

# 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:** National Disease Research Interchange
2. **Reporting Period (start and end date of grant award period):** 1/1/2013-12/31/2013
3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** John T. Lonsdale, PhD
4. **Grant Contact Person’s Telephone Number:** 800-222-6374 x 271
5. **Grant SAP Number:** 4100062214
6. **Project Number and Title of Research Project:** 1 - Susceptibility Genes for Microvascular Complications in Patients with Type 1 Diabetes
7. **Start and End Date of Research Project:** 1/1/2013-12/31/2013
8. **Name of Principal Investigator for the Research Project:** John T. Lonsdale, PhD
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:

\$56,431

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
Cohen	Coordinator	50	\$19,486

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
Lonsdale, John	PI	5
Greenberg, David	Consultant	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

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

Yes \_\_\_\_\_ No X \_\_\_\_\_

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

**11. Leveraging of Additional Funds**

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

Yes      No   X  

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

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

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

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

Yes  No \_\_\_\_\_

If yes, please describe your plans:

We are submitting a grant to NIH. If the NIH grant does not get funded, we will re-apply, both to NIDDK and NEI.

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

Although the genotyping for this project has now been completed it will be several months before the data is fully analyzed. Work on this project is anticipated to continue for the remainder of 2014 and the results will lead to a number of spin-off projects. It is anticipated that the work will be published in 2015.

**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				
<b>Total</b>				

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic				
Unknown				
<b>Total</b>				

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

Unknown				
<b>Total</b>				

**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 \_\_\_\_\_ No X

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

**16. Collaboration, business and community involvement.**

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

Yes \_\_\_\_\_ No 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 ( $\alpha$ ) and beta ( $\beta$ ) should not print as boxes ( $\square$ ) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.**

Aim 1: The linkage analysis of sparse SNP data on chromosome 6 has identified loci that influence risk for diabetic complications. Using dense SNP data that we will acquire, we will analyze the T1D families (n=431) collected by the Human Biological Resource Interchange (HBDI) and will use our newly developed and extensively tested linkage methods to extract the maximum amount of information for linkage to retinopathy, nephropathy, and neuropathy.

Aim 2: We will use our newly-developed association method to find disease-related genes within linkage-identified regions using both family-based and case-control tests of association. The cases (n=188) are T1D patients with complications, and the controls (n=226) are T1D patients

with no complications  $\geq 15$  years after T1D onset. Our test combines information from both family-based and case-control designs, greatly increasing association detection power.

**Aim 3:** Continue our annual program of participant follow-up using the updated family questionnaire to track development or progression of microvascular complications among patients with both T1D and T2D. Data gathered will be an essential component of our primary aim.

#### Progress on Aims:

**Aim 1:** Aim 1 was partially achieved. Previously, linkage analysis of sparse SNP data on chromosome 6 has identified loci that influence risk for diabetic complications. These loci were at 42 cM and 64 cM on chromosome 6. The two loci also showed evidence of interaction with specific HLA alleles. In order to identify the genes that give rise to these loci, we elected to do dense SNP typing of markers under the linkage peaks to use association analysis for disease allele identification.

#### Status of dense SNP typing

DNA samples were ordered for 300 individuals, representing 75 families and sent for typing at the Penn Molecular Profiling Facility at the University of Pennsylvania. That typing took several months and the data is now being cleaned and prepared for analysis. Typing the entire data set would be cost prohibitive, so by judicious sub-setting of the families, we chose those that provide the most information for linkage to retinopathy and nephropathy. Since we found statistically significant evidence for linkage at two loci, we chose the families so that the data coverage for both loci would increase the precision of the location estimate.

**Aim 2:** Aim 1 was not yet achieved. This aim cannot proceed without the SNP typing data. The SNP data is currently being cleaned, that is, tested for Mendelian errors, gene frequency checks, mislabeling of samples, etc. When checking is done, the data will be imported into the database and analyzed. Analysis will consist of case-control analysis (“cases” being T1D patients with complications; controls being T1D patients without complications for 15 years after T1D onset). We have also typed parents of selected families for family-based association analysis. This will augment the power of the data set.

**Aim 3:** Aim 3 was achieved. Our goal was to continue the annual program of participant follow-up using an updated family questionnaire to track development/progression or lack of development/progression of microvascular complications among patients with both T1D and T2D. To this end, we sent 1003 questionnaires to registry participants in 2013. To date, we have received 228 completed questionnaires/updates from individual participants. This corresponds to a response rate of 23%. The information in these updates provides information on a subset of 4,256 of the individuals in the HBDI National Genetics Family Registry. 60 questionnaires were returned due to incorrect addresses. We will continue to follow-up with these families in order to maintain the ability to track development/progression or lack of development and/or progression of microvascular complications.

**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  
 X  No

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

\_\_\_\_\_ Yes  
 X  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

**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:  
\_\_\_\_\_ 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 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.				<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: It is expected that data from this study will be presented in at least one major publication.

