

McLaughlin  
Research



Institute  
for  
Biomedical Sciences

*Scientific Advisory  
Committee*

**David Baltimore, Ph.D.**  
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Professor of Biology  
California Institute of  
Technology

**David Cameron, Ph.D.**  
Professor Emeritus  
Dept. of Biology  
Montana State University

**Neal G. Copeland, Ph.D.**  
Executive Director  
Institute of Molecular and  
Cellular Biology  
Singapore

**Jeffrey A. Frelinger, Ph.D.**  
Professor, Dept. of  
Microbiology and Immunology  
University of North Carolina  
Medical School

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President and Director  
Institute for Systems Biology

**Nancy A. Jenkins, Ph.D.**  
Deputy Director  
Institute of Molecular and  
Cellular Biology  
Singapore

**James A. Spudich, Ph.D.**  
Douglass M. and Nola  
Leishman Professor of  
Cardiovascular Disease  
Department of Biochemistry  
Stanford University

**Irving L. Weissman, M.D.**  
(Chairman)  
V&D Ludwig Professor and  
Director of Stanford Institute  
Of Stem Cell Biology and  
Regenerative Medicine  
Stanford University School  
of Medicine

11/28/11

US NRC Region IV  
ATTN: Carol Hill  
612 East Lamar Boulevard, Suite 400  
Arlington, Texas 76011-4125

Dear Carol,

We request the following amendments to NRC license 25-26973-01, issued to the McLaughlin Research Institute:

1) A change in Radiation Safety Officer from John R. Bermingham, Jr. to Deborah Cabin. Dr. Cabin currently is an Authorized User.

Enclosed are qualifications for Dr. Cabin, including her Curriculum Vitae and an outline of her classroom and laboratory training. Our previous RSO, Dr. John Bermingham, will be on sabbatical in 2012 but will continue as an authorized user. This letter is being sent by email; the original will be sent by traditional mail.

Sincerely,

George A. Carlson, PhD.  
Director, McLaughlin Research Institute  
gac@mri.montana.edu

RECEIVED  
DEC 5 - 2011  
DNMS

**Classroom and Laboratory training, Deborah E. Cabin, Ph.D.:**

<b>Description of Training</b>	<b>Location of Training</b>	<b>Clock Hours</b>	<b>Dates of Training</b>
Radiation physics and instrumentation	1) Dept. of Surgery, Johns Hopkins U. 2) Dept. Physiology, Johns Hopkins U. 3) National Institutes of Health	1) 0.5 2) 0.5 3) 2	1) 08/1987 2) 10/1990 3) 09/22/1998
Radiation protection	1) Dept. of Surgery, Johns Hopkins U. 2) Dept. Physiology, Johns Hopkins U. 3) National Institutes of Health	1) 4 2) 4 3) 2	1) 08/1987 2) 10/1990 3) 09/22/1998
Mathematics pertaining to the use and measurement of radioactivity	1) Dept. of Surgery, Johns Hopkins U. 2) Dept. Physiology, Johns Hopkins U. 3) National Institutes of Health	1) 0.5 2) 0.5 3) 1	1) 08/1987 2) 10/1990 3) 09/22/1998
Radiation biology	1) Dept. of Surgery, Johns Hopkins U. 2) Dept. Physiology, Johns Hopkins U. 3) National Institutes of Health	1) 1 2) 1 3) 1	1) 08/1987 2) 10/1990 3) 09/22/1998
Radiation dosimetry	1) Dept. of Surgery, Johns Hopkins U. 2) Dept. Physiology, Johns Hopkins U. 3) National Institutes of Health	1) 1 2) 1 3) 2	1) 08/1987 2) 10/1990 3) 09/22/1998
Total Hours of Training: 22 Hrs.			

## BIOGRAPHICAL SKETCH

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

NAME Deborah Eileen Cabin		POSITION TITLE Assistant Professor	
eRA COMMONS USER NAME DCABIN			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Johns Hopkins University, Baltimore, MD	B.A.	1978	Biology
Johns Hopkins University School of Medicine	Ph.D.	1996	Physiology
Johns Hopkins University School of Medicine	post-doc	1996-1998	Genetics
NHGRI/NIH, Bethesda, MD	post-doc	1998-2006	Genetics

