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:** 23-Tim2 Expression on Oligodendrocytes: A new Immune System Target

7. **Start and End Date of Research Project:** 7/8/2009 –6/30/2011

8. **Name of Principal Investigator for the Research Project:** James R. Connor, Ph.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:

   $ 46,530

   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
Ponnuru	Postdoctoral Fellow	16.7	$7,174
Alkhateeb	Graduate Student	49.25	$10,962

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
Connor	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
None		

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____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:
Tim-2 Expression on Oligodendrocytes: A New Immune System Target	☐NIH X Other federal (specify:__DoD_) ☐ Nonfederal source (specify:_)	Jun 2010	$692,635	Not Funded
Tim-2 Expression on oligodendrocytes: A new neuroimmune target in multiple sclerosis	☐NIH ☐ Other federal (specify:_____) X Nonfederal source (specify: _MS Society___)	Aug 2011	$582,082	Not Funded

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:

We are planning to submit a NIH grant for the EUREKA funding program in March 2013.

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

The project continues to generate interesting data. The immediate plan is to resubmit the manuscript with the data from the autopsy samples. The second step is to continue to seek funding through NIH and private mechanisms. One area that has recently emerged as a result of this research is the possibility that the Sema4A and Tim-2 receptor interaction may underlie the demyelination associated with cerebral malaria. We plan to investigate this in more detail.

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				

	Undergraduate	Masters	Pre-doc	Post-doc
White				
Black				
Asian				1
Other		1		
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_____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 (α) and beta (ß) should not print as boxes (□) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

Project Overview

Despite the recent advances in our understanding of disease pathogenesis and treatment of multiple sclerosis, this disease still represents a significant source of neurologic disability. Although immunomodulatory drugs are very effective at treating active disease, they are completely ineffective at treating the chronic neurodegenerative phase of MS. To address this, one approach is finding ways of encouraging remyelination by endogenous oligodendrocyte progenitor cells, allowing them to repair myelin and therefore preventing secondary axonal loss and neurodegeneration. We have recently discovered that Tim-2 protein is selectively expressed on cells of oligodendrocyte lineage. Tim-2 is present on mature oligodendrocytes and oligodendrocyte progenitors and functions as receptor for extracellular H-ferritin and Sema4A proteins. Considering that both Sema4A and Tim-2 have an important function in immune regulation and are critical in development of experimental autoimmune encephalomyelitis (EAE), we propose that existence of Tim-2 receptors on oligodendrocytes may predispose these cells to immune attack. There are two specific aims that we intend to accomplish.

Aim 1: Test the hypothesis that Sema4A can be detected in demyelinating plaques, but not in normal white matter from human tissue collected at autopsy. A second hypothesis will be tested concomitantly, that Sema4A staining in the plaques will be colocalized with markers of infiltrating lymphocytes (T cells and B cells) and local central nervous system (CNS) inflammatory cells (astrocytes and microglia).

Aim 2: Test the hypothesis that there will be higher concentrations of Sema4A protein in the Cerebrospinal fluid (CSF) of MS patients compared to controls which will be predictive of clinical diagnosis of MS.

Summary of Research Completed

To investigate the expression of Sema4A protein in MS plaques, we first demonstrated that the Sema4A antibody recognizes Sema4A recombinant protein on a Western blot (Figure 1A). Because Sema3A and Sema4D have been suggested to play a role in the pathogenesis of MS and have been found to be expressed within MS plaques (Williams et al. 2007, Giraudon et al. 2004), we demonstrated that this antibody did not cross-react with these related semaphorin proteins on a native protein immunoblot (Figure 1B). The Figure 1B shows that anti-Sema4A antibody recognizes only native Sema4A-Fc, but not Sema3A-Fc nor Sema4D-Fc. Equal loading of protein is shown with an antibody against the IgG fused domain to rSema4A-Fc, rSema4D-Fc, and rSema3A-Fc. Subsequently, we used the same antibody to evaluate expression and cellular distribution of Sema4A in 5 MS patient plaques and 4 control specimens containing normal human white matter. Table 1 summarizes the histopathological parameters of the specimens used

