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:** Allegheny-Singer Research Institute

2. **Reporting Period (start and end date of grant award period):** 1/1/2011 – 6/30/2012

3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):**
   Rebecca E. Pfeifer, BA CRA

4. **Grant Contact Person's Telephone Number:** 412-359-3137

5. **Grant SAP Number:** 4100054840

6. **Project Number and Title of Research Project:** Project 1: Complement Activation Product C4d Binding to Platelets in Systemic Lupus Erythematosus

7. **Start and End Date of Research Project:** 1/1/2011 – 6/30/2012

8. **Name of Principal Investigator for the Research Project:** Michael Passineau, PhD

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:

   $ 120,273.45

   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
Passineau	Principal Investigator	2.01%	$ 3,365.70
Sanguino	Sr. Research Associate	38.79%	$25,251.02

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
Geguchadze	Sr. Research Associate	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
Ettan Spot Picker	$86,668.00	$75,401.16
Ettan Protective Hood	$2,731.00	$2,375.97

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___X_____ No_____

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

The cost of the Ettan spot picker and protective hood was split evenly between this award and an internal cost center ($77,777.13).

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_____X____ No_____

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:
Proteomic Profiling to Enable Cellomic Fractionation of Sjogren's Salivary Glands	X NIH ☐ Other federal (specify:_____ _____) ☐ Nonfederal source (specify: _____)	02/2012	$ 275,000 direct	$ Not funded
	☐NIH ☐ Other federal (specify:_____ _____) ☐ 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: An NIH R01 grant application is being prepared to expand this research.

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

We will perform a blinded validation study and then attempt to transition our biomarkers to an ELISA-based panel to develop a clinical diagnostic.

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			2	
Unknown				
Total			**2**	

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

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

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

Yes_____ No_____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 acquisition of the Ettan Spot Picker has substantially expanded our proteomic capabilities and this equipment now supports multiple projects within the 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____X_____ No_____

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

We believe we have developed a new diagnostic algorithm for SLE and will continue to work toward commercialization.

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 <u>for the period that the project was funded (i.e., from project start date through end date).</u> 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. <u>Provide detailed results of the</u>

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 (ß) should not print as boxes (□) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

Original Project Aims:

Specific Aim 1. To compare the entire proteome of C4d-positive platelets with C4d-negative platelets in patients with SLE using 2-D difference gel electrophoresis (DiGE) and DeCyder statistical software.
Specific Aim 2. To use mass spectrometry to characterize the 10 most significantly different proteins identified in Aim 1.

Report Summary:

In the previous annual report (June 2011), we reported the purchase of the spot-picker robot and preliminary results of optimization of platelet proteomic profiling. In this final report, we report the final and full completion of the proposed aims of the project. The reviewer should note that the scope of Aim 1 was expanded to include a third experimental cohort (normal, healthy female controls), and we thus report results from 3 (normal controls, C4d- SLE and C4d+ SLE) cohorts in Aim 1 rather than the originally proposed two cohorts.

Summary of Specific Aim 1:

Proteomic Profiling of Platelets

The overall goal of the project is to compare the entire proteome of platelets from different cohorts using two-dimensional difference gel electrophoresis (2D-DIGE). This technique's major innovation is that it allows comparisons of multiple samples on the same gel, dramatically increasing comparative power by eliminating reproducibility problems. Whole-platelet lysates from the various cohorts are labeled with fluorescent dyes Cy2, Cy3 or Cy5 and after electrophoresis, gels are scanned with three different lasers, corresponding to the Cy2-, Cy3- or Cy5-specific wavelengths, allowing creation of an independent image of the gel for each label.

Methods

Our primary technical challenge in performing these experiments is to maximize the number of proteins extracted from platelet samples and to visualize these proteins on the 2-D gel. Based upon earlier literature, we set a goal of visualizing ~1500 individual spots.

Platelet isolation from whole blood: For platelet proteomics studies, we first worked on a method to isolate platelets from whole blood while preventing contamination from other cells. We achieved this goal by performing two consecutive low speed centrifugations. With this method, only platelets remained in the supernatant whereas other blood cells localized in the pellet. A subsequent high speed centrifugation gives a pellet with purified platelets. We then washed the platelets one time with Tyrodes buffer (119 mM NaCl, 5 mM KCl,25 mM HEPES buffer, 2 mM $CaCl_2$, 2 mM $MgCl_2$,6 g/liter glucose, pH to 7.4) and 15% ACD (85mM Sodium Citrate, 62.2mM Citric Acid, 110mM dextrose) to remove plasma proteins and stored a platelet pellet at -80° C for future use. Prostaglandin E was utilized in all centrifugations.