### A. Personal Statement

My area of expertise is in mouse neurogenetics. As a graduate student, I worked on confirming a segmental trisomy mouse model for Down Syndrome by first genetically mapping mouse genes in regions of shared synteny with human Chromosome 21, then building physical contigs for finer mapping, confirming that gene content and order were shared. As a side project, I worked with the mouse neurological mutant weaver, and hoped to continue my career working on central nervous system development. However, as a post-doc, the neurodevelopment project I began working on morphed into a project focusing on the Parkinson's disease-associated protein,  $\alpha$ -synuclein, and the development of progressive mouse models for Parkinson's disease. Instead of studying early developmental phenotypes, I am now using a variety of transgenic approaches to recapitulate in mice the slowly progressive pattern of neurodegeneration seen in Parkinson's disease, and studying the mechanism of  $\alpha$ -synuclein toxicity. Since we know very little about the normal function of Parkinson's disease, I began a major mutagenesis project in mice to identify genes which when mutated cause a more severe phenotype in the absence of  $\alpha$ -synuclein than in wild type mice. The first of these sensitized mutations that we identified was in *Atp7a*, mutations in which cause Menkes disease in humans. This X-linked disorder leads to early death in males, and has a severe neurodegenerative component. The unexpected discovery of a genetic interaction between a gene linked to Parkinson's disease,  $\alpha$ -synuclein, and the Menkes disease gene, *Atp7a*, has brought together my current interest in neurodegeneration and my earlier interest in neurodevelopment.

### B. Positions and Honors

#### Science Employment:

Assistant Professor, 2006 – present, McLaughlin Research Institute, Great Falls, Montana

Faculty Affiliate, 2006 – present, Department of Cell Biology and Neuroscience, Montana State University, Bozeman, MT

Faculty Affiliate, Biomedical and Pharmaceutical Sciences, and member, Center for Functional and Structural Neuroscience, 2006-present, University of Montana, Missoula, MT

Research Technician, 1987-1990, Surgery Department, Johns Hopkins University School of Medicine, Baltimore, MD

#### Awards:

March of Dimes Birth Defects Foundation Predoctoral Fellowship. 1992 - 1994. "Introduction of Yeast Artificial Chromosomes into Embryonic Stem Cells"

#### Memberships in Scientific Societies and committee work:

Member, American Association for the Advancement of Science

Member, International Mammalian Genome Society

Committee for Mouse Chromosome 16: Co-chair, 1996-1999; Chair, 2000

IACUC, McLaughlin Research Institute

Vice-Chair, July 2009 – October 2011; Chair October 2011 - present

Grant reviewer, March 2010 – present, Veteran's Administration, Rehabilitation Research and Development 6: Aging and Neurodegenerative Disease, temporary appointment

## C. Publications

### Peer-Reviewed Publications

Buchman, TG, Cabin, DE, Porter, JM, Bulkley, GB. 1989. Change in hepatic gene expression after shock/resuscitation. *Surgery* 106:283-290.

Buchman, TG, Cabin, DE, Vickers, S, Deutschman, CS, Delgado, E, Sussman, MM, Bulkley, GB. 1990. Expression of four groups of hepatic genes is enhanced after resuscitation from cardiogenic shock. *Surgery* 108: 559-566.

Cabin, D.E. and T.G. Buchman. 1990. HEPG2 Cells Demonstrate Two Patterns of Shock-Induced Gene Expression Which are Independent, Exclusive, and Prioritized. *Surgery* 108: 902-912.

Irving, NG, Cabin, DE, Swanson, DA, Reeves, RH. 1994. Gene order is conserved within the human chromosome 21 linkage group on mouse chromosome 10. *Genomics* 21:144-149.

Cabin, DE, Hawkins, A, Griffin, C, Reeves, RH. 1995. YAC transgenic mice in the study of the genetic basis of Down syndrome. *Prog. Clin. Biol. Res.* 393:213-226.

Mjaatvedt, A.E.\*, D.E. Cabin\*, S.E. Cole, L.J. Long, G. Breitwieser and R.H. Reeves. 1995. Assessment of a mutation in the H5 domain of *Girk2* as a candidate for the *weaver* mutation. *Genome Research* 5: 453-463. PMID:8808466

\*These authors contributed equally

Cabin, D.E., K. Gardiner, and R.H. Reeves. 1996. Molecular Genetic Characterization and Comparative Mapping of the Human *PCP4* Gene. *Somatic Cell and Molecular Genetics* 22: 167-175.

Reeves, R.H., E. Rue, M.P. Citron, and D.E. Cabin. 1997. High Resolution Recombinational Map of Mouse Chromosome 16. *Genomics* 43: 202-208.