in this study. The MS and control patient population were matched well by age (average age 67 and 68, respectively) and gender (male/female ratio was 20%:80% for MS and 25%:75% for controls). In Figure 2, a representative image of immunostaining for Sema4A demonstrates much higher levels of Sema4A immunoreactivity within the plaque compared to normal white matter. Sema4A immunoreactivity was localized in small cells cuffing the blood vessels, which is pathognomonic for infiltrating lymphocytes within the MS plaque. A second group of Sema4A-positive cells observed in the sections were large bloated cells infiltrated within the myelin. These cells are morphologically typical of microglia/macrophages. In each of 5 plaques examined, the Sema4A immunoreactivity was much higher in the plaque compared to normal white matter. We defined the extent of demyelination and distinguished plaque area from normal appearing white matter by staining for myelin basic protein (MBP; Figure 2, C, D) for each plaque used in the study. Collectively, these data demonstrate that there are higher levels of Sema4A protein within the MS plaque compared to normal white matter, and that the chief cellular sources of this protein within the plaque are infiltrating lymphocytes and activated macrophages/microglia.

Figure 1. Anti-Sema4A antibody recognizes Sema4A, but not closely related Sema3A or Sema4D. (A) Recombinant Sema4A-Fc chimera protein was loaded onto a denaturing SDS-PAGE gel and either stained with Comassie or probed with anti-Sema4A antibody on a Western blot (WB). The antibody recognizes the Sema4A-Fc chimera recombinant protein (A), which is of appropriate molecular size (115-120 KDa) for the glycosylated protein. (B) Native (non-denatured) rSema4A-Fc, rSema3A-Fc, and rSema4D-Fc were immobilized onto a nitrocellulose membrane and probed with anti-Sema4A antibody via slot blot. A separate blot was probed with anti-IgG antibody against the fused Fc domain of the semaphorin proteins to show total protein. This representative immunoblot demonstrates that the Sema4A antibody recognizes rSema4A-Fc, but not rSema3A-Fc or rSema4D-Fc.

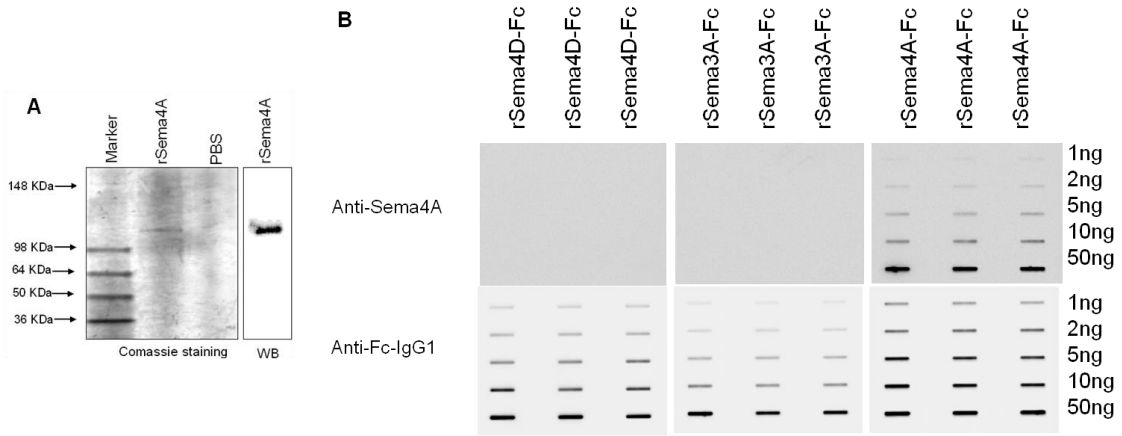


Table 1. Characteristics of MS patients and normal controls used in the study. The tissue specimens from a total of nine patients were used in the study, of which 5 were MS patients and 4 were normal controls. The average age of MS patients and controls were 67 and 68 years, respectively.

MS patient	Primary diagnosis	Age	Gender	Plaque	Path. Classification
1	Multiple Sclerosis	76	F	Active	demyelination, lymphocytic infiltrate (E), microglia present
2	Multiple Sclerosis	84	F	Active	demyelination, lymphocytic infiltrate (D), microglia present
3	Multiple Sclerosis	65	M	Active	demyelination, lymphocytic infiltrate (P, E), microglia present
4	Multiple Sclerosis	62	F	Active	demyelination, lymphocytic infiltrate (E, D), microglia present
5	Multiple Sclerosis	48	F	Active	demyelination, lymphocytic infiltrate (P, E, D), microglia present

Control patient	Primary diagnosis	Age	Gender	Plaque	Path. Classification
1	Normal	66	M	none	Normal white matter
2	Normal	49	F	none	Normal white matter
3	Normal	77	F	none	Normal white matter
4	Normal	80	F	none	Normal white matter

