

December 17, 2008

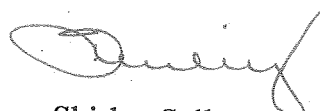
Ms. Teresa W. Borchbeck
Senior Vice President
Endowment & Foundation Services
SunTrust Bank
Post Office Box 620005
Orlando, Florida 32862-0005

Dear Teresa:

It is my pleasure to enclose the fifth progress report on The Evelyn F. McKnight Brain Institute at UAB for the period ending September 30, 2008. The enclosed materials provide information on the outstanding work of the Institute over the past year and follows the report standards provided to us. If you have any questions or need additional information, please do not hesitate to call me at (205) 937-0177 or Daphne Powell, Director of Stewardship, at (205) 934-1807.

As always, please express my heartfelt thanks to the other trustees of the McKnight Brain Research Foundation. UAB continues to be extremely proud of the work being accomplished by Dr. Sweatt and his team. We enjoyed your visit in October and look forward to the April inter-institutional meeting.

Sincerely,



Shirley Salloway Kahn, Ph.D.
Vice President of Development,
Alumni and External Relations

SSK/dbp

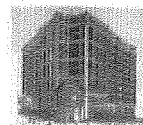
Enclosure

cc: Dr. Carol Z. Garrison
Dr. Robert R. Rich
Ms. Rebecca Gordon

OVERALL TABLE OF CONTENTS

Annual Report for the
McKnight Brain Research Foundation
Report Period: October 1, 2007, through September 30, 2008
Institution: The Evelyn F. McKnight Brain Institute
at The University of Alabama at Birmingham

1.	Summary of scientific achievements since last report	1.2
2.	Publications in peer reviewed journals	1.4
3.	Publications (other)	1.4
4.	Presentations at scientific meetings	1.4
5.	Presentations at public (non-scientific) meetings or events	1.5
6.	Awards (other)	1.5
7.	Faculty	1.5
8.	Trainees including post-doctoral, pre-doctoral, and other	1.7
9.	Clinical/Translational Programs	
	a) New programs	1.7
	b) Update on existing clinical studies	1.7
10.	Technology transfer	1.8
11.	Budget Update	2.0-2.16
	a) Status of matching funds	2.8
	b) Projected budget for coming year	2.2
	c) Extramural funding	2.3
12.	Educational Programs Focusing on Age Related Memory Loss	
	a) Scientific	1.8
	b) Public	1.8
13.	Collaborative programs with other McKnight Institutes, institutions and research programs	1.9
14.	Collaborative programs with non McKnight Institutes, institutions and research programs	1.9
15.	Plans for Future Research and/or Clinical Initiatives	1.9
16.	Endowment Report	2.12
17.	Prohibited Purpose Statement	1.9
18.	Modification to Purpose Statement	1.9
19.	Furtherance of Purpose Statement	1.10
20.	Negative Events Statement	1.10
21.	General Comments	1.10
22.	Submission Signature	1.11
18.	Appendices	Sections 3-6



DEPARTMENT of NEUROBIOLOGY

Annual Report

2008

J. David Sweatt, Ph.D.

Professor

Evelyn F. McKnight Chair, Department of Neurobiology

Director, Evelyn F. McKnight Brain Research Institute

University of Alabama at Birmingham

Shelby Biomedical Multidisciplinary Research Building

1825 University Boulevard

Birmingham, Alabama

35294

CHAIR'S OVERALL REPORT

Annual Report

McKnight Brain Research Foundation Report for Evelyn F. McKnight Brain Institute University of Alabama at Birmingham January – December 2008

This report was prepared by Dr. J. David Sweatt as Director of the Evelyn F. McKnight Brain Institute at the University of Alabama at Birmingham.

This report provides an overview and summary of the activities and accomplishments for 2008 of the UAB MBI as a whole. The format is as follows. The first section is an executive summary prepared according to the suggested format provided by the MBRF. The second section is an overall list of the Investigators of the UAB MBI. In the third section each UAB MBI Investigator with an appointment at the faculty level has prepared his or her own individual annual report for 2008, which is in a shortened and abbreviated format and includes scientific achievements, publications, awards, and collaborations. I also have presented my own individual scientific report as Evelyn F. McKnight Chair, in the final section. The appendices include copies of several documents referred to in the summary.

1. Summary of Scientific Achievements for 2008

As mentioned above, each individual McKnight Investigator's scientific accomplishments are noted in a separate section. The next few paragraphs highlight a few of the principal discoveries from the Institute this year.

This year the Sweatt laboratory continued to investigate the idea that chemical modification of DNA regulates hippocampus-dependent memory formation in the adult CNS. DNA methylation is an epigenetic molecular mechanism that is normally used by cells as part of their development and differentiation program. Thus, gene methylation has previously been studied almost exclusively as a lifelong molecular information storage mechanism put in place during development. Sweatt and his laboratory discovered that epigenetic regulation of the Brain-derived Neurotrophic Factor (BDNF) gene is dynamically regulated in the adult nervous system and that this cellular mechanism is a crucial step in memory formation. This observation will help fundamentally change the accepted paradigm for the cellular roles of chemical modification of DNA, indicating that epigenetic mechanisms like this are actively involved in plasticity and memory formation in the adult nervous system.

Another faculty member, Dr. Lynn Dobrunz is examining the role of short-term synaptic plasticity in hippocampal function. The Dobrunz laboratory, in work partially supported by a McKnight Pilot grant, has shown that target-cell specific short-term plasticity causes large activity-dependent changes in the excitatory

drive to different subsets of interneurons in hippocampus during physiologically derived stimulus patterns. This causes a reduction in excitatory drive to most interneurons relative to pyramidal cells, but a large increase in excitatory drive to somatostatin interneurons relative to both pyramidal cells and other interneurons. These mechanisms help control the dynamic balance between excitation and inhibition in hippocampus and help to regulate the gating of information into the hippocampus, information critically important for long-term memory formation.

In a collaborative project between two McKnight Investigators, Dr. Lori McMahon and Lynn Dobrunz have discovered that interactions between muscarinic acetylcholine receptors and alpha-adrenergic receptors cause induction of long-term depression in hippocampus that is dependent upon ERK activation. This project has important implications for neuromodulation of hippocampal synaptic plasticity in aging.

Several investigators made important discoveries concerning the role of glial cells in synaptic plasticity and regulation of synaptic function. Drs. Harald Sontheimer, Jacques Wadiche, and Vlad Parpura investigate the mechanisms of glial cell function in regulating synaptic transmission and synaptic plasticity. Translational components of this work have resulted in the finding that glial tumors utilize the system Xc glutamate transporter to facilitate tumor growth and invasion. Using animal studies the Sontheimer laboratory showed that tumor expansion is greatly reduced in vivo when system Xc is inhibited using a FDA-approved inhibitor. This led to a phase I clinical trial open for enrollment at UAB that is ongoing.

This year workers in Dr. Parpura's laboratory extended their discovery that the major excitatory neurotransmitter in the CNS, glutamate, can be released exocytotically by a type of glial cell, astrocytes. They found that Ca^{2+} entry through TRPC1 channels contributes to Ca^{2+} signaling in astrocytes and the consequent glutamate release from these cells. This finding has fundamental implications for the potential role of astrocytes in regulating memory, and for astrocytes as a potential site for aging-related memory dysfunction.

Finally, Dr. Gavin Rumbaugh's laboratory studies molecular mechanisms underlying synaptic plasticity and memory formation. This year Dr. Rumbaugh's laboratory made the fascinating discovery that actin-myosin dynamics underlie the stability of LTP at CA1 synapses, a finding that advances our understanding of how the cytoskeleton is regulated in plasticity and memory. In a separate line of research, the Rumbaugh lab discovered that reduced expression of a key synaptic protein, SynGAP, results in a complex and interesting behavioral memory phenotype. This phenotype is similar to mouse models of major mental illness (i.e., schizophrenia) and provides evidence that abnormal synaptic plasticity contributes to neurological and cognitive defects related to memory formation.

2. Publications in Peer Reviewed Journals

Investigators at the UAB MBI published a total of 58 research papers, reviews and commentaries in peer-reviewed journals in 2008. The journals in which these papers were published included many of the leading scientific journals in the discipline of neuroscience: Science, Nature Reviews Neuroscience, Nature Nanotechnology, Nature Neuroscience, Journal of Neuroscience, Biological Psychiatry, Biophysical Journal, Trends in Neuroscience, J. Neurophysiology, etc.

3. Publications (Other)

A. Books

In 2008, David Sweatt published an edited book, *Molecular Mechanisms of Memory*, which is one volume in a series of four books, titled "Comprehensive Handbook of Learning and Memory". Dr. Jack Byrne of the University of Texas served as the Series Editor for all four Volumes. The *Comprehensive Handbook...* is designed to be the definitive comprehensive publication in the area of learning and memory at this point in time. Dr. Sweatt's volume contains chapters by most of the leading scientist in the area of molecular and cellular mechanisms of memory, including chapters by one Nobel laureate and numerous members of the US national scientific academies. Dr. Sweatt's volume is recognized as originating from the UAB McKnight Brain Institute.

Also in 2008, Vlad Parpura Co-Edited a book, *Astrocytes in (Patho)physiology of the Nervous System*, published by Springer Press. This volume is recognized as the most comprehensive and up-to-date book on glial cell function ever published. Most of the leading investigators in the field contributed chapters for this book.

B. Book Chapters

Investigators at the UAB MBI published a total of 10 book chapters in 2008.

4. Presentations at Scientific Meetings (Also Includes Invited Research Seminars)

Investigators at the UAB MBI presented a total of 72 scientific presentations in 2008. UAB MBI Investigators presented their work at numerous prestigious institutions, including: Johns Hopkins, Yale, Emory, Tulane, the University of Wisconsin, UCLA, UT Southwestern, Vanderbilt, Baylor College of Medicine, UC Davis, and the University of Illinois. MBI Investigators also presented their work at prominent national meetings including those sponsored by the Society for Neuroscience, Molecular and Cellular Cognition Society, the NIH, the Neurochemistry Society, and the American Neurological Association.

Please note that the UAB MBI sponsored a number of prominent scientists to come visit UAB and the MBI and give research presentations concerning their own work. A list of MBI-sponsored speakers for 2008 is appended to this report.

5. Presentations at Public (Non-Scientific) Meetings or Events

Investigators at the UAB MBI presented two public-forum presentations in 2008. One was part of a nation-wide network of simultaneous presentations sponsored by the National Association for Research on Schizophrenia and Depression. These presentations occurred at leading neuroscience institutions across the nation.

6. Awards and Honors

Investigators at the UAB MBI received several national-level awards and honors in 2008. Dr. Sweatt was elected a Fellow of the American Association for the Advancement of Science (AAAS). Dr. Sweatt received a CART Award from the Rotary Clubs International. Dr. Gavin Rumbaugh was selected as UAB's sole nominee for the Keck Outstanding Young Scientist Award – winners will be announced next year. Dr. Linda Overstreet-Wadiche, a new recruit to the MBI, received her first R01 grant from the NIH. Dr. Farah Lubin was the recipient of a prestigious K99/R00 Transitions to Independence Award from the NIH. Dr. Courtney Miller was chosen as a platform speaker at the 2008 Molecular and Cellular Cognition Society Meeting. Drs. Tania Roth and Gaston Calfa were recipients of Emerging Scholars Awards from the Civitan International.

7. A. Faculty

Individual faculty reports and brief CV's are attached.

B. Recruitment

As Director of the UAB MBI, I am taking a very selective approach to making appointments of MBI Investigators. My principal criteria for appointments are scientific excellence, research interests, and collegiality. I strongly feel that focusing on these attributes and selecting only the most outstanding individuals as MBI Investigators is the best strategic plan for the long term.

