

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:** Temple University
2. **Reporting Period (start and end date of grant award period):** 1/1/2010-12/31/2013
3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Michel Pontari M.D.
4. **Grant Contact Person’s Telephone Number:** 267-443-7760 or 215-707-8485
5. **Grant SAP Number:** 4100050909
6. **Project Number and Title of Research Project:** Research Project 8 - *Genetic Variations in Inflammation-Related Genes in Patients with Chronic Pelvic Pain Syndrome*
7. **Start and End Date of Research Project:** 12/1/11 to 12/31/2013
8. **Name of Principal Investigator for the Research Project:** Michel Pontari M.D.
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:

\$ 75,251.16

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

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
Pontari, Michel	PI	5
Krynetskiy, Evgeny	Co-investigator/Co-PI	5
John Gaughan	Consultant/Statistician	0.05 one year
Neil Kocher	Research Assistant	0.25 one year
Elizabeth Garvey	Research Assistant	0.25 one year
Brian Cronson	Research Assistant	0.20 one year
Anurag Mishra	Research Technician	0.05 one year
Elton Lukani	Research Assistant	0.05 one year

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
Agilent 2100 Bioanalyzer (Agilent Technologies) with RNA 6000 nano kit and DNA 1000 kit	Allows us to measure RNA- not previously available	\$40,247

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:

Dr. Pontari’s personal departmental overhead recovery research funds estimate: \$15, 983

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 ___x___ No _____

If yes, please describe your plans: Data obtained will be used as preliminary data for NIH grant to look at use of pharmacogenomics to select men with Chronic Pelvic Pain Syndrome (CPPS) for treatment with anti-TNF- α therapy

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

The next step for this research is to use the findings that some men with CPPS have differences in SNP's for TNF- α , and based on our results also have elevated levels of TNF- α mRNA compared to asymptomatic controls, to guide therapy. There are commercially available TNF- α antibodies which are used currently for treating arthritis. To date there have been no positive trials for treatment of men with CPPS. One of the reasons we think is the heterogeneity in phenotype, i.e. men with different reasons for their pain appear similar clinically. There have been no evidence based methods for which to put men in subgroups and then treat only this subgroup with a targeted treatment. Our data serves as a basis for proposing such a trial.

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			1	
Female	1			
Unknown				
Total	1		1	

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

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

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

Yes _____ No _____

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 _____

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

1. The addition of an analyzer for RNA
2. I was able to have a summer first year med student as a research assistant, and he is now going in to Urology
3. I was able to hire a college student who gained experience in research and is now applying to medical school

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 _____

If yes, please describe the collaborations:

16(B) Did the research project result in commercial development of any research products?

Yes _____ No _____

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 _____

If yes, please describe involvement with community groups that resulted from the research project:

17. Progress in Achieving Research Goals, Objectives and Aims.

List the project goals, objectives and specific aims (as contained in the grant agreement). Summarize the progress made in achieving these goals, objectives and aims for the period that the project was funded (i.e., from project start date through end date). Indicate whether or not each goal/objective/aim was achieved; if something was not achieved, note the reasons why. Describe the methods used. If changes were made to the research goals/objectives/aims, methods, design or timeline since the original grant application was submitted, please describe the changes. Provide detailed results of the project. Include evidence of the data that was generated and analyzed, and provide tables, graphs, and figures of the data. List published abstracts, poster presentations and scientific meeting presentations at the end of the summary of progress; peer-reviewed publications should be listed under item 20.

This response should be a DETAILED report of the methods and findings. It is not sufficient to state that the work was completed. Insufficient information may result in an unfavorable performance review, which may jeopardize future funding. If research findings are pending publication you must still include enough detail for the expert peer reviewers to evaluate the progress during the course of the project.

Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project's strategic plan. After the final performance review of each project is complete, approximately 12-16 months after the end of the grant, this Final Progress Report, as well as the Final Performance Review Report containing the comments of the expert review panel, and the grantee's written response to the Final Performance Review Report, will be posted on the CURE Web site.