Sample preparation: We spent a considerable amount of time working on a reliable and reproducible sample preparation. This is the most crucial step in any proteomic profiling study as all samples must be handled in an identical way to guarantee that any differences observed in the proteomic profile are real and are not caused by manipulation artifacts. In addition, depending on the nature of the sample and the pH used for the first dimension, the proteins must be prepared in a specific way to obtain good separation that permits an accurate image comparison of the different protein spots.

To prepare the sample for proteomic profiling, we resuspended the frozen platelet pellet in water (with inhibitors of proteases and phosphatases) and quantified proteins (Pierce BCA Protein Assay Kit, Thermo Scientific). We then precipitated the protein with acetone to remove contaminants and salt and resuspended the pellet in urea-thiourea buffer (30mM Tris, 2 M Thiourea, 7 M urea, 4 % CHAPS, pH 8.5). Finally we labeled the samples with Cy2, Cy3 or Cy5 following the manufacture's protocol (GE Healthcare, Piscataway, NJ.)

2D-DIGE -First dimension: Isoelectric focusing is the step in which proteins are separated based on the pH in which they become neutral. For platelets we decided to use pH values from 4 to 7 and run 18 cm strips. This is based on a preliminary study in which we found that most of the

protein spots concentrated in this pH range. We achieved excellent protein separation by running 15 ug of protein per sample with 0.5% IPG buffer and 10 mM DTT. The first dimension was performed on the Ettan IPGphor 3 Isolectric Focusing Unit (GE Healthcare, Piscataway, NJ.) following the company protocol suggested for this specific strip.
Second dimension After equilibrating the strips with DTT and Iodocetamide, the proteins were separated based on molecular weight using the Ettan DALTsix electrophoresis unit (GE Healthcare, Piscataway, NJ.)

Scanning and analysis: After electrophoresis, each gel was scanned using a Typhon scanner (GE Healthcare, Piscataway, NJ.). Images were analyzed using DeCyder software (GE Healthcare, Piscataway, NJ.).

Results

Experimental Cohorts: Collection of samples for the experiments described above took place between October 2011 and February 2012. We collected platelets from 10 healthy volunteers, 10 systemic lupus erythematosus (SLE) patients with C4d negative platelets and 10 SLE patients with C4d positive platelets. Each sample was analyzed for C4d positivity by flow cytometry using a C4d monoclonal antibody as our group has previously described. The demographic data of the patients used for these experiments is shown in Table 1. Relevant clinical information for SLE patients is shown in Tables 2 and 3**.**

Statistical Analysis: Following acquisition of all gel images, the DeCyder software (GE Healthcare, Piscataway, NJ.) package was used for analysis. The analytical workflow of the DeCyder software is partially illustrated in Figure 2. The first step in the analysis is the loading of gel images into the software and the assignment of an identifier for each protein spot. For comparisons of multiple gels in a study, an internal standard channel (Cy2) is added to each gel, allowing gel-to-gel normalization by the software for statistical analysis of multiple samples across multiple gels. Statistical analysis of the differences among protein spots between each experimental group was performed using ANOVA. A p value less than 0.05 was considered statistically significant, and a p value less than 0.01 was considered highly significant. For platelets, we are able to identify approximately 2300 spots in every gel. ANOVA analysis across the three experimental cohorts indicated a total of 262 protein spots with p values less than 0.05 and 87 protein spots with p values less than 0.01.

A possible biomarker algorithm for diagnosis of SLE: Given the very promising results of our studies, we decided to modify the scope of the project slightly. With 86 highly significant protein spots identified as being different between our study cohorts, we were unable to prioritize these spots in order to perform Aim 2 (spot identification) in a straightforward manner. Given the relative expense of spot identification, we decided to undertake a more complex analysis in order to prioritize spot identification.

The Decyder software includes an Extended Data Analysis module that is capable of using our study design to build panels of biomarkers capable of differentiating between experimental groups. The software will run various discriminatory models based upon all possible permutations of the data in order to build an algorithm that differentiates experimental groups

from one another based upon the smallest number of protein spots. Using this approach, we analyzed the data we were able to identify fourteen proteins that could identify each experimental group with 93.33 % +/- 9.09 accuracy. This accuracy figure is determined by building the model through a training study of the data, then running each sample individually against the model. Results of this analysis are outlined in table 4. As can be seen from these results, our model has an overall 93.33% accuracy, but has *a 100% positive predictive value for diagnosis of SLE*. Negative predictive value for SLE is 96.4%.