CVs with publications for each of the new recruits described below are appended to this report. Three new investigators were recruited to the UAB MBI last year: Dr. Erik Roberson, Dr. Farah Lubin, and Dr. Christina Visscher.

1. **Erik Roberson, M.D., Ph.D.** was recruited to UAB from UCSF. Dr. Roberson's primary appointment is as a tenure-track Assistant Professor in the Neurology Department, and he is appointed as an Investigator of the UAB MBI with a secondary appointment in the Department of Neurobiology. Dr. Roberson's research focuses on using molecular genetic approaches to understand aging-related memory loss. Dr. Roberson also sees patients in the memory disorders clinic here at UAB.

Dr. Roberson is *The William and Virginia Spencer Neuroscience Scholar*. Presentations by Dr. Lee Dockery and David Sweatt at the UAB Endowed Professors and Chairs Dinner, concerning the UAB MBI and the importance of investigating aging-related cognitive dysfunction, led to a development opportunity involving Bill and Virginia Spencer here in Birmingham. Through the combined efforts of the UAB Development Office, the UAB MBI, and the Department of Neurology, the Spencer's committed to a \$500,000 gift to help recruit Dr. Erik Roberson here to the UAB MBI and the Neurology Department.

Dr. Roberson's CV is attached. Dr. Roberson is a clinician-scientist interested in aging-related memory dysfunction. Dr. Roberson obtained his BA *summa cum laude* in Molecular Biology from Princeton. He obtained his MD/PhD at Baylor College of Medicine, where he was a Michael DeBakey Presidential Scholar. His PhD thesis work involved investigating signal transduction mechanisms in memory formation, work he performed as a graduate student in David Sweatt's laboratory. He received his advanced medical training in Neurology at UCSF, where he was resident and Chief Resident. For his research fellowship he trained with Dr. Lennart Mucke at the UCSF Gladstone Institute and the UCSF Memory and Aging Center.

Dr. Roberson's laboratory is housed on the 11th floor of the Shelby Building in the new MBI space that just opened this year. Dr. Roberson's presence will give the MBI an important link to clinically based research on cognitive aging, in addition to benefiting from Dr. Roberson's outstanding program of laboratory research.

2. **Farah Lubin, Ph.D.** was originally recruited to UAB from Baylor College of Medicine. Dr. Lubin's primary appointment is as an Assistant Professor of Neurobiology. Dr. Lubin is an outstanding young scientist who is examining the role of *epigenetic mechanisms and transcription factor regulation in controlling memory*. Dr. Lubin is the recipient of a prestigious K99/R00 Award from the NIH. These highly competitive awards are granted to the most promising young investigators in the country, and help them establish their independent research programs by providing 5 years of support. Dr. Lubin will have her research laboratory

on the 11th floor of the Shelby building, alongside Dr. Roberson. I anticipate that these two stellar young scientists will catalyze each other's research programs.

3. **Kristina Visscher, Ph.D.** was recruited to UAB from Harvard University, and her primary appointment is as an Assistant Professor of Neurobiology. Her work on functional brain imaging is an important complement to the basic science component of the research ongoing at the UAB MBI. We were able to recruit Dr. Visscher in large part because the Civitan International fMRI human imaging center at UAB opened this year. This allowed us to initiate a new area of scientific expertise associated with the MBI, functional and behavioral studies of human cognition. Dr. Harry Sontheimer, a UAB MBI Investigator, is Director of this facility. We plan to continue to capitalize on this opportunity and expand our human clinical studies with additional faculty recruitment in this area next year. Dr. Visscher is interested in *human behavioral and functional imaging in aging-related cognitive decline*. Her presence will allow us to greatly expand our human and clinically based studies of cognitive aging.

8. **Trainees**

A. **Post Doctoral**

Four new postdoctoral fellows were recruited

B. **Pre-Doctoral**

Nine new graduate students were recruited

C. **Other**

Numerous undergraduate work-study students are employed in the MBI laboratories.

9. **Clinical/Translational Programs**

A. **New Programs**

The recruitment of Drs. Visscher and Roberson were described above so I will not reiterate these new initiatives in the clinical/translational area.

B. **Update on Existing Clinical Studies**

Not applicable

10. Technology Transfer

Not applicable

11. Budget Update

A full financial report for 2008 is attached.

12. Educational programs focusing on age related memory loss**A. Scientific**

In 2008 the Evelyn F. McKnight Institute at UAB held a scientific symposium, "Memory and Aging", which most of the Board members were able to attend. The symposium was very successful and helped promote recognition of the MBI here at UAB.

Several prominent national-level scientists came to UAB for a symposium on glial biology organized by Harry Sontheimer, a UAB MBI Investigator. While the symposium did not focus on aging and memory, the symposium generated significant national attention, and provided an excellent opportunity to showcase the MBI at UAB.

In the general realm of scientific education, in 2008 Dr. Sweatt received funding from the NIH for a graduate training program (T32) focusing on cognition and cognitive disorders. This training grant provides an excellent opportunity for recruitment to UAB of graduate students interested in cognitive aging.

Finally, in 2008 the MBI was instrumental in establishing a new undergraduate honors Neuroscience major at UAB that is the only program like it in the country – a joint offering between the undergraduate college and the School of Medicine. This will be a recruiting platform for future medical and graduate students interested in memory research.

B. Public

Last year a film crew and producer from "NOVA Science Now", a PBS-television program produced by WGBH in Boston, visited the UAB MBI. The team filmed a segment highlighting the possible use of HDAC inhibitors to treat aging-related memory disorders. The segment they produced, highlighting work from Dr. Sweatt's lab and including shots filmed at the UAB MBI, was presented on the season premier of NOVA Science Now in 2008.

13. Collaborative Programs with other McKnight Institutes, Institutions and Research Programs

UAB MBI Investigators have identified a total of 13 inter- and intra-MBI collaborations, representing all three other MBIs. More details on these collaborations are noted in the section with the individual investigator's data.

14. Collaborative Programs with Non McKnight Institutes, Institutions and Research Programs

UAB MBI Investigators have identified a total of 28 inter- and intra-institutional collaborations locally, nationally, and internationally.

15. Briefly describe plans for future research and/or clinical initiatives

Drug Trials

While we have not yet undertaken any human drug trials, the Sweatt laboratory is undertaking a drug discovery program investigating the use of Histone DeAcetylase (HDAC) inhibitors as cognition enhancing agents. Specific aspects of this project will investigate the viability of HDAC inhibitors as memory improving agents using rodent models of aging-related cognitive dysfunction. The Sweatt laboratory is collaborating with investigators at the EnVivo Pharmaceuticals for these studies, who are providing novel HDAC inhibitors for evaluation, HDAC inhibitors that are not generally available otherwise. Human clinical pilot studies with one of these compounds are now underway.

While this is at a very early stage, Merck Boston is interested in this line of pursuit and Dr. Sweatt is discussing with Merck scientists the possibility of collaborative studies with them along these lines as well.

16. If applicable, please provide endowment investment results for the report period.

A reporting of funds generated by the Evelyn F. McKnight Chair is included in the overall financial summary.

17. Were any funds used for a Prohibited Purpose during the report period?

No

18. Do you recommend any modification to the Purpose or mandates in the Gift Agreement?

No

19. Did all activities during the report period further the Purpose?

Yes

20. Please describe any negative events (loss of personnel, space, budget, etc.) that occurred during the report period and the possible impact on carrying out the Gift Agreement.

None

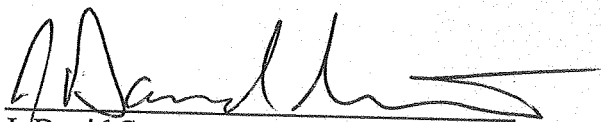
21. Please provide any general comments or thoughts not covered elsewhere – a response is not required. Please respond only if you would like to add something not otherwise covered elsewhere.

The UAB MBI is progressing in accordance with the original strategic plan for the Institute, which was outlined to the Board when the UAB MBI was dedicated in 2006. We have focused on recruiting new faculty members as was originally proposed, and counting the new MBI Director ten new faculty members from outside the institution have been added to the MBI in the last 3 years. The quality of the new investigators has been uniformly excellent.

We also are progressing nicely in developing our research infrastructure as planned. The 11th floor of the Shelby building, i.e. the final third of the MBI physical plant, was completed and we have begun occupancy this year with Drs. Roberson and Lubin occupying new labs there. Two important Core laboratories, the *MBI Mouse Behavioral Assessment Core*, and the *MBI/NIH Blueprint Rodent Physiological Assessment Core*, are in operation and provide an excellent platform for inter-Institute collaborations. These two Cores will provide excellent opportunities for expanded expertise among UAB MBI Investigators in utilizing cutting-edge genetically engineered mouse models relevant to cognitive aging. In addition, these two cores capitalize on scientific strengths of the UAB MBI and will allow for collaborative opportunities with the other two MBI's and UM Center, which in general are not historically strong in the area of mouse genetic engineering.

Finally, as planned we are now developing research programs for drug discovery (based on animal studies of the potential use of Histone De-Acetylase Inhibitors as memory enhancers) and human clinically based research (fMRI and behavioral assessment), continuing our planned expansion into these two important areas of cognitive aging research.

22. Signature, date, and title of person submitting report



J. David Sweatt, Ph.D.
Evelyn F. McKnight Chair
Director, Evelyn F. McKnight Brain Institute
Chairman, Department of Neurobiology
UAB School of Medicine

12/10/08
Date

FINANCE

Projected FY 08-09 Evelyn F. McKnight Brain Institute Budget

Category	Amount
Salary and Benefits	\$550,000
McKnight Recruit Start Up Packages	\$350,000
Recruitment Ads	\$5,000
Other McKnight Brain Institute Support	\$95,000
Total	\$1,000,000

Department of Neurobiology/Evelyn F. McKnight Brain Institute Extramural Funding Report

The Department of Neurobiology/Evelyn F. McKnight Brain Institute currently has active extramural funding of \$4,981,887 in direct costs and \$6,703,226 in total costs broken down as follows:

NIH	\$4,563,408 Direct Costs
NSF	\$ 77,745 Direct Cost
Other Foundations	\$ 340,734 Direct Costs
Total	\$4,981,887 in Direct Costs

A detailed report of grant awards is attached.

