yes, please describe your plans:

Once we complete the 2nd project, national meeting presentation and manuscript preparation/submission will be forthcoming.

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.

The results of the studies detailed herein suggests that we have successfully developed an animal mode for aerosol-challenge of influenza in pregnancy that is closer to the human model of clinical disease (ferret model). Aerosol models of influenza in general are not well established, not to mention pregnancy models. Most of the previous work with influenza challenges have been with intranasal inoculation, not aerosol challenges. It is believed that

the aerosol challenge model better approximates human disease susceptibility and contracting of influenza infection.

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.

The “new discovery” noted herein is the new model creation of influenza in pregnancy that will allow us to better characterize the increased susceptibility among pregnant women and thus understand disease prevention mechanisms to an improved amount.

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.*

Bio-sketch for Richard H. Beigi, MD, MSc.

A. Positions and Honors.

Positions:

1/2004 – 7/2006: CASE School of Medicine, Assistant Professor, Reproductive Biology, Department of Obstetrics and Gynecology, Metro Health Medical Center
8/2006 – Current University of Pittsburgh SOM, Assistant Professor, Reproductive Sciences, Department of Obstetrics/Gynecology /RS, MWH of UPMC

Service:

11/2009 – Current CDC-COCA Critical Care Conference Call Invited Expert: Critical Care of H1N1 in Pregnancy
10/2009 – Current ACOG Representative to the National Vaccine Advisory Committee (NVAC) Working Group
03/2009 NICHD/NIAID: Invited Expert: Pregnancy and Contraception in Microbicide Development Meeting
02/2009 – Current CDC: Invited Expert: Advisory Work-Group to the ACIP: Pertussis (Tdap) Vaccination during Pregnancy
10/2008 CDC: Advisory Committee on Immunization Practices (ACIP). Recommendations from the Anthrax Vaccine in Pregnancy Work-Group

09/2008	NIH/NICHD – Biodefense Expert Working Group Meeting. Rockville, Maryland September 8-9, 2008
05/2008 – Current	NIH/NICHD – Invited Expert: Biodefense – Infectious Diseases Working Group: Antibiotic and Antivirals use in Pregnancy
05-2008 – Current	NIH/NICHD – Invited Expert: Biodefense – Infectious Diseases Working Group: Radiation Exposures in Pregnancy
05-2008 – Current	NIH/NICHD – Invited Expert: Biodefense – Infectious Diseases Working Group: Vaccine use in Pregnancy
05-2008 – Current	CDC – Invited Advisory group to ACIP: Anthrax vaccine in pregnancy
04/2008 – Current	CDC – Invited Expert Working Group: Pandemic Influenza & Pregnancy
04/2007	NIH/NICHD: Invited Study Section Reviewer: HIV Maternal-Child AIDS Network Sites

