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.

1. **Grantee Institution:** The Pennsylvania State 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):** John Anthony, MPA

4. **Grant Contact Person's Telephone Number:** 814 935 1081

5. **Grant SAP Number:** 4100050904

6. **Project Number and Title of Research Project:** 22. Delivery and Mechanism of Action of Novel Therapeutic Agents to Combat ALS

7. **Start and End Date of Research Project:** 9/1/2010 - 6/30/2012

8. **Name of Principal Investigator for the Research Project:** Colin Barnstable, DPhil

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:

   $ 61,800

   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
Snyder, Amanda	Postdoctoral fellow	50	30,000

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
Connor, James	Professor	5
Tombran-Tink, Joyce	Professor	5
Simmons, Zachary	Professor	5
Barnstable, Colin	PI	5

9(D) Provide a list of **all** scientific equipment purchased as part of this research grant, a short description of the value (benefit) derived by the institution from this equipment, and the cost of the equipment.

Type of Scientific Equipment	Value Derived	Cost
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___X____ No_____

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

Department used funds to support unfunded component of faculty salaries.

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:
None	☐NIH ☐ Other federal (specify:_____) ☐ Nonfederal source (specify:_)		$	$

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

Yes__X____ No_____

If yes, please describe your plans:

We need to collect additional data and then reapply for funding

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

The project gave results which were just at the limits of statistical significance. Although we did apply for additional funding it was clear from the reviews that additional animals and dosages would be needed to provide solid statistical support for the proposed aims.

13. New Investigator Training and Development. Did students participate in project supported internships or graduate or post-graduate training for at least one semester or one summer?

Yes___X_____ No_____

If yes, how many students? Please specify in the tables below:

	Undergraduate	Masters	Pre-doc	Post-doc
Male				
Female				1
Unknown				
Total				**1**

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

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

Most cases of ALS are sporadic but the 20% of inherited cases have allowed the identification of some molecular changes that can cause the disease. One of the best studied is a mutation in the superoxide dismutase gene SOD1. Mice expressing the same mutation show many symptoms in common with ALS and undergo progressive degeneration until death.

The long-term objective of our project is to develop a therapy for ALS. The objective of our current work is to determine whether local and sustained delivery of PEDF can prevent degenerative changes seen in the $mSOD1^{G93A}$ mouse model of ALS. To develop sustained funding for this program we need to obtain preliminary data for the following specific aims.

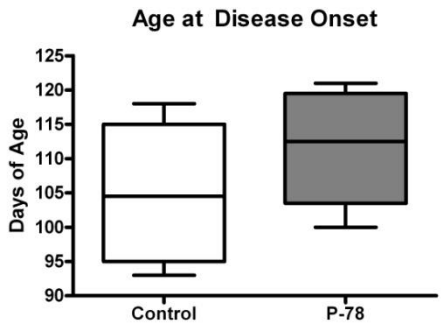
1) To test the hypothesis that encapsulated PEDF can be delivered directly into the CSF via intraventricular infusion and can act to prevent or delay motor neuron death in the $mSOD1^{G93A}$ model of ALS.
2) To determine the mechanism(s) of action of PEDF in this ALS model to optimize the PEDF drug and the route of delivery.

Recombinant PEDF was produced in a highly purified form using standard methods developed by the Tombran-Tink laboratory. A bioactive fragment of PEDF, P-78, was produced in a similar manner and isolated by affinity chromatography using a 6X-his tag present on the fusion protein from which P-78 was cleaved. PEDF and P-78 were used in Alzet minipumps that were implanted in SOD^{G93A} mice. The mice were observed for the development of ALS like symptoms.

We completed the histological analysis of the treated animals and correlated these findings with the functional analysis. As indicated in previous reports the significant expense of obtaining the $SOD1^{G93A}$ mice required us to simplify our experimental plan and limit the aims to a test of the efficacy of PEDF. We treated 4 animals with osmotic minipumps loaded with PEDF but found no significant effect as judged by either performance on a rotorod test or histological analysis. We then repeated these experiments using an active fragment of PEDF, P78. The rationale for this was that the smaller fragment has demonstrated better tissue penetration in a variety of other models of neurodegeneration. $SOD1^{G93A}$ mice were implanted with osmotic minipumps containing P78 in artificial csf, or artificial csf alone as control.