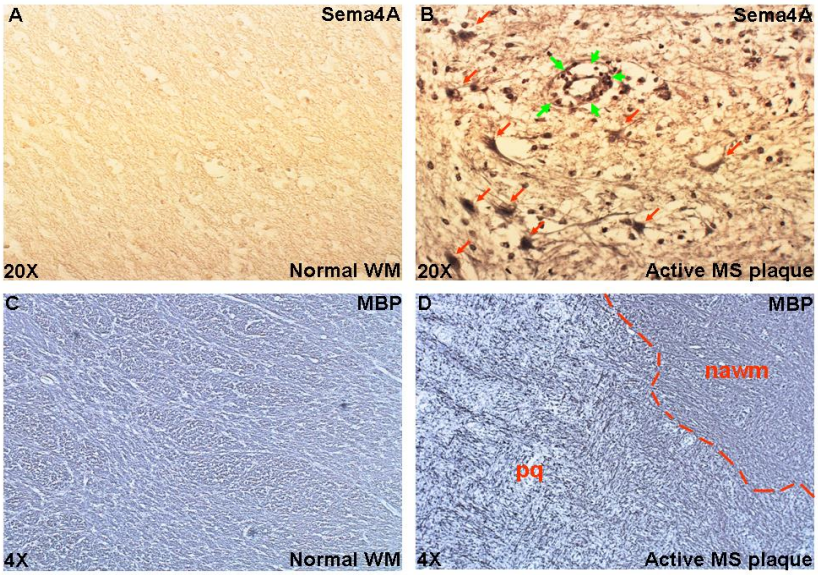
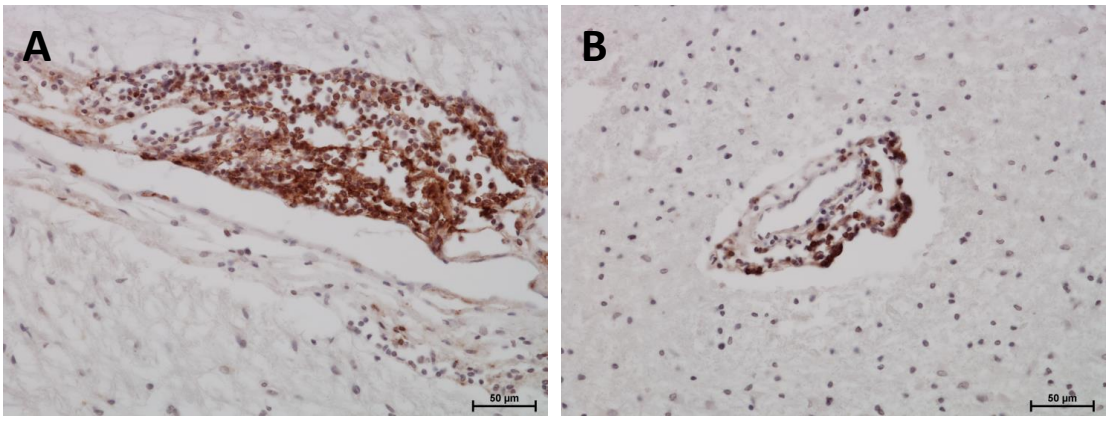


Figure 2. Sema4A is expressed in MS plaques. Sections of normal white matter (A) and those of patients with MS (active plaques, B) were immunostained for Sema4A. Representative images are presented here that demonstrate strong immunoreactivity with Sema4A antibodies in the MS plaque compared to normal white matter. The reaction product was mainly localized in lymphocytes (perivenular cuff, green arrows in B) and in scattered macrophages/microglia (red arrows in B). The size and location of the plaque was determined by immunostaining of the neighboring sections for myelin basic protein (MBP) (C and D). These low powered images demonstrate representative results of MBP immunoreactivity in both

normal white matter and MS plaques. Within the given specimen, the demarcation between the region of strong demyelination/plaque (pq) and normal appearing white matter (nawm), was observed and is indicated by the red dotted line.

To demonstrate that there are lymphocytes in the plaques in the MS tissue that could be the source of Sema4A, we stained samples for CD20, a marker of lymphocytes. A representative section is shown in Figure 3.

Figure 3. CD20+ B cells are detected in blood vessels of active MS plaques in the brain. Paraffin embedded sections were immunostained for the B cell marker CD20 (brown) (A, B) in active MS plaques. Nuclei are counterstained with hematoxylin (blue). There is increased migration of B cells into the blood vessels of the MS plaques of the brain. Representative images are depicted at 20X.