B. Selected Peer-reviewed Publications (Selected from a list of 31)

1. Beigi RH. Pandemic Influenza and Pregnancy: A Call for Preparedness Planning. *Obstet Gynecol* 2007; 109:1193-6.
2. Tabery J, Mackett CW and the University of Pittsburgh Medical Center Pandemic Influenza Task Force's Triage Review Board (Beigi RH). Ethics of Triage in the Event of an Influenza Pandemic. *Disaster Med Public Health Preparedness* 2008; 2:114-8.
3. Farrell RM, Beigi RH. Pandemic Influenza and Pregnancy: An Opportunity to Assess Maternal Bioethics. *Am J Pub Health*. *Am J Pub Health* 2009 2009; 99:S231-S235.
4. Beigi RH, Davis G, Hodges J, Akers A. Preparedness Planning for Pandemic Influenza Among Large United States Maternity Hospitals. *Emerging Health Threats* 2009; e2. doi:10.3134/ehth.09.002.
5. Rasmussen SA, Jamieson DJ, MacFarlane K, Cragan JD, Jennifer Williams J, on behalf of the Pandemic Influenza and Pregnancy Working Group...(Richard Beigi). Pandemic Influenza: Special Considerations for Pregnant Women – Summary of a Meeting of Experts. *A J Pub Health* 2009; 99:S248-S254.
6. Beigi RH, Switzer GE, Meyn LA. Acceptance of a pandemic avian influenza vaccine in pregnancy. *J Reprod Med* 2009; 54:341-46.
7. Lee BY, Bailey RR, Wiringa AE, Assi TM, Beigi RH. Anti-viral Medications for Pregnant Women for Pandemic and Seasonal Influenza: An economic computer model. *Obstet Gynecol* 2009; 114(5):971-980.
8. Broughton DE, Beigi RH, Switzer GE, Raker CA, Anderson BL. Obstetrical Healthcare support staff attitudes and beliefs regarding influenza vaccination in pregnancy. *Obstet Gynecol* 2009; 114(5):981-7.
9. Beigi RH, Wiringa AE, Bailey R, Assi TM, Lee BY. Economic value of seasonal and pandemic influenza vaccination during pregnancy. *Clin Infect Dis* 2009; 49(12):1784-92.

C. Research Support.

1. U01-AI-068633-01: Microbicide Trials Network 4/2008 – Ongoing
NIH/NIAID/NICHD

Protocol Chair: MTN-002: First ever study to be conducted among pregnant women of a topical microbicide for the prevention of HIV. This is a Pharmacokinetic and Placental Transfer evaluation of Term Gravidas undergoing cesarean section.

2. U01-AI-068633-01: Microbicide Trials Network 9/2008 – Ongoing
NIH/NIAID/NICHD
Protocol Co-Chair: MTN-016: HIV Prevention Agent Exposure Registry: EMBRACE Protocol. This is an international pregnancy exposure registry for all women enrolled in HIV prevention investigations.
3. U10-HD-047905-06: Obstetric-Fetal Pharmacology Research Units: 1/2010 – Ongoing
NIH/NICHD:
Site Co-Investigator: Currently we are conducting an investigation of the pharmacokinetics of oseltamivir in pregnancy through this research network that is charged with the investigation of the pharmacokinetics and pharmacodynamics of therapeutic agents in pregnancy
4. ACOG RESEARCH AWARD 4/2007 – 4/2008
Co-Principal Investigator & Mentor
Title: Developing a Comprehensive Immunization Program: Surveying Vaccination Needs and Patient Interest at an Academic Women’s Medical Center.

Bio-sketch for Kelly Stefano-Cole, Ph.D.

A. Positions and Honors:

- | | |
|--------------|--|
| 1994-1998 | Postdoctoral Research Associate, University of Pittsburgh School of Medicine, Department of Molecular Genetics and Biochemistry, Pittsburgh, PA. |
| 1999-2001 | Research Instructor, University of Pittsburgh School of Medicine, Department of Molecular Genetics and Biochemistry, Pittsburgh, PA. |
| 2002-2006 | Assistant Professor, University of Pittsburgh School of Medicine, Department of Medicine, Division of Infectious Diseases, Pittsburgh, PA. |
| 2006-2009 | Assistant Professor, University of Pittsburgh School of Medicine, Department of Immunology, Pittsburgh, PA. |
| 2007-present | Associate Director, Regional Biocontainment Laboratory, University of Pittsburgh School of Medicine, Pittsburgh, PA |
| 2009-present | Associate Professor, University of Pittsburgh School of Medicine, Department of Immunology Pittsburgh, PA. |

Honors:

- | | |
|------|--|
| 2003 | University of Pittsburgh School of Medicine, Dept. of Medicine Junior Faculty Research Award |
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B. Selected Peer-Reviewed Publications (from a list of 40)

1. Cole KS, Alvarez M, Elliott DH, Lam H, Rowles JL, Clements JE, Murphey-Corb M, Montelaro RC, Robinson JE. Rhesus monoclonal antibodies to simian immunodeficiency virus define nine binding domains on the surface envelope glycoprotein. *Virology* 2001; 290:59-73.