Murakami, Y., T. Nobukuni, K. Tamura, T. Maruyama, T. Sekiya, Y. Arai, H. Gomyou, M. Ohki, D. Cabin, P. Frischmeyer, P. Hunt, and R.H. Reeves. 1998. Localization of Tumor Suppressor Activity Important in Non-Small Cell Lung Carcinoma on Chromosome 11q. *Proc. Natl. Acad. Sci.* 95: 8153-8158. PMC:20945

Cabin, D.E., J. W. McKee-Johnson, L. Matesic, T. Wiltshire, E. Rue, A.E. Mjaatvedt, Y.K. Huo, J.R. Korenberg, and R.H. Reeves. 1998. Physical and comparative mapping of distal mouse chromosome 16. *Genome Research* 8: 940-950. PMC:310775

Touchman, J.W., A. Dehejia, O. Chiba-Falek, D.E. Cabin, B.M. Orrison, M.H. Polymeropoulos, and R.L. Nussbaum. 2001. Human and Mouse Alpha-Synuclein Genes: Comparative Genomic Sequence Analysis and Identification of a Novel Gene Regulatory Element. *Genome Research* 11: 78-86. PMC:311023.

Pletcher, M., T. Wiltshire, D.E. Cabin, M. Villanueva, and R.H. Reeves. 2001. Use of Comparative Physical and Sequence Mapping to Annotate Mouse Chromosome 16 and Human Chromosome 21. *Genomics* 74: 45-54.

Cabin D.E.\*, Shimazu K.\*, Murphy D., Cole N.B., Gottschalk W., McIlwain K.L., Orrison B., Chen A., Ellis C.E., Paylor R., Lu B., Nussbaum R.L., 2002. Synaptic vesicle depletion correlates with attenuated synaptic responses to prolonged repetitive stimulation in mice lacking alpha-synuclein. *J Neurosci.* 22:8797-807. PMID:12388586

\*These authors contributed equally.

Cabin, D.E., S. Gispert, D. Murphy, G. Auburger, R.R. Myers, R.L. Nussbaum, 2005. Exacerbated synucleinopathy in mice expressing A53T SNCA on a Snca null background, *Neurobio. of Aging* 26:25-35.

Cabin, D.E., M. Casey, D. Zou. Lack of a-synuclein exacerbates the phenotype of a mouse model of Menkes disease, in revision, PLoS Genetics.

Reviews and book chapters:

Cabin, D.E., A. Hawkins, C. Griffin and R.H. Reeves. 1995. YAC transgenic mice in the study of the genetic basis of Down Syndrome. **Progr. Clin. Biol. Res.** 393:213-226.

Reeves, R.H., D.E. Cabin and B.T. Lamb. 1995. Introduction of YACs into Mammalian Cells. **Current Protocols in Human Genetics**. Unit 5.12. Wiley-Liss, New York.

Cabin, D.E., M.P. Citron, J. McKee-Johnson, A.E. Mjaatvedt, and R.H. Reeves. 1996. Mouse Chromosome 16. Mammalian Genome 6: S271-S280.

Reeves, R.H. and D.E. Cabin. 1997. Mouse Chromosome 16. Mammalian Genome 7: S264-S273.

Korenberg JR, J. Aaltonen, C. Brahe, D. Cabin, N. Creau, J.M. Delabar, J. Doering, K. Gardiner, R.S. Hubert, J. Ives, A. Kessling, J. Kudoh, R. Lafreniere, Y. Murakami, M. Ohira, M. Ohki, D. Patterson, M.C. Potier, J. Quackenbush, R.H. Reeves, Y. Sakaki, N. Shimizu, E. Soeda, C. Van Broeckhoven, M.L. Yaspo. 1997. Report and abstracts of the Sixth International Workshop on Human Chromosome 21 Mapping 1996. Cold Spring Harbor, New York, USA. May 6-8, 1996. Cytogenet. Cell Genet. 79 (1-2): 21-52.

Cabin, D.E and R.H.Reeves. 1998. Mouse Chromosome 16. Mammalian Genome 8: S307-S319 and <http://www.informatics.jax.org/bin/ccr/contents?&year=1998&chr=16>.

Reeves, R.H. and D.E. Cabin. 1999. Mouse Chromosome 16. Mammalian Genome 10: 957, and <http://www.informatics.jax.org/bin/ccr/contents?&year=1999&chr=16>.

Cabin, D.E and R.H.Reeves. 2000. Mouse Chromosome 16. Mammalian Genome 11: 955-956, and <http://www.informatics.jax.org/ccr/searches/contents.cgi?&year=2000&chr=16>.

Reeves, R.H., B.T. Lamb and D.E. Cabin. 2001. Introduction of large insert DNA into Mammalian Cells and Embryos. Current Protocols in Human Genetics. Wiley-Liss, New York.

Cabin, D.E., L.E. Olson, and R.H.Reeves. 2002. Meeting Report: 15<sup>th</sup> International Mouse Genome Conference. Mammalian Genome 13: 229-233.