In addition to the immunostaining, we performed a series of quantitative analyses on MS tissue obtained at autopsy (Figure 3) using an immunoblot approach as described above. The samples are divided as shown below into normal white matter (NAWM), active lesions (AL), chronic active lesions (CAL) and chronic lesions (CL). There is an increase in the non-cleaved form of Sema4a (120kDa) in the chronic lesion compared to the other lesions. The smaller cleaved form (85kDa) is the soluble form and is not significantly different among the different groups.

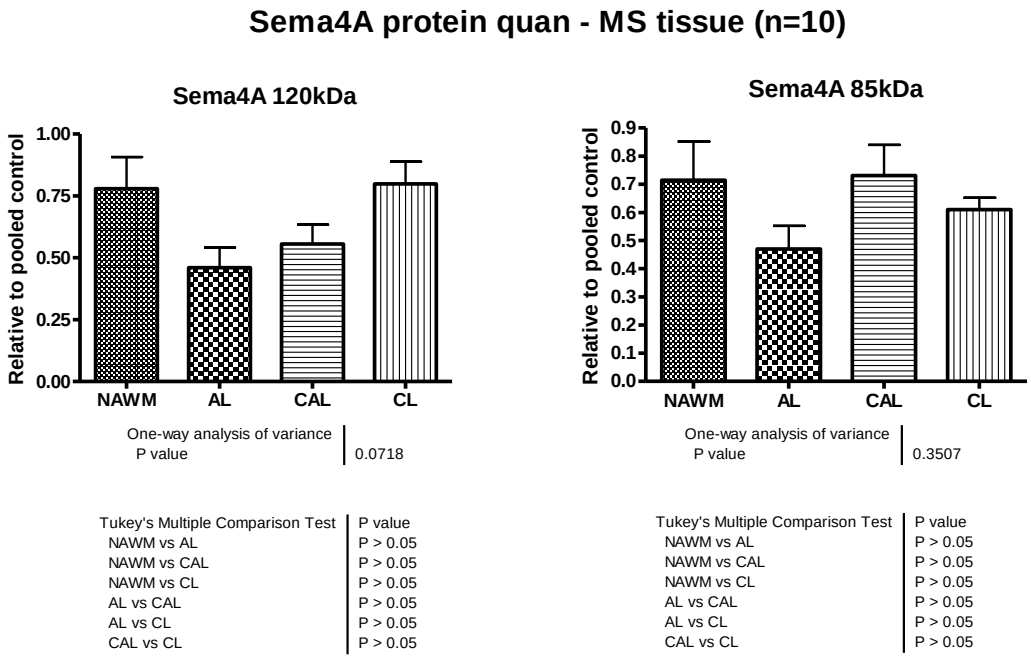


FIGURE 4.

For Aim 2, the goal was to test the hypothesis that there will be higher concentrations of Sema4A protein in the Cerebrospinal fluid (CSF) of MS patients compared to controls which will be predictive of clinical diagnosis of MS. We found that we could not confidently detect Sema4A. We found a band at 55kDa on western blotting that was smaller than any reported band. Acknowledging that this could be some form of cleavage product, we performed antigen competition but could not remove the band at 55kDa convincing us that this was spurious, non-specific binding. We did also try depleting the CSF of Sema4A in one sample by immunoprecipitation and evaluating whether this reduced oligodendrocyte death in a cell culture model, but this experiment was unsuccessful. We have concluded that there are not detectable levels of Sema4a in CSF.

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
__X__ No

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

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

20. Articles Submitted to Peer-Reviewed Publications.

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication or paper submitted for publication, listed in the table, in a PDF version 5.0.5 (or greater) format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, the number of the publication and an abbreviated research project title. For example, if you submit two publications for PI Smith for the "Cognition and MRI in Older Adults" research project (Project 1), and two publications for PI Zhang for the "Lung Cancer" research project (Project 3), the filenames should be:

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

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

Note: The grant agreement requires that recipients acknowledge the Pennsylvania

Department of Health funding in all publications. Please ensure that all publications listed acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

Title of Journal Article:	Authors:	Name of Peer-reviewed Publication:	Month and Year Submitted:	Publication Status (check appropriate box below):
1. None				☐Submitted ☐Accepted ☐Published

20(B) Based on this project, are you planning to submit articles to peer-reviewed publications in the future?