This contract involves the evaluation of a proprietary antimicrobial agent against HIV-1, SIV, influenza and other emerging pathogens in solution and solid phase materials.

Role: Principal Investigator

U01 NIH/NIAID

7/1/2008 – 6/30/2013

Ross (PI)

Virus-Like Particle Vaccines for Pandemic Influenza

This application is designed to compare the immunogenicity of H5N1 pandemic influenza VLP vaccines, based upon a clade 2 isolate, to a single HA protein immunogen in a non-human primate model. We will be evaluating antibody binding properties in serum as a predictor of maturation and correlates of protection.

Role: Consultant

Completed Research Support

Previous Grant Support

R01 NIH/NIAID

6/1/02 – 5/31/07

Cole (PI)

Mechanisms of SIV Neutralization

This study focused on defining the mechanisms of antibody-mediated neutralization of SIV using a unique panel of rhesus monoclonal antibodies.

Role: Principal Investigator

Bio-sketch for Doug Reed, Ph.D.

A. Positions and Honors.

2008–present Aerobiology Manager, Regional Biocontainment Laboratory, University of Pittsburgh, Pittsburgh, PA

2007–2008 Chief, Department of Animal Studies, Center for Aerobiological Sciences, USAMRIID, Fort Detrick, Frederick, MD

2005-2007, Team Leader, Department of Animal Studies, Center for Aerobiological Sciences, USAMRIID, Fort Detrick, Frederick, MD

1999–2005, Microbiologist, Center for Aerobiological Sciences, USAMRIID, Fort Detrick, Frederick, MD

2000-present Member, American Association of Immunologists

2008-present Member, American Society of Microbiology

Army Research & Development Award recipient in 2003

U.S. Army Achievement Medal for Civilian Service, 2005

B. Peer-reviewed publications or manuscripts in press (in chronological order).

1. McElroy, A.K., Bray, M., Reed, D.S., and Schmaljohn, C.S. 2002. Andes virus infection of cynomolgus macaques. *J Infect Dis.* 186:1706-12.
2. Geisbert T., Hensley, L.E., Larsen, T., Young, H.A., Reed, D.S., Geisbert, J.B., Scott, D.P., Kagan, E., Jahrling, P.B., and Davis, K.J. 2003. Pathogenesis of Ebola hemorrhagic fever in cynomolgus macaques: evidence that dendritic cells are early and sustained targets of infection. *Am J Pathol* 163(6):2347-2370.