Department of Neurobiology												
Active Extramural Funding												
Fiscal Year 2008-2009												
Faculty	Role	Percent Effort	Type of Grant and Grant Number	Agency	Grant Period	Title	Current Annual			All Years		
							Direct Costs	F & A	Total	Direct Costs	F & A	Total
Brenner	PI	44%	CR R01 NS39055	NIH	08/2/06-01/31/11	Analyses and Applications of GFAP Transcription	269,166	109,764	378,930	1,082,754	492,653	1,575,407
Brenner	PI	45%	P01 NS042803	NIH-Wisconsin	07/01/08-06/30/13	Alexander Disease: Cellular and Molecular Mechanisms	154,962	69,733	224,695	774,810	348,665	1,123,475
Dobrunz	PI	60%	RO1MH65238-01A revision	NIH	12/01/02-11/30/08	Frequency Dependence of Excitatory Synaptic Transmission	175,000	78,750	253,750	875,000	393,750	1,268,750
Dobrunz	PI	0%	NSF SPIN support	NSF	04/15/05-03/31/09	REU Site: Neuroscience Research for Undergraduates at	77,745	11,300	89,045	233,236	33,900	267,136
Dobrunz	PI	5%	New R03 Grant	NIH	07/01/07-06/30/09	Developmental Changes in Excitatory Synapses in Hippocampus	49,000	22,050	71,050	98,000	44,100	142,100
Dobrunz	PI	10%	New R21 Grant	NIH	09/15/07-07/31/09	A Novel System to Study Postsynaptic Molecules that affect Presynaptic Function	112,500	50,625	163,125	247,500	111,375	358,875
Hablitz	PI	40%	RO1 NS022373 CR	NIH NINDS	04/01/07-03/31/12	Neocortical Epilepsy During Development	218,750	98,438	317,188	1,093,750	492,140	1,585,890
Hablitz	PI	5%	P30PAR-02-059	NIH NINDS	07/1/05-06/30/10	UAB Neuroscience Core Center	322,054	146,535	468,589	1,842,187	706,596	2,548,783
Hablitz	PI	25%	New R21 Grant	NIH	07/01/07-06/30/09	Kainate Modulation of Vesicular GABA Release Evoked by Natural Stimulus Patterns	131,250	59,063	190,313	275,000	123,750	398,750
Lester	PI	30%	R01 DA11940 CR Resub	NIH	06/01/04-03/31/09	Sub-unit Specific Regulation of Neuronal Nicotinic Receptors	162,613	56,914	219,527	875,000	315,000	1,190,000
Parpura	PI	30%	R01 MH069791	NIH	07/01/07-06/30/09	Calcium-Dependent Glutamate Release from Astrocytes	149,339	64,183	213,522	236,714	106,521	343,235
Pozzo-Miller	PI	60%	R01 NS040593	NIH NINDS	08/02/06-01-31/11	Actions of BDNF on Ca2+ Signals in Hippocampal Neurons	218,475	99,406	317,881	1,028,997	456,455	1,485,452

Department of Neurobiology												
Active Extramural Funding												
Fiscal Year 2008-2009												
Faculty	Role	Percent Effort	Type of Grant and Grant Number	Agency	Grant Period	Title	Current Annual			All Years		
							Direct Costs	F & A	Total	Direct Costs	F & A	Total
Pozzo-Miller	PI	25%	New R21 Grant	NIH-NINDS	04/01/07-03/31/09	Role of BDNF in Dendritic Pathologies Caused by Rett-associated MeCP2 Mutations	100,000	45,500	145,500	275,000	125,125	400,125
Pozzo-Miller -	PI		Postdoctoral Fellowship	IRSF	10/01/08-09/30/10	Hippocampal Network Excitability in MECP2 Deficient Mice: A Voltage-Sensitive Dye	50,000	-	50,000	100,000	-	100,000
Pozzo-Miller -	PI		Postdoctoral Fellowship	IRSF	10/01/08-09/30/10	TRPC3-Mediated Membrane Currents as Biosensors of Endogenous BDNF Release: Is	50,000	-	50,000	100,000	-	100,000
Sontheimer	PI	0%	T32GM008111	NIH NIGMS	07/01/08-06/30-13	Predoctoral Training in Cell and Molecular Biology	198,432	12,131	210,563	992,160	60,655	1,052,815
Sontheimer	PI		R01NS036692 CR	NIH NINDS	04/01/08-03/31/13	The Role of Ion Transport in Glioma Cell Migration,	218,750	98,438	317,188	1,093,750	492,190	1,585,940
Sontheimer	PI		R01NS031234 CR	NIH NINDS	03/1/07-11/30/11	Properties and Function of Glia Ion Channels	218,750	98,438	317,188	875,000	393,752	1,818,750
Sontheimer	PI	30%	R01 NS052634	NIH NINDS	07/01/05-06/30/09	Amino-Acid Transport and the Biology of Human Gliomas	219,267	99,766	319,033	925,000	419,332	1,345,490
Sontheimer	PI		R01 NS052634 Minority Supplement	NIH NINDS	01/01/08-04/30/09	Amino-Acid Transport and the Biology of Human Gliomas	8,924	4,016	12,940	35,696	16,063	51,759
Sontheimer/B omben	PI/Mentor		New NRSA	NIH-NINDS	07/01/08-06/30/10	Role of Transient Potential Canonical Channels in Glioma Cell Biology	29,764	-	29,764	29,764	-	29,764
Sweatt	PI	40%	R01MH057014	NIH-NIMH	04/01/06-02/28/10	Biochemical Mechanisms of Long-Term Potentiation	300,032	136,515	436,547	1,331,033	605,620	1,936,653

Department of Neurobiology												
Active Extramural Funding												
Fiscal Year 2008-2009												
Faculty	Role	Percent Effort	Type of Grant and Grant Number	Agency	Grant Period	Title	Current Annual			All Years		
							Direct Costs	F & A	Total	Direct Costs	F & A	Total
Johnston/Sweatt	PI	30%	P01NS037444-07 Subcontract	NIH/NINDS UT-Austin	06/01/06-05/31/09	Project 2: Molecular Mechanisms for Modulation of Hippocampal Neuron Potassium Channels	202,456	91,105	293,561	649,209	295,389	944,598
Sweatt	PI	20%	R01 NS013546 CR	NIH-NINDS	04/01/08-03/31/13	Trophic Interaction of Nerve and Muscle						
Sweatt	Core Director	5%	NIH P30 NS057098	NIH-NINDS	09/04/06-08/31/11	Alabama Neuroscience Blueprint Core Center - Core F	200,900	90,405	291,305	1,025,000	461,250	1,486,250
Sweatt	PI	5%	CART	CART	05/01/08-04/30/10	Epigenetic Mechanisms in Alzheimer's Disease-Related Memory Loss	258,988	82,795	238,056			
Sweatt	PI		NINDS Training Grant	NINDS	04/01/08-03/31/13	Training Program in the Neurobiology of Cognition and cognitive Disorders	100,000	-	100,000	200,000	-	200,000
Sweatt	PI		5R13 MH073327 Conference Grant	NIMH	08/01/07-07/31/10	Molecular and Cellular Cognition Meeting	135,088	8,311	143,399	675,440	41,555	716,995
Sweatt	PI		Pharmaceutical Award	EnvivoPharma, Inc.	11/24/08-11/23/09	En Vivo Research Study	30,000	-	30,000	90,000	-	90,000
							60,734	27,330	88,064			

Department of Neurobiology												
Active Extramural Funding												
Fiscal Year 2008-2009												
Faculty	Role	Percent Effort	Type of Grant and Grant Number	Agency	Grant Period	Title	Current Annual			All Years		
							Direct Costs	F & A	Total	Direct Costs	F & A	Total
Sweatt/Lubin	PI/Mentor		New K99/K00	NIH	03/01/08-02/28/09	Epigenetic mechanisms of gene regulation in long-term memory formation						
Sweatt/ Roth	PI/Mentor		Young Investigator Award	NARSAD	07/01/08-06/30/10	Stress-Induced Changes in DNA Methylation as a Molecular Mechanism Underlying the Long-Term Impact of Caregiver Abuse	78,100	6,248	84,348	598,505	238,495	837,000
Sweatt/Miller	PI/Trainee	0%	1 F32 NS057953-01A1	NINDS	08/01/07-07/31/09	Epigenetic Control of Learning and Memory	30,000	-	30,000	60,000	-	60,000
Wadiche, Linda	PI	20%	Foundation Grant	Epilepsy Foundation	01/01/07-12/31/08	Functional Integration of Newborn Neurons in Epileptogenesis	51,278		51,278	153,822		153,822
Wilson	PI	50%	New RO1 2/03	NIH	01/1/04-11/30/08	The role of Usp 14 in regulating neuronal function	50,000	-	50,000	100,000	-	100,000
Wilson	Core Director	5%	NIH P30 NS057098	NIH-NINDS	09/04/06-08/31/11	Alabama Neuroscience Blueprint Core Center - Core B	197,340	88,803	286,143	1,040,625	468,280	1,508,905
							152,230	68,504	220,734			
							4,981,887	1,825,066	6,703,226	19,012,952	7,242,611	26,806,719
						Total Active Grants						

MCKNIGHT BRAIN RESEARCH INSTITUTE AT UAB
2008 ANNUAL REPORT
FINANCIAL SUPPLEMENT

2.8

In compliance with Section 5.3 of the gift agreement between the Evelyn F. McKnight Brain Research Foundation (MBRF) and UAB, this income and distributions report is provided as a supplement to the annual report on the McKnight Brain Research Institute (MBRI) at UAB.

In compliance with Sections 8.2.2 and 10.3 of said gift agreement, UAB ensures that the contributions from the MBRF and the distributions from the endowed chair have been used solely for the purpose of promoting research and investigation of the brain in the fundamental mechanisms that underlie the neurobiology of memory with a clinical relevance to the problems of age-related memory loss.

In compliance with Sections 6, 8.2.2 and 10.3 of said gift agreement, UAB ensures that no portion of the contributions received from the MBRF or distributions from the endowed chair were used directly or indirectly to construct, purchase, improve, or maintain real property; to pay overhead or indirect costs; or for anything other than direct expenditures in furtherance of the purpose of the fund.

Fiscal Year	Item	MBRF Deposits	Endowment Distributions	MBRF Funds Expended or Encumbered	Matching Funds Expended or Encumbered
2004		\$ 1,000,000			
		\$ 1,000,000			
	Endowed Professorship			\$ 500,000	
	Foster Visit			\$ 223	
	MBRI Ad			\$ 3,016	
	fMRI				\$ 2,900,000
FY04 Totals		\$ 2,000,000	\$ -	\$ 503,239	\$ 2,900,000
2005		\$ 1,000,000			
	Friedlander Salary			\$ 18,780	
	Three Pilot Projects			\$ 120,000	
	MBRI Ads			\$ 3,990	
	Spendable Earnings		\$ 23,654		
	Chair Recruitment				\$ 49,305
	Sontheimer Retention (fMRI)				\$ 694,500
FY05 Totals		\$ 1,000,000	\$ 23,654	\$ 142,770	\$ 743,805
2006		\$ 1,000,000			
	Sweatt Salary			\$ 56,229	
	Endowed Chair Conversion			\$ 1,000,000	
	Move/Furnish Shelby Space				\$ 307,292

MCKNIGHT BRAIN RESEARCH INSTITUTE AT UAB
2008 ANNUAL REPORT
FINANCIAL SUPPLEMENT

2.9

Fiscal Year	Item	MBRF Deposits	Endowment Distributions	MBRF Funds Expended or Encumbered	Matching Funds Expended or Encumbered
	Rumbaugh Salary			\$ 111,960	
	L. Wadiche Salary			\$ 111,960	
	J. Wadiche Salary			\$ 111,960	
	Four Pilot Projects			\$ 160,000	
	Sweatt Start-up Package				\$ 949,000
	L. Wadiche Start-up Package			\$ 700,000	
	J. Wadiche Start-Up Package				\$ 700,000
	Rumbaugh Start-Up Package				\$ 800,000
	Laser				\$ 170,000
	fMRI Upgrade				\$ 150,000
	Lahti Recruitment (fMRI)				\$ 1,275,923
	Akella Appointment (fMRI ops)				\$ 51,542
	Event Facilitation Costs				\$ 10,450
	Spendable Earnings		\$ 66,783		
FY06 Totals		\$ 1,000,000	\$ 66,783	\$ 2,252,109	\$ 4,414,207
2007		\$ 1,000,000			
	Sweatt Salary			\$ 79,478	
	Move/Furnish Shelby Space				\$ 197,428
	Rumbaugh Salary			\$ 116,402	
	L. Wadiche Salary			\$ 93,122	
	J. Wadiche Salary			\$ 116,402	
	V. Parpura Salary			\$ 123,630	
	Three Pilot Projects			\$ 99,000	
	Sweatt Start-up Package (\$65,898 of which went towards establishing the MBRI Physiology and Behavior Cores)				\$ 500,000