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

NAME Lonsdale, John T.		POSITION TITLE	
eRA COMMONS USER NAME (credential, e.g., agency login) JOHNLONSDALE		Vice President, Partnership Development	
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
University of Newcastle Upon Tyne, England, UK	B.Sc (Double First Class Honors)	1981	Biochemistry & Microbiology
University of Newcastle Upon Tyne, England, UK	PhD	1985	Microbial Biochemistry

Please refer to the application instructions in order to complete sections A, B, C, and D of the Biographical Sketch.

## A. Personal Statement

Dr. Lonsdale has extensive experience as PI/Project Leader on numerous research projects in both pharmaceutical industry and academic settings. He is responsible for providing scientific and administrative oversight, and liaison with NIH program officers and IC representatives, in particular as NDRI PI on the NIH-funded Human Tissues and Organs Research resource (HTOR), Genome Tissue Expression (GTEx) and Biospecimen Methodological Study (BMS) projects. He has extensive experience and expertise in all aspects of the provision of human tissues for research, with particular knowledge of those pertaining to researcher recruitment, application processing, protocol development and service.

## B. Positions and Honors

1985-1995 Biochemistry Department, SmithKline Beecham Pharmaceuticals, Brockham Park, England, UK

1995-2001 Assistant Director, Anti-Infectives Research, SmithKline Beecham Pharmaceuticals, Collegeville, PA USA

2001-2002 Director, Microbial Biochemistry - Antimicrobials and Host Defense CEDD, GlaxoSmithKline, Collegeville, PA, USA

2002 Director, Biochemistry - Microbial, Musculoskeletal and Proliferative Diseases CEDD, GlaxoSmithKline, Collegeville, PA, USA

2003-2012 Research Director, NDRI, Philadelphia, PA, USA

2012-2013 VP, Research, NDRI, Philadelphia, PA, USA

2013-present VP, Partnership Development, NDRI, Philadelphia, PA, USA

### C. Selected Peer-reviewed Publications

MC Monti, JT Lonsdale, C. Montomoli, R. Montross, E. Schlag and DA Greenberg. Familial risk factors for microvascular complications and differential male-female risk in a large cohort of American families with type 1 diabetes. *J Clin Endocrinol Metab* 92:4650-4655. 2007.

Lipner EM, Tomer Y, Noble JA, Monti MC, Lonsdale JT, Corso B, Stewart WC, Greenberg DA. HLA class I and II alleles are associated with microvascular complications of type 1 diabetes. *Hum Immunol May*;74(5):538-44. 2013

Lonsdale J, Thomas J, Salvatore M, Phillips R, Lo E, Shad S, Hasz R, Walters G, Garcia F, Young N, Foster B, Moser M, Karasik E, Gillard B, Ramsey K, Sullivan S, Bridge J, Magazine H, Syron J, Fleming J, Siminoff L, Traino H, Mosavel M, Barker L, Jewell S, Rohrer D, Maxim D, Filkins D, Harbach P, Cortadillo E, Berghuis B, Turner L, Hudson E, Feenstra K, Sobin L, Robb J, Branton P, Korzeniewski G, Shive C, Tabor D, Qi L, Groch K, Nampally S, Buia S, Zimmerman A, Smith A, Burges R, Robinson K, Valentino K, Bradbury D, Cosentino M, Diaz-Mayoral N, Kennedy M, Engel T, Williams P, Erickson K, Ardlie K, Winckler W, Getz G, Deluca D, Macarthur D, Kellis M, Thomson A, Young T, Gelfand E, Donovan M, Meng Y, Grant G, Mash D, Marcus Y, Basile M, Liu J, Zhu J, Tu Z, Cox NJ, Nicolae DL, Gamazon ER, Im HK, Konkashbaev A, Pritchard J, Stevens M, Flutre T, Wen X, Dermitzakis ET, Lappalainen T, Guigo R, Monlong J, Sammeth M, Koller D, Battle A, Mostafavi S, McCarthy M, Rivas M, Maller J, Rusyn I, Nobel A, Wright F, Shabalin A, Feolo M, Sharopova N, Sturcke A, Paschal J, Anderson JM, Wilder EL, Derr LK, Green ED, Struwing JP, Temple G, Volpi S, Boyer JT, Thomson EJ, Guyer MS, Ng C, Abdallah A, Colantuoni D, Insel TR, Koester SE, Little AR, Bender PK, Lehner T, Yao Y, Compton CC, Vaught JB, Sawyer S, Lockhart NC, Demchok J, Moore HF. The Genotype-Tissue Expression (GTEx) project. *Nat Genet.* May 29;45(6):580-5. 2013

### D. Research Support

#### ACTIVE

2 U42 OD011158-23 (PI: Lonsdale) 7/1/2013 – 6/30/2018 NIH/OD

#### Human Tissue and Organ Research Resource

The primary mission of the Human Tissue and Organ Research Resource (HTOR) program is to procure and distribute human biomaterials to the biomedical research community.

GTEx RFP 210-120 (PI: Lonsdale) 03/29/13 – 05/31/14 NIH/NCI

#### Genotype-Tissue Expression Project

The primary mission of the GTEx project is to collect and analyze up to 50 tissues from each of approximately 250 deceased donors using methods specially developed to preserve tissues of the highest quality with the lowest possible *post mortem* interval.