Yes___X_____ No_____

If yes, please describe your plans:

We plan to add the data from MS plaques to a paper that demonstrated Sema4a is toxic to oligodendrocytes in culture and then submit the paper to Journal of Neurochemistry for 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	POSITION TITLE
James R. Connor, Ph.D.	Distinguished Professor

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
Thomas More College, Ft. Mitchell, KY	B.A.	05/1975	Psychology
Wright State University, Dayton, OH	M.S.	05/1978	Physiology
University of California, Berkeley, CA	Ph.D.	106/981	Anatomy
Boston University Medical Center, Boston, MA	Postdoc	07/1983	Neuroscience

Personal Statement

I am an internationally recognized leader in the field of brain iron metabolism. The reviews of my first NIH grant on this topic 25 years ago carried the statement from a reviewer that "this PI has the opportunity to start a new field in neurobiology". Since that seemingly prescient comment, I have been privileged to maintain a continuously funded program with funding from 4 different NIH agencies and numerous foundations as I have led investigations into many aspects of brain iron metabolism including, oxidative stress as a consequence of too much brain iron, the role of iron in myelin and oligodendrocyte function, mechanisms and regulation of brain iron transport. My work has relevance to understanding basic pathophysiology of diseases such as Alzheimer's, Parkinson's, multiple sclerosis and restless legs syndrome. In particular, I have focused on iron and oligodendrocytes and have provided evidence over the last 10 years of a novel receptor on oligodendrocytes for iron uptake. This observation led to a series of investigations that resulted in the discovery of a ferritin receptor in the brain. As a result, I have begun to investigate the role of ferritin in oligodendrocyte health and survival. The receptor for ferritin, is Tim-2 and another ligand for this receptor is a member of the semaphorin family of proteins. With this discovery, the data have positioned us to perhaps a novel and significant connection between the immune system and nervous system.

B. Positions and Honors

Professional Positions:

1983-1987 Research Biologist, Veteran's Administration Medical Center, Washington, DC
1983-1987 Assistant Research Professor, Department of Physiology, The George Washington University School of Medicine
1987-1990 Assistant Professor, Department of Anatomy Pennsylvania State University College of Medicine (PSUCOM) Neuroscience & Anatomy, (PSUCOM)
1990-1996 Associate Professor, Department of Neuroscience & Anatomy, (PSUCOM)
1996- Professor, Department of Neuroscience & Anatomy, (PSUCOM)

1999-2002	Vice Chair Department of Neuroscience & Anatomy, (PSUCOM)
2002-2003	Interim Chair Department of Neuroscience & Anatomy, (PSUCOM)
2004-	Professor Neurosurgery, (PSUCOM)
2006	Co-Director, Neuro-oncology Experimental Therapeutic Group (PSU Cancer Institute)
2007	University Distinguished Professor (PSUCOM)

Grant Review Experience:
NIH, NIEHS, Veterans Administration, Department of Defense USDA, NSF, MRC, Wellcome Trust, Israel Academy of Science, Alzheimer's Association, Hong Kong Research Council, American Federation for Aging Research, American Heart Association

Honors and Awards:
Samuel Hinkle Society Outstanding Young Investigator Award, Pennsylvania State University College of Medicine (1990);
Mentored two students awarded Marion Kies Award American Society for Neurochemistry (1999);
Elected Chair of the East Coast Iron Club (2000-2002);
Dean's Lecturer Pennsylvania State University College of Medicine/M.S. Hershey Medical Center (2003)
Named Distinguished Professor Penn State University (2007)
Honorary Professor, Department of Neurology, Tianjin First Center Hospital, Tianjin, China (2008-)

Editorial Boards: *Journal of Neuroscience Research* (1994-); GLIA (2001-); *Fluids and Barriers of the CNS* (2004-); *Current Neurovascular Research* (2004-); *CNS Drug Discovery* (2005-); *Recent Patents on Biotechnology* (2008-), *Journal of Neurochemistry* (Handling Editor; 2011-); *PlosOne* (2012).

C. Selected Peer-reviewed Publications

1. Hulet S, Hess EJ, Debinski W, Arosio P, Bruce K, Powers S, and **Connor JR.** Characterization and distribution of ferritin binding sites in the adult mouse brain. *Journal of Neurochemistry* 72:868-874, 1999.
2. Hulet SW, Powers S, and **Connor JR**. Distribution of transferrin and ferritin binding in normal and multiple sclerotic human brains. *Journal of Neurological Science* 165:48-55. 1999.
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