

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:** The Pennsylvania State University
2. **Reporting Period (start and end date of grant award period):** 1/1/2009- 12/31/2012
3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** John Anthony, MPA
4. **Grant Contact Person’s Telephone Number:** 814-935-1081
5. **Grant SAP Number:** 4100047645
6. **Project Number and Title of Research Project:** 28 - Epithelial/Dendritic Cell Cross-Talk in Acute Kidney Injury
7. **Start and End Date of Research Project:** 7/8/09-6/30/10
8. **Name of Principal Investigator for the Research Project:** William B. Reeves, M.D.
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:

\$ \$75,131

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
Wang	technician	5	3,478

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
Tadagavadi	Post-doctoral fellow	70
Reeves	PI	1%

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
-80 freezer	Ability to store valuable experimental samples and reagents	\$7,000
Agilent Bioanalyzer 2100	Assessment of DNA and RNA samples	28,940

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:

NIH, \$348,980

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:
Epithelial cell/dendritic cell crosstalk in acute kidney injury	<input checked="" type="checkbox"/> NIH <input type="checkbox"/> Other federal (specify:_____) <input type="checkbox"/> Nonfederal source (specify:_)	March 2011	\$1,931,250	\$1,663,875

This is a competitive renewal of grant which was originally supported by the ‘resubmission’ grant. The original grant was funded for two years under ARRA (2009-2011). The funds from the current award supported continuity of research personnel and valuable animal colonies during an interruption in NIH funding in 2009 and was critical to the success of the competitive renewal.

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:

The current NIH award is active through 2016. We will submit a competitive renewal at that time.

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

- a. Determine role of proximal tubule production of TNF in the pathogenesis of ischemic and toxic acute kidney injury using cell specific knockouts developed in our laboratory.
- b. Determine the role of dendritic cell production of TNF in kidney disease using a cell-specific knockout developed in our laboratory.
- c. Determine the role of cell-specific TLR signaling in kidney disease using proximal tubule and dendritic cell deletion of MyD88 mice developed in our laboratory
- d. Establish the mechanism of IL-10 protection using IL-10 chimeras and cell-specific deletion of IL-10 receptors developed in our laboratory.

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			1	
Female				
Unknown				
Total			1	

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

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

This research project has generated research reagents which we are confident will lead to

additional extramural funding and the addition of new investigators. As noted above, these preclinical studies also contributed to the competitive renewal of an NIH grant that has significantly strengthened our institutional research capacity related to kidney disease.

The Agilent Bioanalyzer purchased with this project provides crucial Quality Assessment of DNA and RNA samples necessary before Gene Expression analyses, DNA Library preparation, and other genomics-based assays for almost 70 separate research labs in both Clinical and Basic Science departments.

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

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

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

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

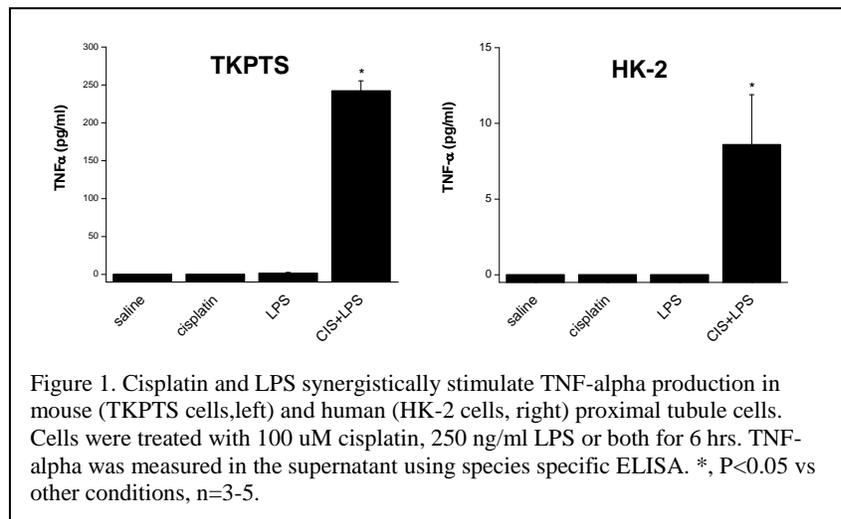
The broad objective of this project is to elucidate how a bidirectional communication between renal epithelial cells and resident renal dendritic cells modulate kidney injury in response to acute renal insults such as ischemia-reperfusion and drug-induced nephrotoxicity. Three specific aims were proposed:

During the award period we achieved each of the specific aims.