There is no limit to the length of your response. Responses must be single-spaced below, no smaller than 12-point type. If you cut and paste text from a publication, be sure symbols print properly, e.g., the Greek symbol for alpha (α) and beta (β) should not print as boxes (\square) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

Specific Aim 1: Test the hypothesis that genetic polymorphisms in candidate genes correlate with the incidence of CP/CPPS. This will be tested in a group of patients with CP/CPPS compared to a group of asymptomatic controls.

Aim 1 was fully completed prior to the start of the project. No project funds were used.

Specific Aim 2: Test the hypothesis that genetic polymorphisms in the promoter regions of candidate genes also modulate their expression, resulting in alterations in the level of mRNA.

This aim was partially achieved. We did obtain enough samples to show a statistical difference between the cases and controls for TNF- α mRNA which supports our hypothesis (page 11). We did not achieve our goal for number of specimens due to:

- (1) Recruitment /sample collection: We had proposed to recruit 60 patients and controls. One of the main difficulties with recruitment was the need to process the specimens the day the blood was drawn. This study did not have a budgeted, dedicated research technician. At the time of application we anticipated other sources of technical help, including technicians in Dr. Krynetskiy's lab, and the Temple Urology resident doing a lab rotation. By the time the study started in earnest, both were no longer available as both positions had been eliminated. Patients were seen in the Urology clinic but in the absence of being able to process the specimen shortly after blood draw, they were not enrolled. Recruitment was best when we used other funds to help fund 2 summer students who could help with sample processing. Moving forward, such a study should have a dedicated technical position. Second, recruitment of controls was more difficult than anticipated, but also limited by the issue described above.
- (2) Poor yield on the RNA. Our yield on the quality control for the specimens we did collect was only 55% that were suitable for analysis. This yield also reduced the final number of specimens.

Focus of research during the funded period:

Methods:

This study was approved by the Temple University Institutional Review Board. All patients who participated in the study provided written informed consent. Inclusion, exclusion and deferral criteria were those as used in the NIH Chronic Prostatitis Cohort study (Schaeffer et al 2002). Men were recruited from Dr. Pontari's clinical practice. Controls were recruited both in the practice and also with posted advertisements. Controls were men with no pelvic pain and met the same exclusion criteria as the CPPS cases. Subjects were characterized by demographics for age, ethnicity, and given symptom questionnaires including a past medical history form as used in the CPCRN study (Schaeffer et al 2002), National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) (Litwin, et al, 1999), the androgen deficiency in aging male questionnaire (ADAM) (Morley JE et al 2000) and the Interstitial Cystitis Symptom and Problem Index, and the American Urologic Association symptom index.

Patients were consented in the Urology clinic. 5-8 ml of blood were obtained and placed on ice. Extraction of total RNA from blood was performed using Biorobot EZ1 installed in the Haines Center for Pharmacogenomics and stored at -80°C . The RNA was analyzed with the Agilent 2100 bioanalyzer using the Agilent RNA 6000 Nano Kit provided from Agilent Technologies (Waldbronn, Germany). The assay quantitative accuracy and reproducibility of quantitation are reported as being 20 % coefficient of variation (standard deviation/ mean) for ladder and sample 10 % coefficient of variation for sample respectively. The reagents and reagent mixes were refrigerated at 4°C . Dye and dye mixtures were protected from light. All reagents were allowed to equilibrate to the room temperature for 30 minutes before use. Samples were kept on ice during the experiment.

RNA analyzation:

Initially quality control was performed on the available samples of RNA by capillary gel electrophoresis. 550 μL of RNA gel matrix (red) was pipetted in to into a spin filter, and centrifuged at $1500\text{ g} \pm 20\%$ for 10 min at room temperature. 65 μL of filtered gel was aliquotted into 0.5 mL RNase- free microcentrifuge tubes. RNA dye concentrate (blue) was equilibrate to room temperature for 30 min. The RNA dye concentrate (blue) is vortexed for 10 s, and then added 1 μL of dye into a 65 μL aliquot of filtered gel; this solution is vortexed, and then centrifuged at 13000 g for 10 min at room temperature. Nine μL of the gel-dye mix was loaded into wells containing an RNA chip on the chip priming station. As a marker, 5 μL of RNA marker (green) was put in each well. One 1 μL of prepared ladder and 1 μL of sample was added to the well. The chip is then vortexed for 1 min at 2400 rpm. Each RNA chip contains an interconnected set of microchannels that is used for separation of nucleic acid fragments based on their size as they are driven through it electrophoretically.