MCKNIGHT BRAIN RESEARCH INSTITUTE AT UAB
2008 ANNUAL REPORT
FINANCIAL SUPPLEMENT

2.10

Fiscal Year	Item	MBRF Deposits	Endowment Distributions	MBRF Funds Expended or Encumbered	Matching Funds Expended or Encumbered
	V. Parpura Start-Up Package			\$ 250,000	\$ 750,000
	Akella Appointment (fMRI ops)				\$ 39,181
	D. Knight Recruitment (fMRI)				\$ 507,948
	Furniture for Evelyn F. McKnight Student Resource Room and Student Conference Room			\$ 11,091	
	Neurolynx Data Acquisition Recording System (MBRI/NIH Blueprint Rodent Physiological Assessment Core)			\$ 46,595	\$ 49,867
	Furniture for 11th Floor Conference Room			\$ 8,539	
	Spendable Earnings		\$ 67,194		
FY 07 Totals		\$ 1,000,000	\$ 67,194	\$ 944,259	\$ 2,044,424
2008		\$ 1,000,000			
	Sweatt Salary			\$ 83,020	
	Rumbaugh Salary			\$ 116,402	
	L. Wadiche Salary			\$ 98,942	
	J. Wadiche Salary			\$ 116,402	
	V. Parpura Salary			\$ 123,630	
	F. Lubin Salary			\$ 9,819	
	Three Pilot Projects			\$ 124,000	
	Evelyn F. McKnight Interdisciplinary Retreat			\$ 10,434	\$ 4,000
	F. Lubin Start Up Package			\$ 250,000	\$ 450,000
	McKnight Recruitment Ads			\$ 5,530	
	E. Roberson Start Up Package			\$ 125,000	\$ 700,000

MCKNIGHT BRAIN RESEARCH INSTITUTE AT UAB
2008 ANNUAL REPORT
FINANCIAL SUPPLEMENT

2.11

Fiscal Year	Item	MBRF Deposits	Endowment Distributions	MBRF Funds Expended or Encumbered	Matching Funds Expended or Encumbered
	Sweatt Start Up Package				\$ 176,000
	Spendable Earnings		\$ 75,731		
FY 08 Totals		\$ 1,000,000	\$ 75,731	\$ 1,063,179	\$ 1,330,000
Grand Totals		\$ 6,000,000	\$ 233,362	\$ 4,905,555	\$ 11,432,436

Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging

Date Established: 10/1/2004

This endowment was initially created as an endowed professorship which was converted to an endowed chair by the University's Board of Trustees at its meeting on February 3, 2006.

Current Occupant: John David Sweatt, M.D.

Occupancy Date: February 3, 2006

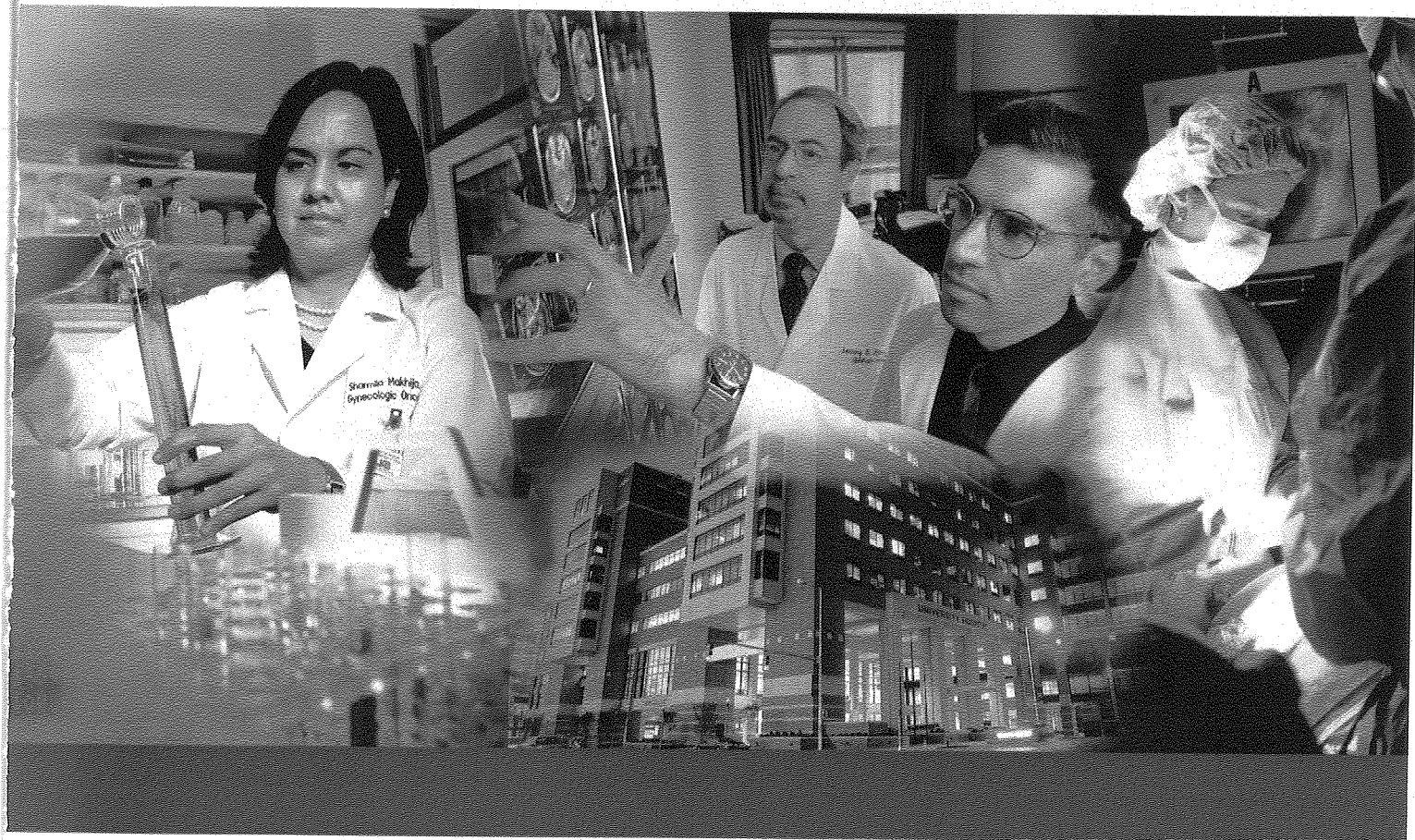
Total Contributions: \$1,500,000 ¹

Market Value at 9/30/08: \$1,512,729 ²

**Projected Spendable
Earnings for FY 2008/09:** \$81,958 ³

-
1. Contributions may be added to endowment principal at any time.
 2. Market value is the principal and reinvested earnings plus market appreciation.
 3. The projected spendable earnings amount was calculated using 5% of a moving market average of the unit value of the University System's Pooled Endowment Fund for the previous twelve quarters ended December 31, 2007.

INSPIRATION UNDERSTANDING SUCCESS INGENUITY INNOVATION



UAB Pooled Endowment Fund Investment Report

as of September 30, 2008

UAB Development Office

Investment Report

In 1978, the University's Board of Trustees created The University of Alabama Pooled Endowment Fund (UAPEF) managed by the Chancellor's Office. The Board adopted an investment policy and established an Investment Committee, which oversees investment activities, monitors performance of professional money managers, and ensures the prudent control of the investment of funds. The Investment Committee is responsible for recommending investment objectives and policies and for implementing such policies. The Board seeks to enhance the value of individual endowments by pooling these assets. A pool of assets provides more options for investment, stronger diversification, superior returns and lower management fees.

The UAPEF had a ten-year annualized investment return of 7.9% for the period ending December 31, 2007, compared to a return of 6.8% for the custom index.* For the quarter ending September 30, 2008, the UAPEF posted a -9.6% return. The Board of Trustees is committed to a diversified investment strategy in order to preserve the real purchasing power of the principal and to provide a stable source of perpetual financial support to the University.

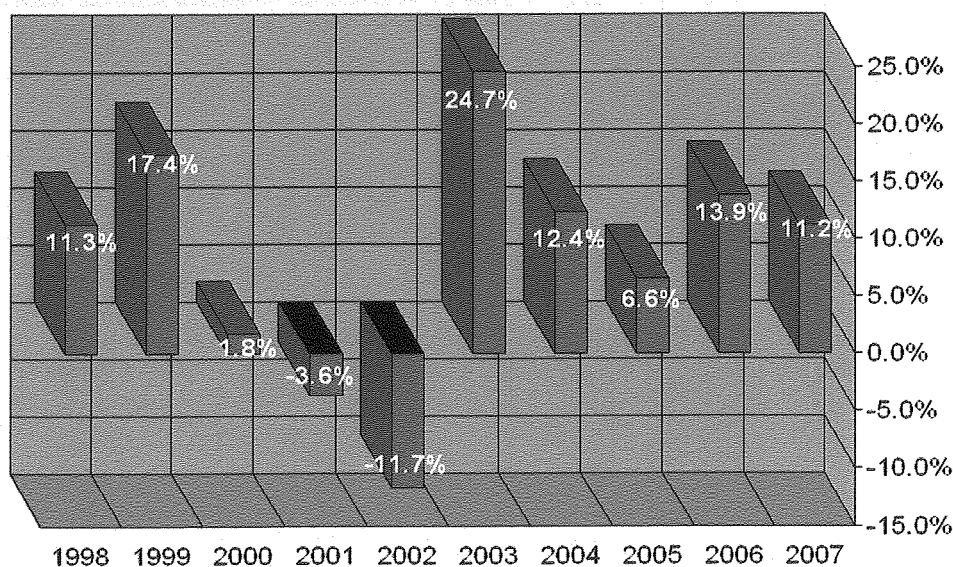
As of September 30, 2008, the market value of the UAPEF was \$862.3 million. Of this amount, 34.5%, or \$297.2 million, is attributable to UAB and the Hospital. As state assistance shrinks and the costs of higher education rise, endowment support becomes more critical to the University's growth and ability to maintain its standards of excellence.

Asset Allocation

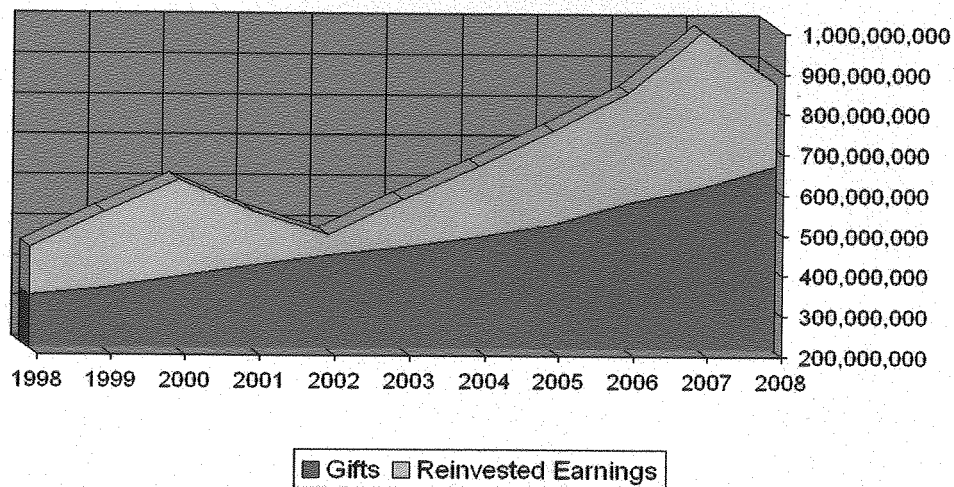
The Board seeks superior investment returns through professional money management. Assets of the UAPEF are managed by 43 professional investment firms. The UAPEF also has an investment consultant, Hammond Associates, with expertise in investment policy development, spending policy analysis, manager evaluation and selection, and performance evaluation. The Board believes multiple external managers provide (1) greater diversification of investment philosophy, judgment, investment opportunity and risk exposure; (2) a positive influence on performance through long-term competition; and (3) a broader basis on which to compare and judge investment performance.