Specific Aim 1. Confirm the presence of defective TLR4 signaling in proximal tubule epithelial cells. Renal epithelial cells of mouse and human origin will be cultured in vitro and exposed to TLR4 agonists.

Prior published work from our laboratory, and others, indicated that renal proximal tubules express TLR4. We have also reported that renal proximal tubule cells are capable of producing TNF-alpha. It was surprising, then, to find that treatment of cultured murine proximal tubule cells (TKPTS cells) and human proximal tubular cells (HK-2 cells) with LPS, the prototypic TLR4 ligand, elicited rather small amounts of TNF-alpha production (Fig. 1). Several lines of evidence indicate that the failure to respond to LPS is not due to a lack of surface expression of TLR4 and/or CD14. First, we published that LPS resulted in activation of NFkB and increased TNF-alpha mRNA transcription. Second, LPS does stimulate TNF-alpha production in the presence of cisplatin (Fig. 1).

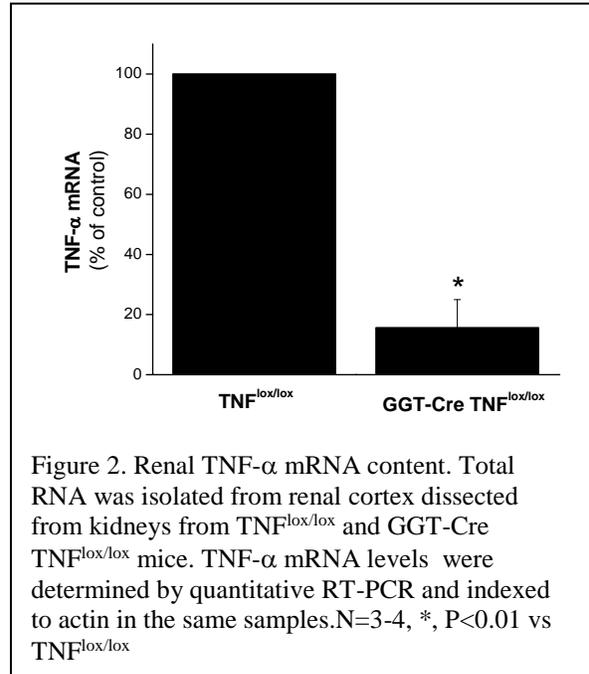
Third, when TKPTS cells were transfected with a TLR4 expression vector, LPS-induced TNF-alpha production remained undetectable while TNF-alpha production in response to the combination of LPS and cisplatin more than doubled (128 ± 9 vs 289 ± 27 pg/ml, $P=0.005$, $n=4$). These results indicate that TLR4 is present on TKPTS cells, has access to LPS, and that pathways leading to NFkB activation are intact. In spite of this, little TNF-alpha protein is produced in response to LPS, suggesting a defect in mRNA translation.



Specific Aim 2. Demonstrate specific TNF-alpha gene recombination in the proximal tubules of GGT-cre/TNF flox/flox mice. Proximal tubules will be microdissected from GGT-cre/TNFflox/flox mice and DNA recombination and mRNA expression of TNF-alpha will be determined.

We successfully used the cre recombinase approach to generate mice with a deletion of the TNF-alpha gene specifically in the proximal tubule epithelium. A mouse with its TNF-alpha gene flanked by LoxP sites was provided by Dr. Sergei Nedospasov. This mouse has been used by Dr. Nedospasov to create specific TNF-alpha deletion in T cells and monocytes (Grivennikov, 2005). These 'floxed' TNF-alpha mice (TNF^{flox/lox}) were bred with GGT-Cre transgenic mice (kindly provided by Dr. Eric Neilsen) to create a proximal tubule TNF-alpha knockout. The GGT-Cre mice were shown by Iwano et al to express Cre only in proximal tubules, not in the renal medulla, and not in brain, liver, spleen, muscle, lung, adrenal gland or bone marrow. Moreover, expression of GGT-Cre was delayed until 7-14 days post-partum, ensuring recombination occurs only late in renal development. Using Rosa26 reporter mice, a high efficiency (over 95%) of recombination in the proximal tubule was observed. Thus, it was expected that GGT-Cre/TNF^{flox/lox} mice would have near complete and specific deletion of TNF-laphain the proximal tubule.