Following the confirmation of RNA quality, samples with adequate quality RNA were quantified by qRT-PCR with TaqMan gene expression kit using GAPDH endogenous control. TNF- α RNA label was normalized by the relative standard curve method using sample 8014 for normalization.

PCR methods: samples were prepared using the following components: RNase-free water (variable); 10X TaqMan RT Buffer (volume/tube: 1.0 mL; final concentration: 1X); 25mM MgCl_2 (volume/tube: 2.2 mL; final concentration: 5.5 mM); deoxyNTPs Mixture 2.5 mL (volume/tube: 2.0 mL; final concentration: 500 mM per dNTP); Random Hexamers 50 mM (volume/tube: 0.5 mL; final concentration: 2.5 mM); RNase inhibitor 20 U/L (volume/tube: 0.2 mL; final concentration: 0.4 U/mM); MultiScribe Reverse Trascriptase 50 U/mL (volume/tube: 0.25 mL; final concentration: 1.25 U/mL); total volume/tube 6.15 mL.

Thermal cycling parameters for reverse transcriptase reactions: Incubation for 10 min at 25°C ; Reverse Transcription for 30 min at 48°C ; Reverse Transcription Inactivation for 5 min at 95°C .

Results:

A total of 24 patients and CPPS and 16 controls were recruited and had blood drawn and processed. There were differences in past medical history as men with CPPS were much more likely to self report a history of allergy/sinusitis (62.5% vs 43.7%) and GI disease (29.0% vs 6.3%).

Results of questionnaires in men with CPPS vs controls

Mean score \pm S dev	CPPS cases	Controls
ADAM questionnaire	3.52 \pm 0.44	0.40 \pm 0.0
NIH-CPSI total	16.48 \pm 7.22	0.71 \pm 0.82
AUA symptoms score	10.75 \pm 7.51	1.57 \pm 1.63
ICSI IC symptom index	5.95 \pm 4.68	1.35 \pm 1.27
ICPI IC Problem Index	4.39 \pm 4.20	0.36 \pm 0.74

From 40 samples included in the study, 22 had good RNA quality and the rest 18 had poor RNA quality which precluded their use. Values are listed as relative to patient 8014, used as a standard for the curve.

cases TNF mRNA	
8013B	0.889826
8019B	1.368918
8014B	1
8032	0.802611
8011B	0.728576
8038	0.708071
8015B	0.679806
8016B	0.45333
8033	0.411638
8043	0.369423
8017B	0.277099
8007	0.122031
8041	0.016502
8044	0.016502
8039	0.795692
mean	0.576002
st dev	0.383996

:

controls TNF mRNA	
8012B	0.551366
8037	0.476575
8042	0.363632
8010B	0.097319
8027	0.016502
8034	0.016502
8036	0.016502
mean	0.219771
stdev	0.236484

The mean of the CPPS patients is 0.57 relative to the index compared to 0.21 for the controls, or between 2-3 times the amount of TNF- α mRNA on average per patient. By a 2 tailed

unpaired T test this is statistically significant ($p= 0.016$) despite the small number of patients. The correlation of level of TNF- α mRNA in a given patient correlates better with the pain score (question 4 on the NIH-CPSI) $r= 0.46$ than with the total NIH-CPSI score, $r= 0.05$.

Summary: We were able to perform the study with the purchase of the RNA analyzer, and have unique data. Despite our difficulty in recruitment/processing and also our yield of the RNA collected, the amount of TNF- α mRNA was significantly greater ($p=0.016$) in men with CPPS than controls. This data helps support the idea of some men with CPPS having not only a greater frequency of SNP's for TNF- α genes but overall the men with CPPS also had more mRNA for TNF- α compared to controls. This can be used as data to support further applications to investigate the use of medications to target TNF- α for treatment in selected men with CPPS.

References:

Litwin MS, McNaughton-Collins M, Fowler FJ, Jr, Nickel JC, Calhoun EA, Pontari MA, et al. The national institutes of health chronic prostatitis symptom index: Development and validation of a new outcome measure. chronic prostatitis collaborative research network. J Urol 1999; 162: 369-75.