*The Custom Index reflects a blend of 55% S&P 500 Index, 15% MSCI EAFE Index, 15% Lehman Aggregate Index, 5% NCREIF Index, and 10% 90-Day T-Bill+3%. Prior to third quarter 2004, the Custom Index reflected the Pooled Endowment Fund's previous asset allocation.

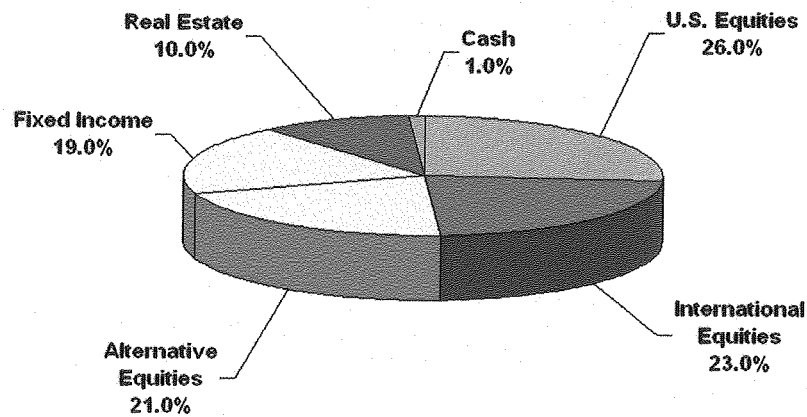
UAPEF Rates of Return: 12/31/1998-12/31/2007



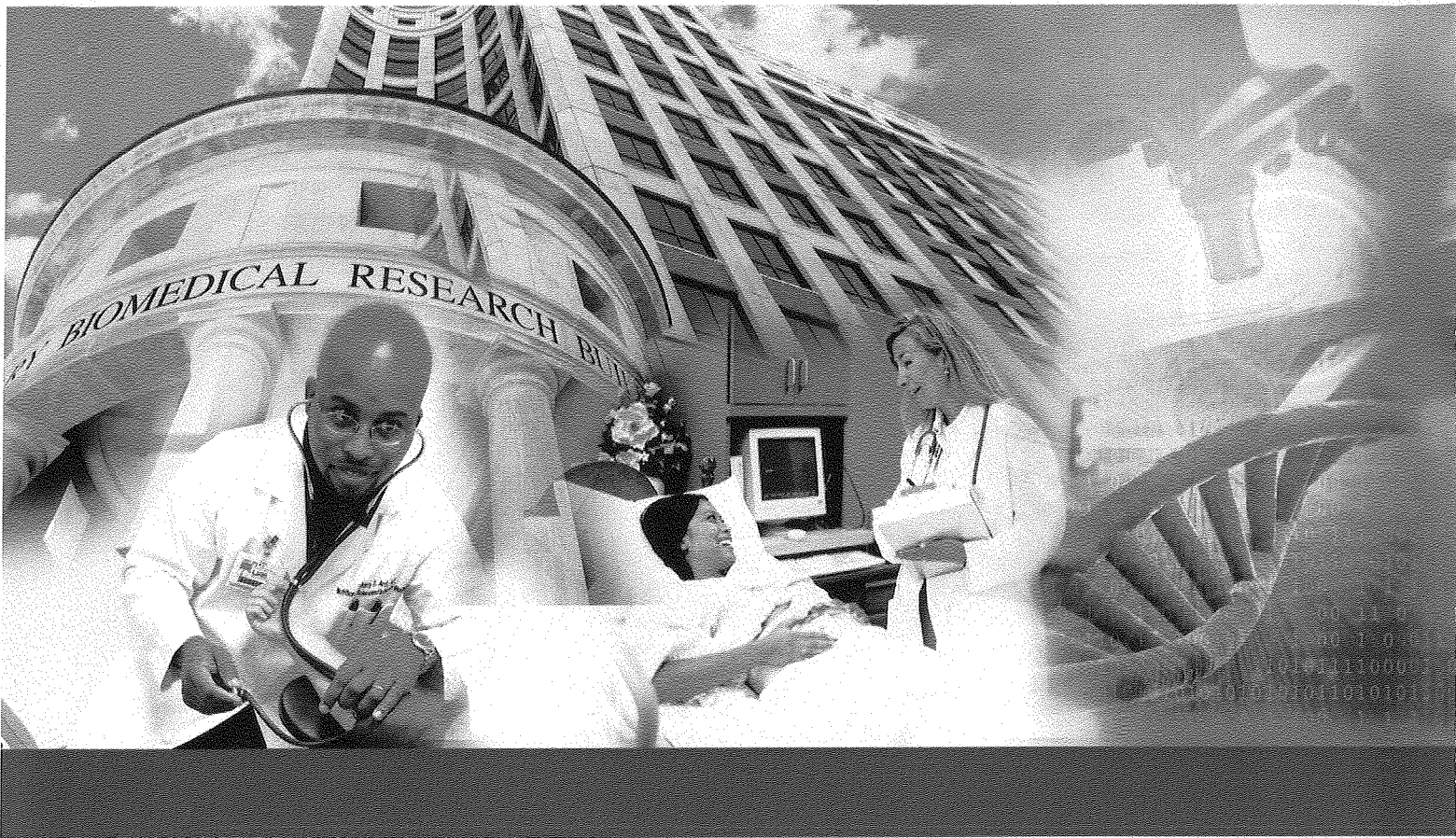
UAPEF Growth in Endowment Funds September 30, 1998 - September 30, 2008



Asset Allocation at 09/30/08



KNOWLEDGE SPIRIT ACHIEVEMENT DISCOVERY OPPORTUNITY VISION



UAB UNIVERSITY DEVELOPMENT

Daphne B. Powell
Director of Stewardship
AB 1228
1530 3rd Avenue South
Birmingham, Alabama 35294-0112
205.934.1807
daphnep@uab.edu

This publication was produced in house.

INDIVIDUAL FACULTY REPORTS

Investigators of the UAB McKnight Brain Institute:

- J. David Sweatt, Ph.D.
 E. F. McKnight Chair, Dept of Neurobiology
 Director, Evelyn F. McKnight Brain Institute
Area of Interest: Signal transduction and transcriptional control in memory and aging.
- John Hablitz, Ph.D.
 Professor, Neurobiology
 Associate Director, Evelyn F. McKnight Brain Institute at UAB
Area of Interest: Modulation of excitability in neocortical circuits.
- Harry Sontheimer, Ph.D.
 Professor, Neurobiology
 Director, Center for Glial Biology in Medicine, at UAB
Area of Interest: Cell biology of glial function.
- Michael Brenner, Ph.D.
 Professor, Neurobiology
Area of Interest: Glial cell biology, Alexander Disease.
- David Standaert, M.D./Ph.D.
 Professor of Neurology
 Director, UAB Movement Disorders Center
Area of Interest: Striatal molecular and cellular biology, Parkinson's Disease.
- Robin Lester, Ph.D.
 Associate Professor, Neurobiology
Area of Interest: Nicotinic receptors in CNS function.
- Lucas Pozzo-Miller, Ph.D.
 Associate Professor, Neurobiology
Area of Interest: Mechanisms controlling dendritic spine morphology.
- Lori McMahon, Ph.D.
 Associate Professor, Physiology and Biophysics
Area of Interest: Hormonal control of synaptic plasticity in aging.
- Anne Thiebert, Ph.D.
 Associate Professor, Neurobiology
Area of Interest: PI-3-Kinase signal transduction in neuronal cell biology.
- Lynn Dobrunz, Ph.D.
 Assistant Professor, Neurobiology
Area of Interest: Regulation of short-term synaptic plasticity in the hippocampus.
- Scott Wilson, Ph.D.
 Assistant Professor, Neurobiology
Area of Interest: The ubiquitin/proteasome system in neuronal function.

Recent UAB McKnight Institute New Faculty Recruits:

2006 Recruits:

- Linda Overstreet Wadiche, Ph.D. (Recruited from the Vollum Institute)
 Assistant Professor, Neurobiology
Area of Interest: Adult neurogenesis in the dentate gyrus.
- Jacques Wadiche, Ph.D. (Recruited from the Vollum Institute)
 Assistant Professor, Neurobiology
Area of Interest: Synaptic plasticity and function in the cerebellum.

Gavin Rumbaugh, Ph.D. (Recruited from Johns Hopkins)
 Assistant Professor, Neurobiology
Area of Interest: Actin-myosin dynamics and MAPK signaling in plasticity and memory.

2007 Recruits:

David Knight, Ph.D. (Recruited from the NIH)
 Assistant Professor, Psychology
Area of Interest: Human imaging approaches to investigating memory.
 Vlad Parpura, M.D., Ph.D. (Recruited from the Univ. of California, Riverside)
 Associate Professor, Neurobiology
Area of Interest: Imaging approaches to investigating synaptic and glial cell function.
 Tong Ye, Ph.D. (Recruited from Duke University)
 Assistant Professor, Neurobiology
Area of Interest: In vivo imaging, 2-photon imaging.

2008 Recruits:

Kristina Visscher, Ph.D. (Recruited from Harvard)
 Assistant Professor, Neurobiology
Area of Interest: Human imaging approaches to investigating memory.
 Erik Roberson, M.D., Ph.D. (Recruited from the Univ. of California, San Francisco)
 Assistant Professor, Neurology and Neurobiology
Area of Interest: Using genetically engineered mice to investigate aging-related memory dysfunction. Dr. Roberson also sees patients at the aging-related memory disorders clinic here at UAB.
 Farah Lubin, Ph.D. (Recruited from Baylor College of Medicine and UAB)
 Assistant Professor, Neurobiology
Area of Interest: Epigenetic mechanisms in memory formation and memory dysfunction.

UAB McKnight Research Scientists:

Courtney Miller, Ph.D.
 Scientific Director, UAB McKnight Rodent Behavior Core
Area of Interest: DNA methylation in memory formation.
 Susan Campbell, Ph.D.
 Scientific Director, UAB McKnight Synaptic Plasticity Core
Area of Interest: Epigenetic control of neuronal biophysical properties.
 Eric Roth, Ph.D.
 Scientist, UAB McKnight Synaptic Plasticity Core
Area of Interest: Place cells in the hippocampus.

UAB McKnight Pilot Grant Awardees 2008:

The 3rd Annual Evelyn F. McKnight Brain Research Foundation Research Grant award winners were chosen from a group of highly competitive applications. Three projects were selected to receive a maximum of \$33,000 each for the year. The 2008

awardees were: Dr. Inga Kadish, Department of Cell Biology; Dr. David Clark, Department of Neurology; and Dr. Anne Theibert, Department of Neurobiology. Using different approaches, each recipient will be investigating various aspects of processes likely to be involved in normal aging. The awards allow the recipients to gather sufficient preliminary data for preparation of applications for extramural NIH funding.

Inga Kadisha, Ph.D.

Assistant Professor, Cell Biology

Area of Interest: Astrocyte inflammatory responses in aging-related memory loss.

Anne Thiebert, Ph.D.

Associate Professor, Neurobiology

Area of Interest: PI-3-Kinase signal transduction in neuronal cell biology.

David Clark, M.D.

Assistant Professor, Neurology

Area of Interest: Human neurimaging approaches to understanding aging-related memory loss.