These results were not anticipated in the original aims of the grant, and thus represent an expansion of the overall scientific scope. Accordingly, we have scaled back slightly the scope of Aim 2 as outlined below.

Summary of Specific Aim 2

We have identified 5 protein spots from our biomarker panel and are in the process of identifying 9 more. However, we respectfully submit that the identities of these proteins are redacted due to intellectual property considerations. We plan to publish the identities of the biomarkers and the overall diagnostic algorithm in the future, once appropriate patents have been filed. Appropriate acknowledgement of this PA DoH grant will be made at the time of public disclosure of results.

Table 1: Demographic data for the patients participating in this study.

	Healthy	SLE C4d Negative	SLE C4d Positive
Total Number of participants	10	10	10
Mean age (years)	39.53	50.01	49.28
Range	(25 - 55)	(31 - 65)	(31 - 66)
Sex			
Female	9	10	9
Male	1	0	1
Race			
White	8	9	10
African American	2	1	0

Table 2: Disease manifestations in SLE patients by C4d status

Symptoms	Lupus C4d Negative	Lupus C4d Positive
Joint	9	9
Malar	7	2
Discoid	1	0
Photosensitivity	8	5
Oral Ulcer	3	4
Serositis	4	5
Neurologic	2	0
Renal	2	3
Criteria for SLE Dx	6.4	5.8

Table 3: Medication regimens of SLE patients according to C4d status

Medication	SLE C4d Negative (Number of patients)	SLE C4d Positive (Number of Patients)
NSAIDs	6	2
Clopidrogel	0	2
Anticoagulant	5	4
Prednisone	6	7
Immunosuppressant	10	9
HTA	8	7
Statins	3	3
Antidepressant	5	6

	Healthy Volunteers	SLE – Platelets C4d Negative	SLE- Platelets C4d Positive
Healthy Volunteers	10	1	0
SLE Platelets C4d Negative	0	8	0
SLE Platelets C4d Positive	0	1	10
Error	**0**	**2**	**0**

Table 4

Proteomic Profiles: 2-D DiGE experiments were performed on platelet proteomes from each experimental cohort as described. Representative proteomic images obtained from these experiments are shown in Figure 1.