Morley JE, Charlton E, Patrick P, Kaiser FE, Cadeau P, McCreedy D, Perry HM 3rd. Validation of a screening questionnaire for androgen deficiency in aging male. Metabolism. 2000; 49: 1239-1242.

O'Leary MP, Sant GR, Fowler FJ Jr, Whitmore KE, Spolarich-Kroll J. The interstitial cystitis symptom index and problem index. Urology 1999; 49(5A Suppl):58-63.

Schaeffer AJ, Landis JR, Knauss JS, Propert KJ, Alexander RB, Litwin MS, et al. Demographic and clinical characteristics of men with chronic prostatitis: The national institutes of health chronic prostatitis cohort study. J Urol 2002; 168: 593-8.

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

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 _____ No _____

If yes, please describe your plans:

21. Changes in Outcome, Impact and Effectiveness Attributable to the Research Project.

Describe the outcome, impact, and effectiveness of the research project by summarizing its impact on the incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of outcome, impact or effectiveness of the research project. If there were no changes, insert “None”; do not use “Not applicable.” Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

None

22. Major Discoveries, New Drugs, and New Approaches for Prevention Diagnosis and Treatment.

Describe major discoveries, new drugs, and new approaches for prevention, diagnosis and treatment that are attributable to the completed research project. If there were no major discoveries, drugs or approaches, insert “None”; do not use “Not applicable.” Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

This research further supports the idea of using pharmacogenomics to select men with Chronic Pelvic Pain Syndrome for treatments targeting TNF- α

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 Michel A. Pontari		POSITION TITLE Professor of Urology	
eRA COMMONS USER NAME (credential, e.g., agency login) Pontari01			
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
Wake Forest University	B.A.	05/82	Biology
Penn State Univ. Sch. of Medicine, Hershey, PA	M.D.	05/86	Medicine
Yale New Haven Hospital, New Haven, CT		12/91	Surgery, Urology
Boston Univ. Med Ctr, Boston, MA		06/92	Neurourology and Female Urology

A. Personal Statement

I have participated in the Chronic Prostatitis Collaborative Research Network (CPCRN) and Urologic Pelvic Pain Collaborative Research Network (UPPCRN) as a principal investigator. Currently I am involved in the Multidisciplinary Approach to Pelvic Pain (MAPP) project on the executive committee, in charge of Prostatitis/Chronic Pelvic Pain Syndrome. As part of all three networks, I have been involved with the drafting of the protocol. As part of the CPCRN, I was part of the team that developed the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI). Currently I am on the Patient Reported Outcomes (PRO) team with MAPP, and we are working with the FDA in the development of a patient reported outcome measure for patients with chronic pelvic pain. I have experience with recruitment of subjects in the CPCRN, and three subsequent clinical trials as part of the CPCRN and UPPCRN. As part of the CPCRN, our study of risk factors for CP/CPPS described the systemic diseases that are more prevalent in patients with prostatitis, helping to further the idea that urinary symptoms are likely not only caused by urinary tract pathology.

B. Positions and Honors

Positions and Employment

1992 -1998 Assistant Professor, Department of Urology, Temple University School of Medicine
 1998-2000 Acting Chief, Department of Urology, Temple University School of Medicine
 2000- Vice Chairman, Department of Urology, Temple University School of Medicine
 1998- 2006 Associate Professor, Department of Urology, Temple University School of Medicine
 2006- Professor of Urology, Department of Urology, Temple University School of Medicine

Other experience and Professional Memberships

1994- Member, American Urological Association
1998- Member, Society for Urodynamics and Female Urology
1992- Member, Philadelphia Urological Society
1994- 1999 Clinical Advisory Committee, Delaware Valley Chapter of MS Society
2002- Member, Executive Board of Philadelphia Urological Society
2002-2007 Member of DSMB for NIH sponsored MIST trial
2003- Member, Society for Infection and Inflammation in Urology (SIU)
2003- Member, Epidemiology of Interstitial Cystitis Task Force, NIH/NIDDK
2005 Co-Chair, NIH Scientific Workshop on Chronic Pelvic Pain/Chronic Prostatitis
2006- Invited participant, Urologic Diseases in America Project, Prostatitis
2007: Invited participant, NIDDK Prostate Basic and Clinical Science Strategic Planning Meeting
2007-2008 Advisory Panel for NIDDK meeting: Defining the Urologic Chronic Pelvic Pain Syndromes: A New Beginning, Bethesda MD, June 2008
2008-2010 Editor for Current Bladder Reports, section on voiding dysfunction
2009-2012 Member, Core Curriculum Committee, American Urologic Association
2009- Member, International Consultation on Incontinence, Research Society
2011 President, Society for Infection and Inflammation in Urology (SIU)
2012 Member, Committee of International Consultation on Urological Diseases, section on Chronic Prostatitis/Chronic Pelvic Pain Syndrome