**McKnight Brain Research Foundation
Annual Report
2008**

**J. David Sweatt, Ph.D.
Evelyn F. McKnight Chair
University of Alabama, Birmingham**

This is an individual report for Dr. Sweatt as Evelyn F. McKnight Endowed Chair.

1. Summary of Scientific Achievements for 2008

While a number of discoveries are described in the research publications listed in section 2 below, I will highlight only two of the principal discoveries from the laboratory this year.

One of the most important projects that we have pursued since I joined the Evelyn F. McKnight Institute concerns our investigations into whether methylation of DNA regulates hippocampus-dependent memory formation. DNA methylation is a covalent chemical modification of DNA catalyzed by DNA methyltransferases (DNMTs). DNA methylation is a potent mechanism for regulating gene expression, and DNA methylation is associated with transcriptional silencing. Gene methylation has previously been studied almost exclusively as a lifelong molecular information storage mechanism put in place during development. However, long-term memory formation in the adult nervous system also requires selective changes in gene expression. In one series of studies published this year we determined the contribution of DNA methylation to learning-induced changes in *Brain-derived Neurotrophic Factor (BDNF)* gene expression in the adult hippocampus. Contextual fear learning induced differential regulation of exon-specific *bdnf* mRNAs (I, IV, VI, IX) that was associated with changes in *bdnf* DNA methylation and altered local chromatin structure. Infusions of a DNA methyltransferase inhibitor significantly altered *bdnf* DNA methylation and triggered changes in exon-specific *bdnf* mRNA levels, indicating that altered DNA methylation is sufficient to drive differential *bdnf* transcript regulation in the hippocampus. In addition, NMDA receptor blockade prevented memory-associated alterations in *bdnf* DNA methylation, resulting in a block of altered *bdnf* gene expression in hippocampus and a deficit in memory formation. These results suggest epigenetic modification of the *bdnf* gene as a mechanism for isoform-specific gene readout during memory consolidation. The paper containing these results (Lubin et al, *Journal of Neuroscience* 2008) was cited by The Faculty of 1000 as one of the most important papers published in the biomedical sciences in 2008.

A second series of studies investigated molecular epigenetic mechanisms underlying life-long perpetuation of memory. Childhood maltreatment and early trauma leave lasting imprints on neural mechanisms of cognition and emotion. Using a rat model of infant maltreatment by a caregiver, we investigated whether early-life adversity leaves lasting epigenetic marks at the *Brain-derived Neurotrophic Factor (BDNF)*

gene in the CNS. In these experiments, during the first postnatal week we exposed infant rats to stressed caretakers that predominately displayed abusive behaviors. We then assessed DNA methylation patterns and gene expression throughout the life span, as well as DNA methylation patterns in the next generation of infants. We found that early maltreatment produced persisting changes in methylation of *BDNF* DNA that caused altered *BDNF* gene expression in the adult prefrontal cortex. Furthermore, we observed altered *BDNF* DNA methylation in offspring of females that had previously experienced the maltreatment regimen. These results highlight an epigenetic molecular mechanism potentially underlying lifelong and transgenerational perpetuation of changes in gene expression and behavior incited by early experience. This work is now in press in *Biological Psychiatry*, and was highlighted at a press conference at the annual Society for Neuroscience meeting this year.

Overall our work received considerable press attention this year, being profiled in a number of newspaper and magazine articles. In addition, our work was highlighted nationally on PBS as part of the NOVA series of television programs.

2. Publications in Peer Reviewed Journals

Miller, C.A., Campbell, S., and Sweatt, J.D. DNA methylation and histone acetylation work in concert to regulate memory formation and synaptic plasticity. (2008) *Neurobiology of Learning and Memory* 89:599-603 .

Bracchi-Ricard, V., Brambilla, R., Levenson, J., Hu, W.H., Bramwell, A., Sweatt, J.D., Green, E.J., and Bethea, J.R. (2008) Astroglial nuclear factor-kappaB regulates learning and memory and synaptic plasticity in female mice.. *J Neurochem.* 104:611-23 .

Nicholas, A.P., Lubin, F.D., Hallett, P.J., Vattam, P., Ravenscroft, P., Bezard, E., Zhou, S., Fox, S.H., Brotchie, J.M., Sweatt, J.D., Standaert, D.G. (2008) Striatal histone modifications in models of levodopa-induced dyskinesia. *J. Neurochem.* 106:486-94.

Samuels, I.S., Karlo, J.C., Faruzzi, A.N., Pickering, K., Herrup, K., Sweatt, J.D., Saitta, S.C., and Landreth, G.E. (2008) Deletion of ERK2 Mitogen-Activated Protein Kinase Identifies Its Key Roles in Cortical Neurogenesis and Cognitive Function. *J. Neurosci.* 28 6983-6995.

Ahn, H.J., Hernandez, C.M., Levenson, J.M., Lubin, F.D., Liou, H.C., and Sweatt, J.D. (2008) c-Rel, an NF-kappaB family transcription factor, is required for hippocampal long-term synaptic plasticity and memory formation. *Learning and Memory* 15:539-49.

Lugo, J.N., Barnwell, L.F., Ren, Y., Lee, W.L., Johnston, L.D., Kim, R., Hrachovy, R.A., Sweatt, J.D., Anderson, A.E. (2008) Altered phosphorylation and localization of the A-type channel, Kv4.2 in status epilepticus. *J. Neurochem.* 106:1929-40.

Schrader, J.A., Ren, Y., Cheng, F., Bui, D., Sweatt, J.D., and Anderson, A.E. (2008) Kv4.2 is a locus for PKC and ERK/MAPK cross-talk. *Biochemical J.*, in press.

Lubin, F.D., Roth, T.L., and Sweatt, J.D. (2008) Epigenetic regulation of BDNF gene transcription in the consolidation of fear memory. *J. Neuroscience* 28: 10576-10586.

Roth, T.L., Lubin, F.D., Funk, A.J., and Sweatt, J.D. (2009) Lasting epigenetic influence of early-life adversity on the BDNF gene. *Biological Psychiatry*, in press.

Klann, E., and Sweatt, J.D. (2008) Protein synthesis is a trigger for long-term memory formation. *Neurobiology of Learning and Memory* 89:247-59

Roth, T.L., and Sweatt, J.D. (2008) Rhythms of memory. *Nature Neuroscience* 11:993-4.

Sweatt, J.D. (2009) Experience-Dependent Epigenetic Modifications in the Central Nervous System. *Biological Psychiatry*, in press.

3. Publications (Other)

Books

Sweatt, J.D., Ed. *Molecular Mechanisms of Memory*
One volume in a series of four books, "Comprehensive Handbook of Learning and Memory". Jack Byrne, Series Editor. 2008, Elsevier, Ltd.

In preparation: Sweatt, J.D., *Mechanisms of Memory, 2nd Edition*
To be published in mid 2009 by Elsevier/Academic Press

Book Chapters

Sweatt, J.D. Cellular Basis of LTP. In: Comprehensive Handbook of Learning and Memory: Molecular Mechanisms of Memory. J.D. Sweatt, ed., J.H. Byrne, series editor. in press. Elsevier, London, 2008.

Sweatt, J.D. The NMDA Receptor. In: Comprehensive Handbook of Learning and Memory: Molecular Mechanisms of Memory. J.D. Sweatt, ed., J.H. Byrne, series editor. in press. Elsevier, London, 2008.

Byrne, J.H. LaBar, K.S., LeDoux, J.E., Schafe, G.E., Sweatt, J.D. and Thompson, R.F.. Learning and Memory: Basic Mechanisms. In Byrne and Roberts, eds, Molecular Neuroscience, Academic Press/Elsevier. 2008 (in press).

4. Presentations at Scientific Meetings (also includes invited research seminars)

UC Davis, Molecular Biology Seminar Series
 University of Pittsburgh, Department of Neuroscience
 Northwestern University School of Medicine
 Molecular and Cellular Cognition Society, invited speaker, FENS satellite meeting
 FENS Symposium speaker
 American Neurological Association, invited speaker 2008 annual meeting
 UPenn, Mahoney Institute
 Northwestern Univ, Children's Memorial Research Center
 Nature Neuroscience/IPSEN Conference on Epigenetics in Behavior, invited speaker
 Vanderbilt, Pharmacology Dept Post-doctoral Training Program
 EnVivo Pharmaceuticals
 Constellation Pharmaceuticals

Invited for 2009 -

Case Western, Department of Neuroscience
 Harvard, Children's Hospital Program in Neurobiology
 NYU, Center for Neural Science
 Weill Cornell Medical School, Neuroscience Colloquium
 Neuroscience Center Dartmouth, Neuroscience Day keynote speaker

5. Presentations at Public (Non-Scientific) Meetings or Events

Lecture - "The Neurobiology of Creativity", UAB Medical Scientist Training Program *Art in Medicine* lecture series

6. Awards and Honors

Elected Fellow of the American Association for the Advancement of Science (AAAS)
 Rotary Clubs International CART Award, 2008

7. Faculty Reports - N/A

8. Trainees

A. Post doctoral

B. Pre-Doctoral

I recruited one new student to my laboratory this year, Faraz Sultan. Faraz is an outstanding M.D./Ph.D. student supported by the UAB Medical Scientist Training Program. Faraz is an honors graduate from Rice University and will be working on the role of DNA methylation in controlling memory-associated signal transduction mechanisms in the CNS.

C. Other

I had a total of approximately 20 post-doc and grad student applications for my laboratory this year.

9. Clinical/Translational Programs – N/A**10. Technology Transfer - N/A****11. Budget**

See attached overall report

12. Education Programs focusing on age related memory loss

See attached overall report

13. Collaborative programs with other McKnight Institutes, institutions and research programs

University of Arizona – We are continuing a very fruitful collaboration with Carol Barnes concerning the possible role of DNA methylation in controlling aging-related transcriptional alterations in the CNS. I anticipate that we will publish our first jointly-authored paper next year, in a high-profile journal.

University of Florida – We are continuing our collaboration with Tom Foster to investigate alterations in chromatin structure and histone post-translational modifications in memory-impaired aged rats.

University of Miami – We have completed a collaboration with John Bethea at UM, investigating NF-kappaB regulation of synaptic plasticity and memory formation. This project is described in the publication this year by Bracchi-Ricard et al., listed in section 2 above.

UAB – We are collaborating with a number of McKnight investigators here at UAB, including Farah Lubin, David Standaert, Scott Wilson, and Gavin Rumbaugh. Our collaboration with the Standaert lab resulted in the publication by Nicholas et al listed in section 2 above.

14. Collaborative programs with non McKnight Institutes, institutions and research programs

Emory – collaborating with Steve Traynelis on Protease Activated Receptor 1 (PAR1) in plasticity and memory.

Case Western – we have a long-standing collaboration with Gary Landreth concerning generation and characterization of ERK2 MAPK isoform-specific knockout mice.

Tulane – we are collaborating with Laura Schrader on K Channel Interacting Protein and Kv4.2 regulation.

Baylor College of Medicine – collaborating with Jim Lupski on mouse models of Smith-Magenis Syndrome.

University of Texas, Houston – collaborating with Jim Knierem on place cell recordings.

University of Dundee, Scotland – collaborating with Simon Arthur to investigate the role of Mitogen- and Stress-activated Kinase (MSK) in chromatin regulation and synaptic plasticity.

Karolinska Institute, Stockholm, Sweden – collaborating with Agneta Nordberg on chromatin regulation in mouse models of early-stage Alzheimer's Disease/Mild Cognitive Impairment. We also are working with the Nordberg lab to investigate alterations in chromatin structure in human normal aging and dementia using human post-mortem tissue.