We crossed the TNF^{flox/lox} and GGT-cre mice for 2 generations and obtained the desired GGT-Cre/TNF^{flox/lox} mice. Our analysis showed a dramatic reduction in renal cortical TNF-alpha mRNA in GGT-Cre/TNF^{flox/lox} mice compared with TNF^{flox/lox} mice (Figure 2).



Specific Aim 3. Generate a dendritic cell-specific TNF-alpha knockout mouse. TNF flox/flox mice will be bred with a dendritic cell specific cre-transgenic mouse to create a dendritic cell-specific TNF knockout.

Using the same strategy as in Aim 2, we produced a mouse with a dendritic cells specific deletion of TNF alpha. Specifically, we bred the TNF-alpha^{flox/lox} mouse with a CD11c-cre mouse. CD11c is an integrin expressed specifically by myeloid dendritic cells. After two generations of breeding, we obtained the desired CD11c-cre/TNF^{flox/lox} mouse. To test the efficiency and specificity of TNF deletion in dendritic cells, spleen cells from the CD11c-cre/TNF^{flox/lox} and TNF-alpha^{flox/lox} mice were fractionated into dendritic cells (CD11c), macrophages (CD11b) and T cells (CD4) by flow sorting. Figure 3 shows PCR analysis of genomic DNA. The TNF gene was efficiently deleted in CD11c cells which carried the cre

recombinase. In contrast, CD11b and CD4 positive cells had no gene deletion.

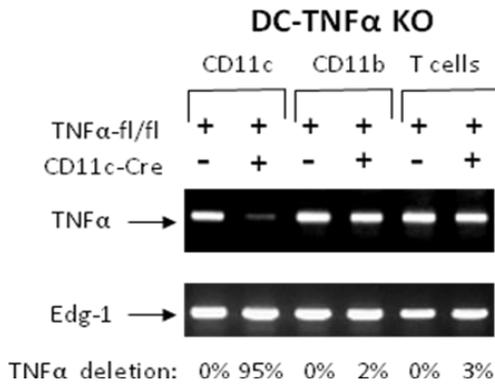


Figure 3 – TNF gene deletion in dendritic cells of CD11c-cre/TNF^{lox/lox} mice.

MyD88 is a key signaling intermediate shared by all TLR receptors except TLR3, as well as by IL-18R and IL-1R. Many of the pro-inflammatory actions of TLR4 agonists are transduced through MyD88 while TRIF signaling mediates type I interferon production. We crossed the CD11c-cre mouse, which expresses cre recombinase in dendritic cells with a mouse in which exon 3 of the MyD88 gene is flanked by LoxP sites (MyD88^{fl/fl}). After backcrossing the CD11c-cre/MyD88^{fl/WT} F1 generation with the MyD88^{fl/fl} mice, we obtained the desired CD11c-cre/MyD88^{fl/fl} mice, in which recombination within the MyD88 gene in DCs interrupts MyD88-dependent TLR4 signaling (DC-MyD88 knockout). We purified DCs, macrophages and T cells from the spleen of both the DC-MyD88 knockout and MyD88^{fl/fl} mice and amplified the MyD88 gene by PCR. There was almost complete loss of the MyD88 gene in DCs, but not macrophages or T cells from the DC-MyD88 knockout mice. Likewise, DCs, macrophages and T cells from the MyD88^{fl/fl} mice produced large amounts of TNF-alpha in response to either TLR4 or TLR9 stimulation, TLR4 or TLR9 agonists, as expected. In contrast, DCs from the DC-MyD88 knockout mice did not respond to either agonist whereas macrophages and T cells responded normally. These results demonstrate that MyD88 recombination occurs with high efficiency in DCs with little recombination in macrophages or T cells.

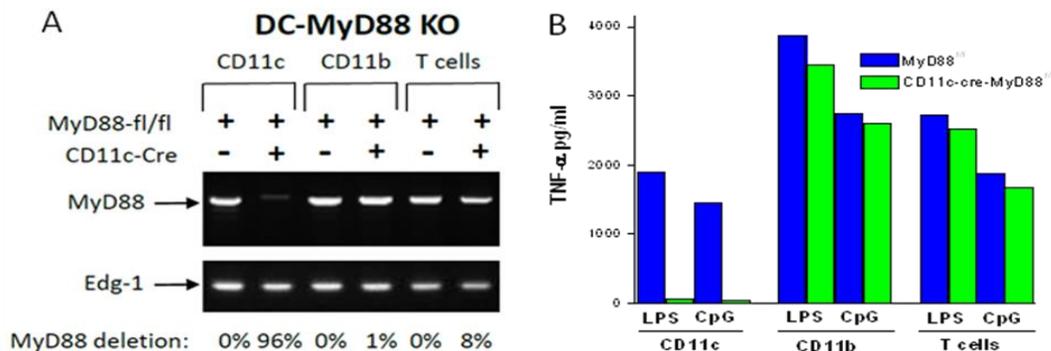


Figure 4 – MyD88 gene deletion (A) and TNF production (B) in dendritic cells of CD11c-cre/MyD88^{lox/lox} mice