From these experiments we have preliminary data that supports the use of P-78 as a viable treatment to directly impact the course of ALS symptomology and survival in $SOD1^{G93A}$ mice. In Figure 1, the data demonstrate that P-78 delays the age of symptom onset, as assessed by Rotarod performance.

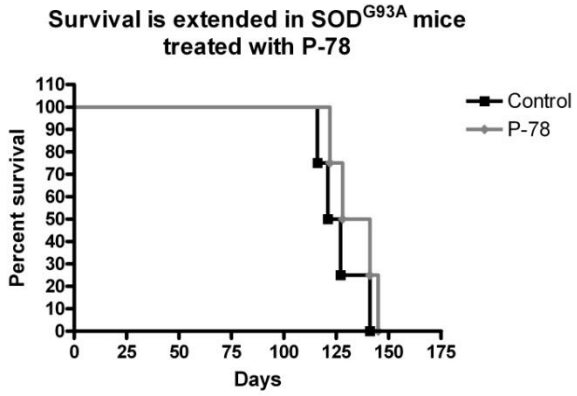
Figure 1



Infusion of P-78 delays disease onset in SOD1^{G93A} mice. Rotarod behavioral assessment was used to determine the age at which animals lacked the ability to stay on the rotating rod for 3 minutes. Intracerebroventricular (i.c.v) infusion of P-78 (concentration 600ug/mL) is achieved via an osmotic mini-pump linked to a cannula that is targeted to lateral ventricles in the brain. The control animals were infused with artificial cerebrospinal fluid (CSF). Median age of onset for the control group was 104.5 days while P-78 delayed onset of disease to 112.5 days. N = 4 in each group.

We have also collected behavioral data that demonstrates that survival is extended by P-78 infusion in these same SOD1^{G93A} mice (Figure 2). Endpoint criterion is based on the inability of the animal to right itself when placed on its side; if the animal is unable to right itself after 30 seconds, endpoint has been reached.

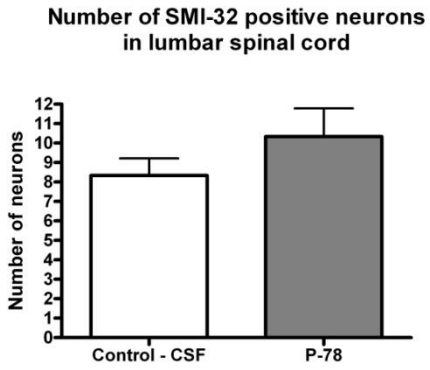
Figure 2



Infusion of P-78 extends survival in the SOD1^{G93A} mouse model of ALS. Median survival time for control (artificial CSF-infused mice) was 124 days and mice that received P-78 infusion survived 134.5 days longer, which is an 8% increase in survival time. N = 4 in each group.

Cell count data of SMI-32 (Neurofilament H non-phosphorylated)-immunopositive cells in the ventral horn of the lumbar spinal cord demonstrated that P-78 treatment results in a greater number of surviving motor neurons at endpoint (Figure 3).

Figure 3



The SOD^{G93A} mice that were treated with P-78 infusion had 12% more neurons than animals given the control infusion of artificial CSF. These cell count data are in agreement with the extended lifespan and delayed disease onset data observed in the P-78 - treated animals.
N = 3 mice in each group. The average cell counts from 7-9 tissue sections were used to obtain a value for each animal; this average was used to calculate group means for comparisons.

Although the limited funds available limited the number of animals we could treat, the results do support the hypothesis that the p78 fragment of PEDF has potential therapeutic benefit for the treatment of ALS.

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, 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.				☐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:

As indicated above we are seeking funds to extend our preliminary data. When this is done we expect that we will have sufficient significant data to justify publication in a quality journal.

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.

The research did provide support for the idea that PEDF can serve as a protective factor to lessen the degeneration in a mouse model of ALS. With additional work we believe that versions of this protective factor would be useful in human therapy.

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.