3. Reed, D.S., Hensley, L., Geisbert, J., Jahrling, P.B., and Geisbert, T. 2004. Depletion of peripheral blood T lymphocytes and NK cells during the course of Ebola hemorrhagic fever in cynomolgus macaques. *Viral Immunology* 17(3): 390-400.
4. Reed, D.S., Lind, C.M., Sullivan, L.J., Pratt, W., and Parker, M. 2004. Aerosol infection of cynomolgus macaques with enzootic strains of Venezuelan Equine Encephalitis. *J Infect Dis.* 189:1013-7.
5. Reed, D.S., Lind, C.M., Lackemeyer, M., Sullivan, L.J., Pratt, W., and Parker, M. 2005. Genetically engineered, live attenuated vaccines protect nonhuman primates against aerosol challenge with a virulent IE strain of Venezuelan equine encephalitis virus. *Vaccine*: 23(24) pp. 3139-3147.
6. Reed, D.S., Larsen, T., Sullivan, L.J., Lind, C.M., Lackemeyer, M.G., Pratt, W.D., and Parker, M.D. 2005. Aerosol exposure to western equine encephalitis virus causes fever and encephalitis in cynomolgus macaques. *J Infect Dis.* 192(7):1173-82
7. Reed, D.S., Lackemeyer, M.G., Garza, N.L., Norris, S., Gamble, S., Sullivan, L.J., Lind, C.M., Raymond, J.L. 2007. Severe encephalitis in cynomolgus macaques exposed to aerosolized Eastern Equine Encephalitis virus. *J Infect Dis.* 196:441-450.
8. Rubins, K. H., Hensley, L.E., Wahl-Jenson, V., Daddario, K.M., Young, H., Reed, D.S., Jahrling, P.B., Brown, P.O., Relman, D.A., Geisbert, T.W. 2007. The temporal program of peripheral blood gene expression in the response of non-human primates to ebola hemorrhagic fever. *Genome Biology* 8(8)R174:1-14.
9. Fritz, E.A., Geisbert, J.B., Geisbert, T.W., Hensley, L.E., Reed, D.S. 2008. Cellular immune response to Marburg virus infection in cynomolgus macaques. *Viral Immunol.* 21(3):355-64.
10. Geisbert, T.W., Daddario-Dicaprio, K.M., Geisbert, J.B., Reed, D.S., Feldmann, F., Grolla, A., Stroher, U., Fritz, E.A., Hensley, L.E., Jones, S.M., Feldmann, H. 2008. Attenuated recombinant vaccines protect nonhuman primates against aerosol challenge with Ebola and Marburg viruses. *Vaccine.* 26(52):6894-6900.
11. Rossi, C.A., Ulrich, M., Norris, S., Reed, D.S., Pitt, M.L.M., Leffel, E.K. 2008. Identification of a surrogate marker for infection in the african green monkey model of inhalational anthrax. *Infect Immun.* 76:5790-5801.
12. Martin, S.S., Bakken, R.R., Lind, C., Reed, D.S., Price, J.L., Koehler, C., Parker, M.D., Hart, M.K., Fine, D.L. 2009. Telemetric analysis to detect febrile responses in mice following vaccination and challenge with Venezuelan equine encephalitis virus. *Vaccine* 27:6814-23
13. Roy, C.J., Reed, D.S., Wilhelmsen, C., Hartings, J., Norris, S., Geisbert, J., Jahrling, P., Steele, K.E. 2009. Pathogenesis of aerosolized Eastern Equine Encephalitis virus in guinea pigs. *Virology J.* 6:170.
14. Alves, D.A., Glynn, A.R., Lackemeyer, M.G., Garza, N.L., Buck, J.G., Reed, D.S. 2010. Aerosol exposure to the Angola strain of Marburg virus causes lethal viral hemorrhagic fever in cynomolgus macaques. *Vet Pathol.* In Press.

C. Research Support.

Ongoing Research Projects:

1. S1008576. Cell Mediated Immunity following LVS vaccination in Mice. 2009-2010. Study Director. 20% effort. Tularemia Vaccine Development Team, NIAID subcontract through Dynport Vaccine Company

Completed Research Projects:

1. H.H.0003_07_RD_B. Development of replicon-based vaccines for alphaviruses. Co-Investigator. 2004-2008. NIH/DOD funded. Project objective: evaluate the efficacy of replicon based alphavirus vaccines against aerosol challenge with 3 alphaviruses.
2. X.X.009_06_RD_B. Animal models of aerosol infection with filoviruses. Principal Investigator. 2006-2008. DOD funded. Objective of project was to develop rodent and nonhuman primate models for use in efficacy studies to evaluate vaccines or therapeutics for protection against aerosol challenge with Marburg or Ebola virus
3. H.H.0002_07_RD_B. Live Attenuated WEE and EEE Viruses for a Combined Equine Encephalitis Vaccine. Co-Investigator. 2001-2008. DOD funded. Project objective was to evaluate the efficacy of live, attenuated alphaviruses as vaccines against aerosol challenge with three alphaviruses (Venezuelan, Western, and Eastern equine encephalitis) in animal models.
4. W81XWH-06-C-0390. Novel viral biowarfare agent identification & treatment. Principal Investigator. 2006-2008. Congressional/DOD funded. Develop novel therapeutics for treatment of Venezuelan equine encephalitis.