18. Extent of Clinical Activities Initiated and Completed. Items 18(A) and 18(B) should be completed for all research projects. If the project was restricted to secondary analysis of clinical data or data analysis of clinical research, then responses to 18(A) and 18(B) should be “No.”

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

Yes
 No

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

Yes
 No

If “Yes” to either 18(A) or 18(B), items 18(C) – (F) must also be completed. (Do NOT complete 18(C-F) if 18(A) and 18(B) are both “No.”)

18(C) How many hospital and health care professionals were involved in the research project?

_____ Number of hospital and health care professionals involved in the research project

18(D) How many subjects were included in the study compared to targeted goals?

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

18(E) How many subjects were enrolled in the study by gender, ethnicity and race?

Gender:

Males
 Females
 Unknown

Ethnicity:

Latinos or Hispanics
 Not Latinos or Hispanics
 Unknown

Race:

American Indian or Alaska Native
 Asian
 Blacks or African American
 Native Hawaiian or Other Pacific Islander
 White

_____ Other, specify: _____
_____ Unknown

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

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

19(A) Did this project involve, in any capacity, human embryonic stem cells?

_____ Yes
 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, listed in the table, in a PDF version 5.0.5 format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, the number of the publication and an abbreviated research project title. For example, if you submit two publications for PI Smith for the “Cognition and MRI in Older Adults” research project (Project 1), and two publications for PI Zhang for the “Lung Cancer” research project (Project 3), the filenames should be:

Project 1 – Smith – Publication 1 – Cognition and MRI
Project 1 – Smith – Publication 2 – Cognition and MRI
Project 3 – Zhang – Publication 1 – Lung Cancer
Project 3 – Zhang – Publication 2 – Lung Cancer

If the publication is not available electronically, provide 5 paper copies of the publication.

Note: The grant agreement requires that recipients acknowledge the Pennsylvania Department of Health funding in all publications. Please ensure that all publications listed acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

Title of Journal Article:	Authors:	Name of Peer-reviewed Publication:	Month and Year Submitted:	Publication Status (check appropriate box below):
1. Endogenous IL-10 attenuates cisplatin nephrotoxicity: role of dendritic cells	Raghu Tadagavadi W.Brian Reeves	Journal of Immunology	February 2010	<input type="checkbox"/> Submitted <input type="checkbox"/> Accepted <input checked="" type="checkbox"/> Published
2. TNF-alpha mediates increased susceptibility to ischemic AKI in diabetes	Guofeng Gao Binzhi Zhang Ganesan Ramesh Daniel Betterly Raghu Tadagavadi Weiwei Wang W. Brian Reeves	Am Journal of Physiology: Renal Physiology	September 2012	<input type="checkbox"/> Submitted <input type="checkbox"/> Accepted <input checked="" 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:

1. Relative roles of dendritic cell and proximal tubule derived TNF α in cisplatin nephrotoxicity.
2. Relative roles of dendritic cell and proximal tubule derived TNF α in ischemia-reperfusion injury.
3. Role of macrophage and proximal tubule derived TNF α in obstructive uropathy

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 – these are preclinical studies.

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 established a new paradigm for dendritic cells in acute renal failure, namely, that dendritic cells protect against renal injury. We also determined that endogenous IL-10 is a potent protective mechanism which could be manipulated therapeutically. We have created mouse models which will enable us to dissect the sources of TNF-alpha which mediates various forms of kidney injury.