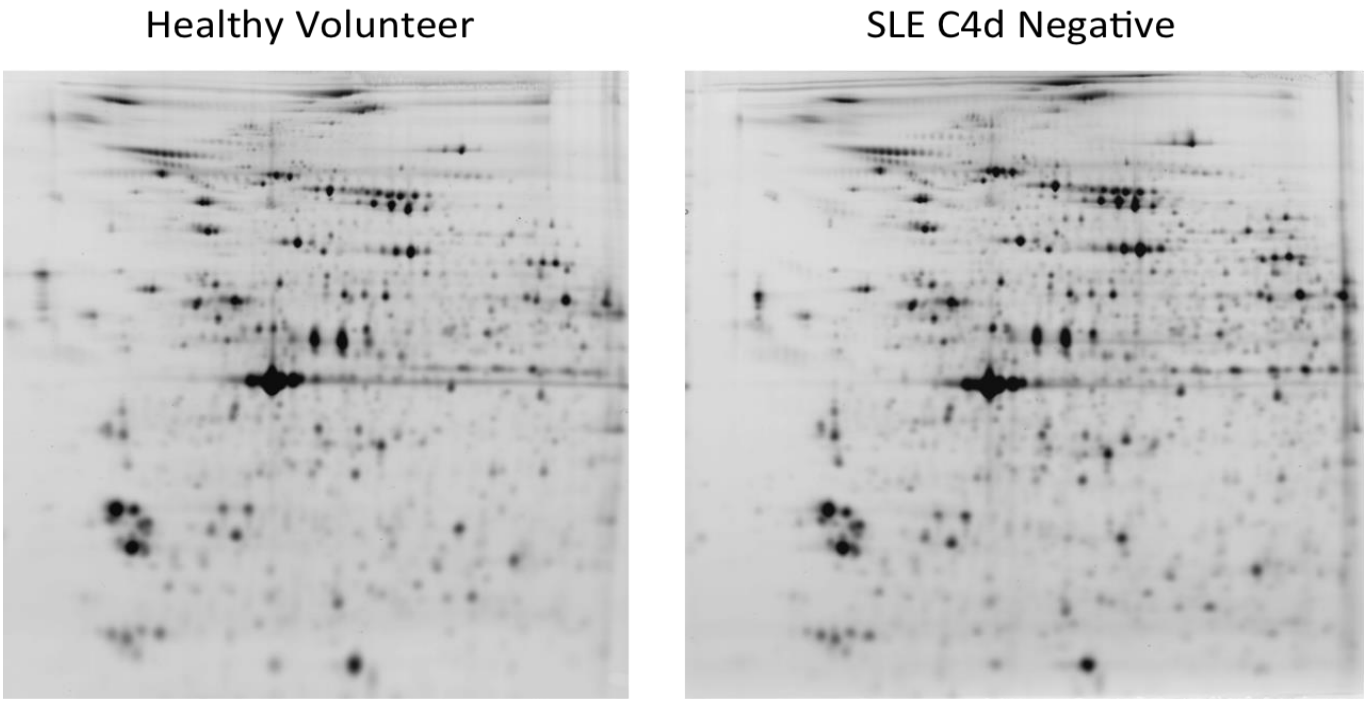
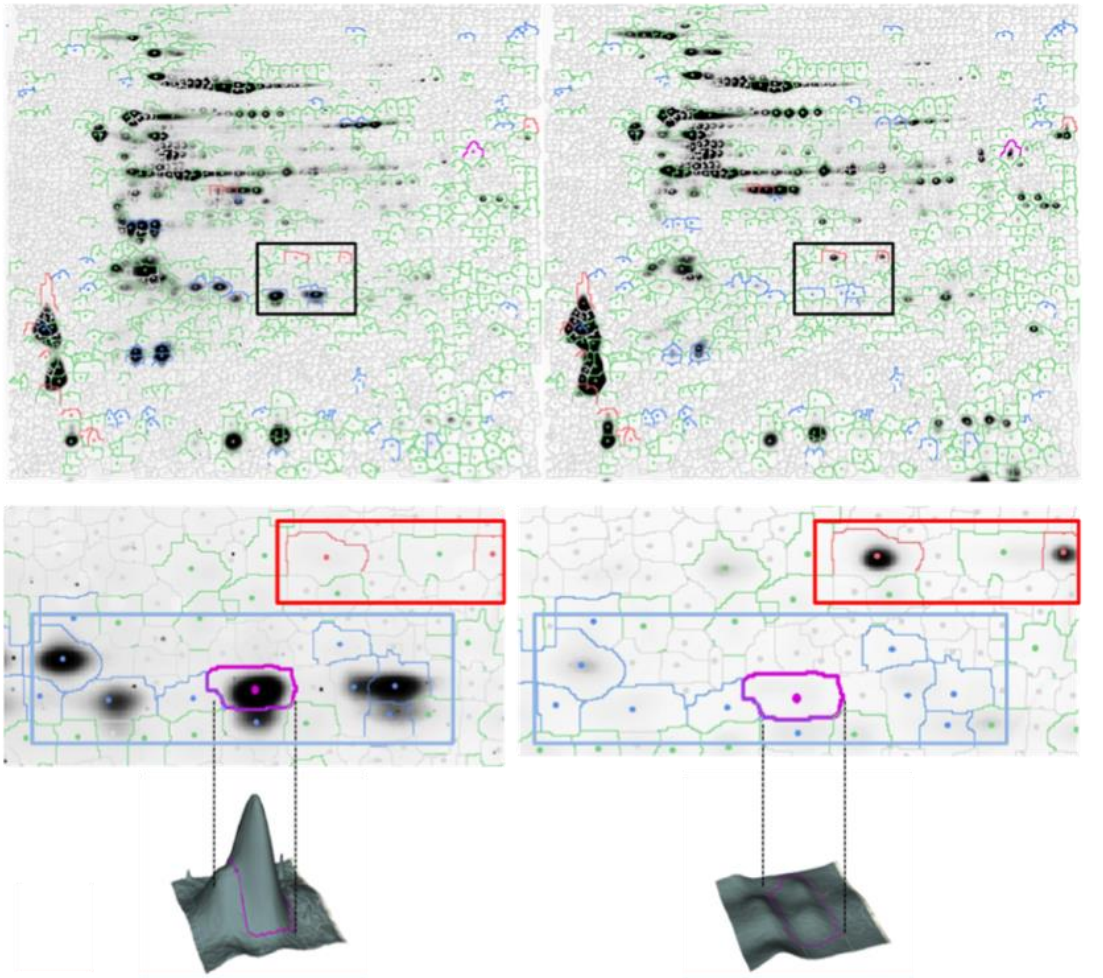


Figure 1. Proteomic profiles of platelets from SLE subjects versus healthy volunteers. These images are representative of results obtained from two samples compared *on the same gel* using DiGE.