EnVivo Pharmaceuticals – we are collaborating on a project for evaluating next-generation histone de-acetylase inhibitors as memory-enhancing agents. One of these novel compounds is entering human trials.

Merck – we are collaborating with investigators at Merck, utilizing genetically engineered mice to determine which histone de-acetylase isoforms are relevant to memory enhancement.

15. – 21. See Overall Report

John J. Hablitz, Ph.D., Professor and Vice Chair

1. Summary of Scientific Achievements for 2008

We discovered that presynaptic NMDA receptors regulate GABA release and synaptic plasticity in developing neocortex. These receptors are altered in an animal model of cortical dysplasia. We are investigating if similar changes occur in human cortical dysplasia.

2. Publications

Campbell, S.A., Mathew, S. S., and Hablitz, J.J. Pre- and postsynaptic effects of kainate on layer II/III pyramidal cells in rat neocortex. *Neuropharmacology* 2007, 53: 37-47.

Mathew, S.S., Pozzo-Miller, L. and Hablitz, J.J. Kainate modulates presynaptic GABA release from two vesicle pools. *J. Neurosci.* 2008, 28:725-731.

Mathew, S.S. and Hablitz, J.J. Calcium release via activation of presynaptic IP3 receptors contributes to kainate-induced IPSC facilitation in rat neocortex. *Neuropharmacology* 2008, 55: 106-116.

Campbell, S.A. and Hablitz, J.J. Altered glutamate transport enhances excitability in a rat model of cortical dysplasia. *Neurobiology of Disease* (In Press).

Hablitz, J.J. Dopamine modulation of neurotransmission: Relationship to epilepsy. In *Encyclopedia of epilepsy*, P. Schwartzkroin Ed. Elsevier (In Press).

Hablitz, J.J. GABA vesicles at synapses: Are there two distinct pools? *The Neuroscientist* (Invited Article, Submitted).

3. Presentations

Invited Speaker, Department of Neuroscience, Baylor College of Medicine, March 2008, "Presynaptic Ionotropic Receptors and Synaptic Plasticity".

Invited Speaker, Department of Biomedical Sciences, Creighton University School of Medicine, May 2008, "Disorders of Brain Development and Cortical Excitability".

4. Awards/Honors Received

UAB Graduate Dean's Award for Excellence in Mentorship, 2008.

5. Collaborations

None

Harald Sontheimer, Ph.D., Professor

1. Summary of Scientific Achievements for 2008

We showed that glial tumors utilize the system Xc glutamate transporter to facilitate tumor growth and invasion. Using animal studies we show that tumor expansion is greatly reduced in vivo when system Xc is inhibited using a FDA approved inhibitor. This led to a phase I clinical trial open for enrollment at UAB.

We were able to use three dimensional confocal time-laps imaging to show that ClC-3 Cl⁻ channels are mechanistically linked to cytoplasmic and chromatin condensation of dividing cells. This finding challenges hitherto held notions concerning cell volume changes in dividing cells and define a new pharmacological target to treat cancer.

We will soon submit data to show that Kir4.1 in astrocytes is down regulated following spinal cord injury in vivo and that it can be restored by application of estrogen. The increased expression of Kir4.1 enhances K⁺ buffering and correlates with white matter sparing and strong behavioral improvements in these animals.

2. Publications

McCoy, E. and Sontheimer, H. Water channel expression and function in normal and malignant glial cells. GLIA, 55:1034-1043 (2007).

Ernest, N.-J., and Sontheimer, H. Extracellular glutamine is a critical modulator for regulatory volume increase in human glioma cells. Brain Res. 1144:231-238 (2007).

Habela C.W. and Sontheimer, H. Cytosolic volume condensation is an integral part of mitosis. Cell Cycle, 6:1613-1620 (2007).

Olsen, M.L., Campell, S.L., and Sontheimer, H. Differential distribution of Kir4.1 in spinal cord astrocytes suggests regional differences in K⁺ homeostasis. J. Neurophysiol., 98: 786-93 (2007).

Lyons, S.A., Chung, W.J., Weaver, A.K., Ogunrinu, T. and Sontheimer H. Autocrine glutamate signaling promotes glioma cell invasion. Cancer Research, 67:9463-9471 (2007).

Higashimori, H. and Sontheimer, H. Role of Kir4.1 Channels in Growth Control of Glia. GLIA, 55: 1668-1679 (2007).

A.K. Weaver, M.L. Olsen, M. B. McFerrin and H. Sontheimer. BK Channels are Coupled to IP3-receptors via Lipid Rafts: a Novel Mechanism for Coupling [Ca²⁺]_i to Channel Activation, J. Biol. Chem., 282:31558-68 (2007).

Bomben V. and Sontheimer H., Inhibition of transient receptor potential canonical (TRPC) channels impairs cytokinesis in human malignant gliomas. Cell Proliferation, 41:98-121 (2008).

Ernest, N.-J, Habela, C.W. and Sontheimer, H. Cytoplasmic condensation is both necessary and sufficient to induce apoptotic cell death. J. Cell Sci., 121:290-297 (2008).

Sontheimer, H., An unexpected role for ion channels in brain tumor metastasis. Exp Biol Med. Apr 29. [Epub ahead of print] (2008).

Sontheimer, H., A role for glutamate in growth and invasion of primary brain tumors. J Neurochem. 105:287-95 (2008).

Sontheimer, H. Sontheimer, H. Chlorotoxin (TM-601): A Cl⁻ Channel Blocker Used To Treat Malignant Glioma. Goodman and Gilman's Pharmacology Update (2008).

M.L. Olsen and H. Sontheimer, Ionic Channels in Glia, Encyclopedia of Neuroscience, 3rd Edition, Larry Squire (ed.) Elsevier, in press 2007.

Ernest, N.-J. and H. Sontheimer, Glioma, Encyclopedia of Neuroscience, 3rd Edition, Elsevier, in press 2007

Sontheimer, H. Role of ion channels and amino-acid transporters in the biology of astrocytic tumors. In: Astrocytes in (patho)physiology of the nervous system (Parpura V, Haydon PG, eds), pp x-XX. Boston, MA: Springer, in press 2007

Lyons, S.A., and Sontheimer H. Peritumoral Epilepsy. Encyclopedia of Basic Epilepsy, Phil Schwartzkroin (ed.) Elsevier, in press 2008.

Olsen, M.L., and Sontheimer, H. Functional Implications for Kir4.1 Channels in Glial Biology: From K⁺ Buffering to Cell Differentiation, J. Neurochem., in press.

Habela, C.W, Olsen M,L., Sontheimer, H. ClC3 is a critical regulator of the cell cycle in normal and malignant glial cells. J. Neuroscience, in pr

3. **Presentations**

Burton Horowitz Lecture, University of Nevada School of Medicine, "Ion channels and amino-acid transporters support the growth and invasion of primary brain tumors" (12/6/07)

American Society for Neurochemistry, San Antonio, TX, "Biological changes that support the growth and invasion of malignant gliomas", (3/03/08)

USA-Japan Joint Meeting for Glial Research, Philadelphia, PA, "Ion channels and amino acid transporters aid the biology of glial-derived brain tumors", (3/20/08)

Gordon Conference, Mechanisms of Epilepsy, Colby College, MA. "Glutamate release from gliomas facilitates tumor growth and triggers peritumoral seizures" (8/3/2008).

Woods Hole Marine Biological Laboratories; Astrocytes, (8/14/07).

6th International Symposium on Volume Regulation in Health and Disease; Salzburg, Austria Cl^- and K^+ channels promote cell volume changes that support the invasion of malignant brain tumors into normal brain, (9/20/07)

Yale University; Ion Channels & Amino-acid Transporters support the Growth and Invasion of Primary Brain Tumors; (10/17/2007)

International Meeting on Ion channels and Cancer, Castle Ringberg Max Planck Society; Role of ion channels in glioma invasion (11/25-28, 2007)

University of Texas Health Science Center; Ion channel and amino-acid transporters support the growth and invasion of primary brain tumors,; (4/04/08)

4. Awards/Honors Received
None

5. Collaborations
None

Michael Brenner, Ph.D., Professor

1. Summary of Scientific Achievements for 2008

While we have not made any discoveries in the past year that I would consider "key," the following briefly summarizes our progress.

In our GFAP transcription studies we have demonstrated the importance of several regions of the GFAP promoter for activity, have begun to construct targeting vectors to make BAC transgenics, and have preliminary data indicating that insulator elements thought to have the ability to confer position independent expression of genes fail to do so in transgenic mice.

In our Alexander disease studies we have worked with collaborators to identify several unusual mutations, including a frameshift and missense mutation very near the C-terminal of the protein. We have also begun a proteomic analysis of the composition of the protein aggregates that characterize this disease.

2. Publications

Quinlan, R.A., Brenner, M., Goldman, J.E. and Messing, A. (2007) GFAP and its role in Alexander disease. *Exp. Cell Res.* 313:2077-2087.

This is an invited review; I wrote a few paragraphs.

Howard, K.L., Hall, D.A., Moon, M., Agarwal, P., Newman, E., and Brenner, M. (2008) Adult-Onset Alexander Disease with Progressive Ataxia and Palatal Tremor. *Mov. Disord.* 23:118-122.

A figure from this paper was featured on the cover of the journal; E. Newman was a SPIN student.

Lee, Y., Su, M., Messing, A., Su, M. and Brenner, M. (2008) GFAP promoter elements required for region-specific and astrocyte-specific expression. *Glia* 56: 481-493.

Essentially all the work was done by Youngjin Lee, my graduate student.

Liu, B., Wang, S., Brenner, M., Paton, J.F., and Kasparov, S. (2008) Enhancement of cell-specific transgene expression from a Tet-Off regulatory system using a transcriptional amplification strategy in the rat brain. *J Gene Med.* 10:583-592.

I contributed a new, compact GFAP promoter that we developed and assisted with writing the paper.

Brenner, M., Goldman, J.E., Quinlan, R.A. and Messing, A. (2008). Alexander disease: a genetic disorder of astrocytes. In Parpura, V. and Haydon, P., *Astrocytes in (patho)physiology of the nervous system*, Springer, in press.

3. Presentations

Plenary speaker for the 11th International Congress on Neuronal Ceroid Lipofuscinosis (Batten Disease), Rochester, NY, July 14-17, 2007.

Seminar presentation, "What Studies Of The GFAP Gene Tell Us About Astrocytes In Health And Disease" Southern Research Institute, Birmingham, AL, 13 August 2007.

Speaker in a symposium "Glial Cells and Neurological Disease" for the 39th Annual Meeting of the American Society for Neurochemistry, San Antonio, TX, 1-5 March 2008.

Speaker at the United Leukodystrophy Foundation meeting on Alexander disease, DeKalb, IL, 11-12 April, 2008.

4. Awards/Honors Received

Paper in Movement Disorders featured as cover art (publication #82, 2008)

5. Collaborations

The NINDS Program Project Grant I am part of to study Alexander disease involves a joint collaborative effort among the following labs:

Maiken Nedergaard, MD., DMSc.
Professor, Department of Neurological Surgery
University of Rochester
Rochester, NY

James E. Goldman, M.D., Ph.D.
Professor of Pathology & Director, Division of Neuropathology
Columbia University College of Physicians & Surgeons
New York, NY

Mel Feany, M.D., Ph.D.
Associate Professor of Pathology
Brigham and Women's Hospital
Harvard Medical School
Boston, MA

Albee Messing, VMD PhD
Professor of Neuropathology
Waisman Center on Mental Retardation & Human Development and
Department of Comparative Biosciences
University of Wisconsin-Madison
Madison, WI

I also have a collaboration to produce a conditional endothelin knock mouse with

Vittorio Gallo, Ph. D.