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	POSITION TITLE
Colin J. Barnstable	Professor and Chair
eRA COMMONS USER NAME (credential, e.g., agency login)	
BARNSTCJ	

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
University College, Oxford, UK	B.A.	05/75	Biochemistry
Wolfson College, Oxford, UK	D.Phil	06/78	Genetics
Harvard Medical School, Boston, MA	Post-doc	08/78-06/80	Neurobiology

A. Personal Statement

For several decades my research group has focused on the molecular mechanisms governing development and degeneration in the mammalian CNS. Our work in this area was slowed for approximately two years when I moved to Penn State because of a cascade of delays in construction that resulted in a lack of lab space. We then moved into newly renovated lab space and our research productivity is now getting back to normal. In addition to studying the expression and function of individual genes and signal pathways, we have taken a broader unbiased approach to define the transcriptome of one portion of the CNS, the retina, as well as some of the global mechanisms regulating its development. In recent years we have examined some of the signal pathways regulating rod photoreceptor development and also those regulating cell death of several retinal cell types. In parallel with the studies in this proposal we are currently studying the mouse retinal epigenome in order to elucidate the ways in which changes in chromatin organization can influence gene expression. Since 1980 my work has been funded by grants from the NIH, and other organizations, that have also supported the training of many students and postdoctoral associates. Many of these now hold leadership positions in science and medicine in several countries.

B. Positions and Honors

Positions and Employment

1980-1983	Instructor & Assistant Professor, Department of Neurobiology, Harvard Medical School
1983-1988	Assistant (83-85) and Associate (85-88) Professor, The Rockefeller University
1988-1993	Associate Professor (tenured), Department of Ophthalmology & Visual Science, and Section of Neurobiology, Yale University School of Medicine
1992-1993	Co-Director, Yale Interdepartmental Neuroscience Program
1993-2006	Professor and Vice Chair of Research, Department of Ophthalmology & Visual Science, Yale University School of Medicine
2006 -	Professor and Chair, Department of Neural and Behavioral Sciences, Pennsylvania State University College of Medicine.
2006-2008	Director, Penn State Hershey Neuroscience Research Institute

2006-2008	Co-Director Penn State Neuroscience Institute
2007-	Professor of Psychiatry, Pennsylvania State University College of Medicine.
2011-	Research Director, Penn State Hershey Eye Center

Other Experience

1984-1991	Associate Editor, Journal of Neuroscience
1986-	Editorial Board, Molecular Neurobiology
1989-1992	NEI Vision Research Review Committee
1993- 2004	Scientific Advisory Board, RP Research Foundation, Canada (Chair, 1998-2000)
1994- 2001	Editorial Board, Journal of Neurochemistry
1995-	Editorial Board, Journal of Molecular Neuroscience (Editor-in-Chief, 1995-1999)
1997- 2000	NIH Vis B Study Section (Chair 1999 – 2000)
1998-	Scientific Advisory Board, Macular Vision Research Foundation
2003-2008	Editorial Board, Experimental Eye Research
2005-	Co-Editor, "Ophthalmology and Visual Science" book series, Humana/Springer Press
2007-	Co-Editor-in-Chief, Journal of Ocular Biology, Diseases and Informatics.
2007-	Regular Ad Hoc member of study sections for SBIR grants, K awards and R01 special panels

Honors

1984-1986	Alfred P. Sloan Research Fellow
1988	Demuth Swiss Medical Foundation International Award in Neuroscience
1988-1996	Jules & Doris Stein Research to Prevent Blindness Professor
1999-2001	Senior Scientific Investigator, Research to Prevent Blindness, Inc.

C. Selected peer-reviewed publications (from a total of 176).
Most relevant to the current application

Popova EY, Xu X, DeWan AT, Salzberg AC, Berg A, Hoh J, Zhang SS, **Barnstable CJ**. Stage and gene specific signatures defined by histones H3K4me2 and H3K27me3 accompany mammalian retina maturation in vivo. PLoS One. 2012;7(10):e46867. [PCMID: PMC3682587]

Pinzon-Guzman C, Zhang SS, **Barnstable CJ**. Specific protein kinase C isoforms are required for rod photoreceptor differentiation. J Neurosci. 2011, 31:18606-17. [PMCID: PMC3256583]

Liu MG, Li H, Xu X, **Barnstable CJ**, Zhang SS. Comparison of gene expression during in vivo and in vitro postnatal retina development. J Ocul Biol Dis Infor. 2008, 1:59-72. [PMCID: PMC2802513]

Zhang SSM, Xu X, Liu MG, Zhao H, Soares MB, **Barnstable CJ**, Fu XY. A biphasic pattern of gene expression during mouse retina development. *BMC Dev. Biol.* 2006, **6**:48. [PMCID: PMC1633734]

Zhang SS, Wei J, Qin H, Zhang L, Xie B, Hui P, Deisseroth A, Barnstable CJ, Fu XY. STAT3-mediated signaling in the determination of rod photoreceptor cell fate in mouse retina. Invest Ophthalmol Vis Sci. 2004, 45: 2407-2412