Fold	% Homologous	% Different	% Increased	% Decreased
1.5	60.4	39.6	16.3	23.3
2	79.6	20.4	6.1	14.3
3	91.6	8.4	1.3	7.1
4	94.6	5.4	0.4	5
5 or greater	96	4	0	4

Figure 2. **Representative DeCyder analysis**. Gel images are parsed into individual protein spots, as shown in the top panel. Middle panel shows magnification of a region showing differences between the Cy3 and Cy5 images. The bottom panel shows the final summary of all differences between the two samples.

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?

___X___Yes
_____No

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

____X__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?

____2__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?

___30___Number of subjects originally targeted to be included in the study
____30__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:
___2___Males
____28__Females
_____Unknown

Ethnicity:
_____Latinos or Hispanics

_____Not Latinos or Hispanics
____30__Unknown

Race:
_____American Indian or Alaska Native
_____Asian
__3____Blacks or African American
_____Native Hawaiian or Other Pacific Islander
__27____White
_____Other, specify:_____
_____Unknown

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

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

19(A) Did this project involve, in any capacity, human embryonic stem cells?
_____Yes
____X__ No

19(B) Were these stem cell lines NIH-approved lines that were derived outside of Pennsylvania?
_____Yes
_____ No

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

20. Articles Submitted to Peer-Reviewed Publications.

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication 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, 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.				☐Submitted ☐Accepted ☐Published
2.				☐Submitted ☐Accepted ☐Published
3.				☐Submitted ☐Accepted ☐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 have completed a blinded validation study and filed a patent, we will publish our results.

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.

We believe we have conceived of a new diagnostic algorithm for SLE but this requires further refinement before becoming a diagnostic.

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__X____ No_____

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: Redacted

b. Name of Inventor(s): Michael Passineau, Angela Sanguino, Joseph Ahearn, Ramaz Geguchadze

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

Redacted

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

If yes, indicate date patent was filed:

e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No___X
If yes, indicate number of patent, title and date issued:
Patent number:

Title of patent:
Date issued:

f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes_____ NoX__

If yes, how many licenses were granted?_____

g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes___ No___X

If yes, describe the commercial development activities:

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

Yes_____X____ No_____

If yes, please describe your plans:

Redacted.

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 in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Passineau, Michael Joseph	Assistant Professor
eRA COMMONS USER NAME (credential, e.g., agency login) mjpassineau	

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
Cedarville College	B.A.	06/95	Bible/Chemistry
University of Miami	Ph.D.	12/01	Neuroscience
University of Alabama at Birmingham	Postdoctoral	12/05	Gene Therapy
University of Alabama at Birmingham	Postdoctoral	2/07	Gene Therapy

A. Positions and Honors

Positions and Employment

2003-2005 Postdoctoral Fellow, Gene Therapy Center, Division of Human Gene Therapy, UAB
1/2006-3/2007 Postdoctoral Scholar, UAB School of Dentistry
3/2007-6/1/2008 Instructor, Department of Oral and Maxillofacial Surgery, UAB School of Dentistry
4/2007-6/1/2008 Associate Scientist, UAB Gene Therapy Center
8/2007-6/1/2008 Associate Scientist, UAB Center for Metabolic Bone Disease
6/1/2008- Research Scientist, Allegheny-Singer Research Institute
6/1/2008- Assistant Professor, Drexel University School of Medicine
5/1/2010- Adjunct Professor, Carnegie Mellon University
2011- Director, Gene Therapy Program, Allegheny-Singer Research Institute

Experience and Professional Memberships

2007- Member, International Association for Dental Research
2008- Member, American Association for the Advancement of Science
2008- Member, American Society for Cell and Gene Therapy
2009- Member, American Thoracic Society
2010- Member, American Heart Association

Honors

2006	Colgate Research in Prevention Award (Intl Association for Dental Research)
2006	Bloc Travel Award (American Association for Dental Research)
2003-2005	Ruth L. Kirchstein National Service Award
1999	Finalist, Student Research Competition, National Neurotrauma Society
1994	American Heart Association Summer Fellow

C. Selected Peer-reviewed Publications

- Geguchadze RN, Machen L, Zourelias L, Gallo PH, **Passineau MJ**. An AAV2/5 Vector Enhances Safety of Gene Transfer to the Mouse Salivary Gland. J Dent Res. 2012 Feb 3.
- Borovjagin AV, Dong J, **Passineau MJ**, Ren C, Lamani E, Mamaeva OA, Wu H, Keyser E, Murakami M, Chen S, Macdougall M. Adenovirus gene transfer to amelogenesis imperfecta ameloblast-like cells. PLoS One. 2011;6(10):e24281. Epub 2011 Oct 7.
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