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 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 Reeves, W. Brian	POSITION TITLE Professor of Medicine		
eRA COMMONS USER NAME WREEVES			
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 <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
Pennsylvania State University, University Park, PA	B.S.	1977	Pre-Med
Jefferson Medical College, Philadelphia, PA	M.D., cum laude	1979	Medicine
University of Texas Medical School, Houston, TX	Resident	1979-1982	Internal Medicine
University of Texas Medical School, Houston, TX	Chief Resident	1982-1983	Internal Medicine
University of Texas Medical School, Houston, TX	Fellow	1983-1986	Nephrology

A. Positions and Honors.

Professional Experience:

1986-1988 Assist. Professor, Division of Nephrology, University of Texas at Houston
 1988-1994 Assist Professor, Division of Nephrology, University of Arkansas for Medical Sciences
 1994-2000 Assoc Professor, Division of Nephrology, University of Arkansas for Medical Sciences
 2000-present Professor, Chief, Division of Nephrology, Penn State College of Medicine
 2005-present Vice Chair, Department of Medicine, Penn State College of Medicine

Activities:

1989-2005: Scientific Peer Review Committees for the American Heart Association
 1994-1996: Review Committee for the Young Investigator Award, National Kidney Foundation
 1995-2000: Research Committee, Arkansas Chapter of the National Kidney Foundation
 1999-2000: Research Committee, Heartland Affiliate of the American Heart Association
 2002-2005: Research Committee, AHA Pennsylvania Affiliate
 2005-present: Grant Review Committee, American Society of Nephrology
 2007/2008: NIH PBKD Study Section (ad hoc member)
 2009: NIH ZRG1 DKUS-K Study Section
 2010: NIH ZDK1 GRB-S Special Emphasis Panel. PKD Research and Translation Core Centers
 Editorial Boards: Kidney International (1995-2003); Am. J. Physiology: Renal Physiology (1997-2001)

Honors:

Alpha Omega Alpha, Squibb-American Heart Association Clinician Scientist Award, 1985-1990,
 American Heart Association Established Investigator Award 1995-2000

B. Selected Peer-Reviewed Publications (Selected from 59 peer-reviewed publications)

1. Zhang, B., Ramesh, G., Uematsu, S., Akira, S., Reeves, W. B. TLR4 signaling mediates inflammation and tissue injury in nephrotoxicity. J Am Soc Nephrol, 19:923-932, 2008.
2. Reeves, W.B., Kwon, O., Ramesh, G. Netrin-1 and kidney injury. II. Netrin-1 is an early biomarker of acute kidney injury. Am. J. Physiol: Renal Physiol. 294:F731-F738, 2008.
3. Adalsteinsson, V., Parajuli, O., Kepics, S., Gupta, A., Reeves, W.B., and Hahm, J-I.

- Ultrasensitive Detection of Cytokines Enabled by Nanoscale ZnO Arrays. *Analytical Chemistry*, 80:6594-6601, 2008.
4. Ghahramani N, Reeves WB and Hollenbeak C. Association between increased body mass index, calcineurin inhibitor use, and renal graft survival. *Exp Clin Transplant* 6:199-202, 2008. PMID: 18954297
 5. Yura, RE, Bradley GS, Ramesh G, Antonetti, DA, Reeves WB and Bond JS. Meprin A Metalloprotease Modulates the Host Response to Lipopolysaccharide. *Am. J. Physiol: Renal Physiol*. 296:F135-F144, 2009
 6. Wang, W, Reeves, WB, Pays, L, Mehlen, P & Ramesh, G: Netrin-1 overexpression protects kidney from ischemia reperfusion injury by suppressing apoptosis. *Am J Pathol*, 175:1010-8, 2009.
 7. Wang, H, Malvadkar, N, Koytek, S, Bylander, J, Reeves, WB & Demirel, MC: Quantitative analysis of creatinine in urine by metalized nanostructured parylene. *Journal of Biomedical Optics* 15:027004-5, 2010.
 8. Tadagavadi, R, Reeves, WB. Dendritic cells ameliorate nephrotoxic acute kidney injury. *J Am Soc Nephrol*. 21: 53-63, 2010. PMID: 19875815
 9. Saadulla, L, Reeves, WB, Irely, B, Ghahramani, G. Impact of computerized order entry and pre-mixed dialysis solutions for continuous veno-venous haemodiafiltration on selection of therapy for acute renal failure. *J of Medical Systems*. 2010. In press.
 10. Lin, L, Bu, G, Mars, WM, Reeves, WB, Tanaka, S, & Hu, K. tPA activates mitogenic signaling involving LDL receptor-related protein 1-mediated p90RSK and GSK3 β pathway. *Am J Pathol*. 2010, In press.
 11. Tadagavadi, R. Reeves, WB. Endogenous IL-10 attenuates cisplatin nephrotoxicity: role of dendritic cells. *J. Immunol*. 2010, in press.