Ad hoc reviewer for NIDDK

Special Emphasis Grant Review Panel March 2003 March 2006, November 2006, December 2007, March 2008, October 2008
SBIR grants: August 2009, December 2009, June 2010
NIH UKGD study section: November 1997, September 2008, February 2011
LURN RFA July 2012

BIOGRAPHICAL SKETCH

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

NAME Krynetskiy, Evgeny	POSITION TITLE Associate Professor		
eRA COMMONS USER NAME (credential, e.g., agency login) ekrynetskiy			
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
Moscow State University, Moscow, Russia	M.S.	1974	Chemistry
Moscow State University, Moscow, Russia	Ph.D.	1980	Bioorganic Chemistry
Moscow State University, Moscow, Russia	D.Sc.	1995	Bioorganic Chemistry

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

A. Personal Statement

During my career, I had a chance to receive training and expertise in major areas pertinent to this project, e.g. in bioorganic chemistry and human genetics. As a visiting scientist, I had an opportunity to work at St. Jude Children's Research Hospital where my collaborators and I discovered one of the first polymorphisms recognized in pharmacogenetically-based chemotherapy. This finding proved the concept that pharmacogenetic profile of a patient is an important characteristic in leukemia treatment with thiopurines. Moreover, we were able to develop a genotyping assay predictive of a dangerous, potentially fatal hematopoietic toxicity which is now used worldwide for genotyping childhood patients with acute lymphoblastic leukemia. I continue my studies in Pharmacogenomics at Temple University: I co-authored in a number of papers on genetic determinants of pharmacotherapy of gastroparesis, and concussion susceptibility. In these studies, I developed a number of tools for analysis of patients which have been successfully used in my subsequent studies on pharmacologically important polymorphisms. I am confident that, using these tools, our team is in a good position to address pharmacogenetic/pharmacogenomic problems. I have the expertise necessary to carry out this translational, multidisciplinary study because of my previous experience as a PI or a co-Investigator on several university- and NIH-funded grants, and collaborative work with other researchers. My collaborator, Dr. Pontari, and other members of the project, have demonstrated complementary skills and knowledge in the fields essential for the success of this project. My previous publications in the field of Pharmacogenetics/Pharmacogenomics evidence my competency as a researcher, and the relevance of my skills and knowledge for this project.

B. Positions and Employment

1974-1976 Research Assistant, Belozersky Laboratory for Molecular Biology and Bioorganic Chemistry, Moscow State University, Moscow, Russia

1980-1984 Assistant Member, Laboratory of Molecular Biology of Leukemia, Central Institute for Blood Transfusion, Moscow, Russia

1984-1989 Associate Member, State Institute for Drug Control, Moscow, Russia

1993-1995 Karnofsky Fellow, Department of Pharmaceutical Sciences, St. Jude Children's Research Hospital, Memphis, Tennessee, USA

1996-2005 Investigator, Department of Pharmaceutical Sciences, St. Jude Children's Research Hospital, Memphis, Tennessee, USA

1997-2005 Associate Professor, College of Graduate Health Studies, University of Tennessee, Memphis, Tennessee, USA

2005-present Associate Professor, School of Pharmacy, Temple University, Philadelphia, PA

2006-present Director, Jayne Haines Center for Pharmacogenomics and Drug Safety, Temple University School of Pharmacy, Philadelphia, PA

Other Experience and Professional Memberships

1997-present American Association for Cancer Research

2001-present American Society for Biochemistry and Molecular Biology

2007-present American Association of Colleges of Pharmacy

2005 American Association for Clinical Chemistry

1996-2004 International Society for the Study of Xenobiotics