Additional selected publications – in chronological order

Zhang SSM, Liu MG, Zhang C, Fu XY and **Barnstable CJ**. STAT3 activation in response to growth factors or cytokines participates in precursor proliferation of neuronal retina. *Exp Eye*

Res. 2005, **81**, 103-115.
Klein RJ, Zeiss C, Chew EY, Tsai JY, Sackler RS, Haynes C, Henning AK, SanGiovanni JP, Mane SM, Mayne ST, Bracken MB, Ferris FL, Ott J, **Barnstable C**, Hoh J. Complement factor H polymorphism in age-related macular degeneration. *Science*. 2005, **308**, 385-389. [PMCID: PMC1512523]
Zhang SS, Xu X, Li J, Liu MG, Zhao H, Soares MB, **Barnstable CJ**, Fu XY. Comprehensive in silico functional specification of mouse retina transcripts. *BMC Genomics*. 2005, **6**, 40. [PMCID: PMC1083414]
Li H, Tran VV, Hu Y, Mark Saltzman W, **Barnstable CJ**, Tombran-Tink J. A PEDF N-terminal peptide protects the retina from ischemic injury when delivered in PLGA nanospheres. *Exp Eye Res.* 2006, 83:824-33.
DeWan A, Liu M, Hartman S, Zhang S, Liu DTL, Zhao C, Tam POS, Chan WM, Lam DSC, Snyder M, **Barnstable CJ**, Pang CP, Hoh J. *HTRA1* Promoter Polymorphism in Wet Age-related Macular Degeneration. *Science* 2006, **314**, 989-992.
Zhang C, Li H, Liu MG, Kawasaki A, Fu XY, **Barnstable CJ**, Zhang SSM. STAT3 activation protects retinal ganglion cell layer neurons in response to stress. Exp Eye Res 2008, **86**:991-997.
Volpert KN, Tombran-Tink J, **Barnstable C**, Layer PG. PEDF and GDNF are key regulators of photoreceptor development and retinal neurogenesis in reaggregates from chick embryonic retina. *JOBDI* 2009, **2**:1-11. [PMCID: PMC2802504]
Liu Y, Leo LF, McGregor C, Grivitishvili A, **Barnstable CJ**, Tombran-Tink J. Pigment epithelium-derived factor (PEDF) peptide eye drops reduce inflammation, cell death and vascular leakage in diabetic retinopathy in Ins2(Akita) mice. Mol Med. 2012, 18:1387-1401. [PMCID: PMC3533643]
Popova EY, Grigoryev SA, Fan Y, Skoultchi AI, Zhang SS, **Barnstable CJ**. Developmentally regulated linker histone h1c promotes heterochromatin condensation and mediates structural integrity of rod photoreceptors in mouse retina. J Biol Chem. 2013 Jun, 288:17895-178907. [PCMID: PMC3682587]
Huang P, Huo Y, Lou LX, Li H, **Barnstable CJ**, Zhang C, Zhang SS. CD4 Positive T Helper Cells Contribute To Retinal Ganglion Cell Death In Mouse Model of Ischemia Reperfusion Injury. Exp Eye Res. 2013 Jun 20S0014-4835(13)00156-5. [Epub ahead of print]

C. Research Support

Ongoing Research Support

R01 EY13865 (Barnstable) 01/01/09 – 12/31/13
NIH/NEI
Molecular Analysis of Retinal Ganglion Cell Death
The major goals of this renewal application are to study the anti-apoptotic role of mitochondrial uncoupling proteins and to study their potential regulation by a variety of neurotrophic factors.

No Number Assigned (Barnstable) 04/01/2007-03/31/2014
Macula Vision Research Foundation
Molecular Mechanisms of Retinal Neuroprotection
The major goal of this award is to define the molecular causes of macular degeneration and the effects of specific mutations on photoreceptor structure and survival.

Completed Research Support

1 S10 OD010756-01A1 05/01/2012-05/31/2013
NIH
Leica SP5 confocal microscope for live-cell imaging
This is an equipment ward for a new shared confocal microscope

JDRF Grant Key: 17-2008-1049 (Tombran-Tink) 09/01/2008 – 08/31/2010

Juvenile Diabetes Research Foundation
Developing PEDF Therapeutics for Diabetic Retinopathy
The major goal of this project is to test the efficacy of PEDF and PEDF peptide biomimetics when applied in different ways to the eyes of animals with diabetic retinopathy.