Cabin, D.E. and G. Carlson. 2008. Gene Mapping to Gene Targeting: Application of Mouse Genetics to Human Disease, in The Molecular and Genetic Basis of Neurological and Psychiatric Disease, ed. R.N. Rosenburg et al., Lippincott, Williams, & Wilkins, Philadelphia, PA

## D. Research Support

### Current

**1 R01-NS062121-01A1** Cabin (PI) 9/30/2008 – 7/31/2013

NIH/NINDS

Mutant human a-synuclein toxicity in mice

Major goals: The major goals of this project are 1) to generate a progressive mouse model of Parkinson's disease for the study of early stages of the disease in regions such as brainstem and enteric nervous system, and 2) to understand the mechanism of toxicity of  $\alpha$ -syn1 R21 NS077289-01uclein, a protein linked to sporadic Parkinson's disease and a familial form of the disease, using both transgenic mice and cell culture systems.

### Completed

**NIH P20 RR015583-07** Bridges (PI) 04/01/06 – 04/30/10

NIH/NCRR

COBRE Center for Structural and Functional Neuroscience

The major goals of this project are to enhance biomedical research in Montana by creating a Center of Biomedical Research Excellence to facilitate research in the structure and function of CNS proteins.

Role: Sub-project PI (Cabin) project period 5/01/08-4/30/09. Sub-project involved work to better understand the normal function of SNCA so that its contribution to Parkinson's disease can be assessed.

McLaughlin  
Research

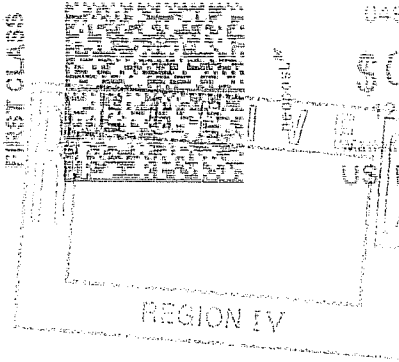


Institute  
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Biomedical Sciences

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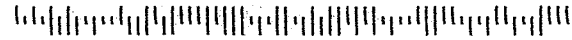
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12/02/2011

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US NRC Region IV  
ATTN: Carol Hill  
612 East Lamar Boulevard, Suite 400  
Arlington, Texas 76011-4125

76011 76011



RECEIVED

DEC - 5 2011

DNMS

No 576481

DEC - 5 2011

This is to acknowledge the receipt of your letter/application dated 11/28/11, and to inform you that the initial processing, which includes an administrative review, has been performed.

DATE

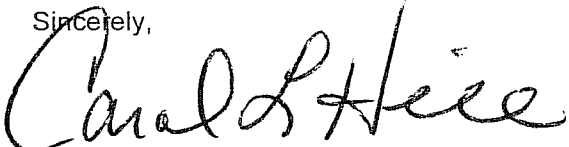
- There were no administrative omissions. Your application will be assigned to a technical reviewer. Please note that the technical review may identify other omissions or require additional information.
- Please provide to this office within 30 days of your receipt of this card:

The action you requested is normally processed within 90 days.

- A copy of your action has been forwarded to our License Fee & Accounts Receivable Branch, who will contact you separately if there is a fee issue involved.

Your action has been assigned **Mail Control Number** No. 576481.  
When calling to inquire about this action, please refer to this mail control number.  
You may call me at (817) 860-8103.

Sincerely,

  
Licensing Assistant

BETWEEN:

Accounts Receivable/Payable  
and  
Regional Licensing Branches

[ FOR ARPB USE ]  
INFORMATION FROM LTS

Program Code: 03620  
Status Code: Pending Amendment  
Fee Category: 3M  
Exp. Date: 09/30/2015  
Fee Comments: 3M IS CORRECT  
Decom Fin Assur Req: N

**License Fee Worksheet - License Fee Transmittal**

**A. REGION**

**1. APPLICATION ATTACHED**

Applicant/Licensee: MCLAUGHLIN RESEARCH INSTITUTE  
Received Date: 12/05/2011  
Docket Number: 3030962  
Mail Control Number: 576481  
License Number: 25-26973-01  
Action Type: Amendment

**2. FEE ATTACHED**

Amount: \_\_\_\_\_

Check No.: \_\_\_\_\_

**3. COMMENTS**

Signed: Carol R. Hice  
Date: 12/5/11

**B. LICENSE FEE MANAGEMENT BRANCH (Check when milestone 03 is entered / / )**

1. Fee Category and Amount: \_\_\_\_\_

**2. Correct Fee Paid. Application may be processed for:**

Amendment: \_\_\_\_\_

Renewal: \_\_\_\_\_

License: \_\_\_\_\_

3. OTHER \_\_\_\_\_  
\_\_\_\_\_

Signed: \_\_\_\_\_

Date: \_\_\_\_\_