Professor of Pediatrics, Pharmacology and Physiology

George Washington University School of Medicine

and

Director, Center for Neuroscience Research

Children's National Medical Center

Washington, D.C.

Lynn Dobrunz, Ph.D., Associate Professor

1. Summary of Scientific Achievements for 2008

My lab has shown that target-cell specific short-term plasticity causes large activity-dependent changes in the excitatory drive to different subsets of interneurons in hippocampus during physiologically derived stimulus patterns. This causes a reduction in excitatory drive to most interneurons relative to pyramidal cells, but a large increase in excitatory drive to somatostatin interneurons relative to both pyramidal cells and other interneurons. These mechanisms help control the dynamic balance between excitation and inhibition in hippocampus and help to regulate the gating of information into hippocampus from entorhinal cortex.

My lab discovered that developmental changes occur in short-term plasticity at temporoammonic synapses onto CA1 pyramidal cells that are opposite of those that occur at Schaffer collateral synapses. The mechanism of these changes is also different; it is caused by a developmental decrease in the initial release probability at temporoammonic synapses and a disynaptic mechanism involving mGluR1 receptors and GABAB receptors at Schaffer collateral synapses. These studies shed light on normal developmental mechanisms in hippocampus and pave the way for future studies investigating short-term plasticity in animal models of developmental disorders.

In collaboration with Dr. Lori McMahon, we have discovered that interactions between muscarinic receptors and alpha-adrenergic receptors cause induction long-term depression in hippocampus that is dependent upon ERK activation.

In collaboration with Dr. Scott Wilson, we have shown that two deubiquitinating enzymes, Usp-14 and UCH-L1 have different effects on synaptic function and plasticity, with the effects of the loss of Usp-14 being more severe. Because the loss of Usp-14 and UCH-L1 both cause ubiquitin depletion, this shows that ubiquitin depletion is not responsible for the severity of phenotype with loss of Usp-14.

2. Publications

*Speed, H.E. & L.E. Dobrunz. 2008. Developmental decrease in short-term facilitation at Schaffer collateral synapses in hippocampus is mGluR1 sensitive. J. Neurophysiol 99:799-813.

*Scheiderer, C.L., M.E. McCutcheon, L.E. Dobrunz, & L.L. McMahon. 2008. Coactivation of M1 muscarinic and $\alpha 1$ adrenergic receptors stimulates ERK and induces long-term depression at CA3-CA1 synapses in rat hippocampus. J. Neurosci 28:5350-5358.

*Speed, H.E. & L.E. Dobrunz. 2008. Changes in short-term facilitation are opposite at temporoammonic vs. Schaffer collateral synapses in early postnatal development. Hippocampus, in press.

*Walters, B.J. , Campbell, S.L., P.C. Chen, L.E. Dobrunz, J.A. Wilson, K. Artavanis-Tsakonas, H.L. Ploegh, A.P. Taylor, D.G. Schroeder, G.A. Cox, & S.M. Wilson. Differential effects of Usp14 and Uch-L1 on the ubiquitin-proteasome system and synaptic activity. Molecular and Cellular Neuroscience, in press.

3. **Presentations**

Dobrunz, L.E. (Chair) and D.F. Buonomano (Co-Chair). 2007. Society for Neuroscience Minisymposium. Short-term Synaptic Plasticity: What is it and what is it good for? Society for Neuroscience Annual Meeting, San Diego, CA.

Dobrunz, L.E. 2007. Mechanisms of target-cell specific short-term plasticity at excitatory synapses in hippocampus. In Society for Neuroscience Minisymposium, Short-term Synaptic Plasticity: What is it and what is it good for? Society for Neuroscience Annual Meeting, San Diego, CA.

Northwestern University School of Medicine, Department of Physiology, departmental seminar

University of Illinois at Chicago School of Medicine, Neuroscience Program, departmental seminar

Brudnick Neuropsychiatric Research Institute, University of Massachusetts School of Medicine, Worcester MA, departmental seminar

4. **Awards/Honors Received**

Promoted to Associate Professor, University of Alabama at Birmingham

5. **Collaborations**

None

Vladimir Parpura, M.D., Ph.D., Associate Professor

1. Summary of Scientific Achievements for 2008

We determined that the Ca^{2+} entry through TRPC1 channels contributes to Ca^{2+} signaling in astrocytes and the consequent glutamate release from these cells (Malarkey et al, 2007).

We experimentally determined the activation free energy for single molecule interactions between two synaptic proteins syntaxin 1A and synaptobrevin 2, using an atomic force microscope and the Jarzynski equality of non-equilibrium thermodynamics (Liu et al, 2008).

2. Publications

Malarkey, E.B., Parpura, V. (2007) Applications of carbon nanotubes in neurobiology. *Neurodegenerative Dis.* 4: 292- 299.

Ni, Y., Malarkey, E.B., Parpura, V. (2007) Vesicular release of glutamate mediates bidirectional signaling between astrocytes and neurons *J. Neurochem.* 103: 1273-1284.

Malarkey, E.B., Parpura, V. (2008) Mechanisms of glutamate release from astrocytes. *Neurochem Int* 52: 142-154.

Malarkey, E.B., Ni, Y., Parpura, V. (2008) Ca^{2+} entry through TRPC1 channels contributes to intracellular Ca^{2+} dynamics and consequent glutamate release from astrocytes. *Glia* 56:821-835.

Montana, V., Liu, W., Mohideen, U., Parpura, V. (2008) Single molecule probing of exocytotic protein interactions using force spectroscopy. *Croat Chem Acta* 81:31-40.

2008 Liu, W., Montana, V., Parpura, V.*, Mohideen, U*. (2008). Comparative Energy Measurements in Single Molecule Interactions. *Biophys J* 95: 419-425.* corresponding authors

In Press:

Sucapane, A., Cellot, G., Prato, M., Giugliano, K., Parpura, V.*, Ballerini, L.* (2008) Interactions between cultured neurons and carbon nanotubes: A nanoneuroscience vignette. *J Nanoneurosci.* In Press

* corresponding authors

Parpura, V., Mohideen, U. (2008). Molecular form follows function: (un)snaring the SNAREs. *Trends Neurosci.* In Press

2008. Reyes, C.R., Parpura, V. (2008) Models of astrocytic Ca^{2+} dynamics and epilepsy, *Drug Discov Today Dis Models*, In Press

BOOKS (Technical/Refereed):

Parpura, V., Haydon P.G. (Eds.) Astrocytes in (patho)physiology of the nervous system. Springer, Boston, MA, 2008; In Press.

INVITED CHAPTERS IN EDITED BOOKS (Technical/Refereed):In Press:

2008 Malarkey, E.B., Parpura, V. (2008) Mechanisms of transmitter release from astrocytes. In: Parpura, V., Haydon P.G. (Eds.) Astrocytes in (patho)physiology of the nervous system. Springer, Boston, MA, 2008.

PROCEEDINGS (Technical/Refereed):In Press

Liu, W., Parpura, V. (2009) Single molecule probing of SNARE proteins by atomic force microscopy, *Ann. N. Y. Acad. Sci.*

COMMENTARIESIn Press

Parpura, V. (2008) Instrumentation: Carbon nanotubes on the brain, *Nat. Nanotechnol.* 3: 384-385. [News&views]

3. **Presentations**

07/10/07 "Tripartite synapse-astrocytic regulation of glutamate", "Glutamate in vineyards"- an international conference on neuropharmacology of glutamate, Hunter Valley Resort, Pokolbin, NSW, Australia.

07/12/07 "Spatio-temporal characteristics of exocytosis in astrocytes", Brain and Mind Research Institute, University of Sydney, NSW, Australia

07/15/07 "Spatio-temporal characteristics of exocytosis in astrocytes" in Symposium entitled "Regulated exocytosis of neuroligands from astrocytes" (organizer: Vladimir Parpura; chair: David Pow, University of New Castle, NSW, Australia), 7th International Brain Research Organization (IBRO) World Congress of Neuroscience, Melbourne, VIC, Australia

10/15/07 "Spatio-temporal characteristics of exocytosis in astrocytes", International workshop on neuron-glia interactions: Information processing and engineering perspectives, Pisa, Italy

10/17/07 "Tripartite synapse-astrocytic regulation of glutamate", Croatian Society for Biochemistry and Molecular Biology, Rijeka, Croatia

10/18/07 "Spatio-temporal characteristics of exocytosis in astrocytes", Center for Neuroscience B.R.A.I.N., University of Trieste, Trieste, Italy

10/20/07 "Mechanisms of glutamate release from astrocytes"

NEUROTRAIN-Neuroscience Training in Europe, Autumn School

"Neuron-glia interactions in health and disease", Dubrovnik, Croatia

10/29/07 "Spatio-temporal characteristics of exocytosis in astrocytes", Institute François Magendie, Research Center ISERM U862, University of Bordeaux, 2, Bordeaux, France

01/15/08 "Comparative validation of energy measurement in single SNARE/exocytotic protein interactions", Institute of Complex Adaptive Matter (ICAM)/ International ICAM (I2CAM) Annual Conference, Santa Fe, NM

1/29/08 "Connexin 43 regulates contact-directed distribution of exocytotic fusion sites on astrocytes" in Panel "Connexins in Physiology and Pathophysiology of the CNS" (organizer and chair: Vladimir Parpura, UAB), 41th Winter Conference on Brain Research (WCBR), Snowbird, UT

3/1/08 "Tripartite synapse-astrocytic regulation of glutamate", in Pre-meeting workshop "Glial Neuronal Interactions: Cutting Edge Approaches to Modeling CNS Function & Disease" (organizers: Monica J. Carson, University of California, Riverside, CA; Bruce R. Ransom, University of Washington Medical School, Seattle; and Vladimir Parpura, UAB) 39th Annual Meeting of the American Society for Neurochemistry, San Antonio, TX.

3/3/08 "Neurobiology at the interface of nanotechnology: vignettes from the laboratory" in Workshop entitled "Nanotechnology and Neuroscience" (organizer and chair: Vladimir Parpura) 39th Annual Meeting of the American Society for Neurochemistry, San Antonio, TX.

3/18/08 "Spatio-temporal characteristics of exocytosis in astrocytes" in Session "Transmitter release and uptake", USA-Japan Joint Meeting for Glial Research, Philadelphia, PA

4/29/08 "Regulation of exocytotic release of glutamate by vesicular glutamate transporters and cytoplasmic glutamate in astrocytes", 13th International Symposium on Hepatic Encephalopathy and Nitrogen Metabolism. Albano Terme, Italy

4/30/08 "Mechanisms of glutamate release from astrocytes", Istituto Consiglio Nazionale delle Ricerche di Neuroscienze Dipartimento di Scienze Biomediche Sperimentali, University of Padua, Italy

5/23/08 "Spatio-temporal characteristics of exocytosis in astrocytes" in Session "Neurons and astrocytes", International Meeting Mechanisms(s) of exocytosis 2008. Ljubljana, Slovenia.

6/13/08 "Tripartite synapse-astrocytic regulation of glutamate", Department of Neurotoxicology, Medical Research Centre, Polish Academy of Sciences, Warsaw, Poland

6/14/08 "Carbon nanotubes and neurons: a nanoneuroscience vignette" in Session "Nanoparticles and Brain Edema" (Organizer: Sharma SH, Uppsala University, Sweden), 14th International Symposium on Brain Edema and Brain Tissue Injury, Warsaw, Poland

6/25/08 "Tripartite synapse-astrocytic regulation of glutamate" in Session "Astrocyte-neuron interactions", 8th Biennial Meeting of the Asian-Pacific Society for Neurochemistry, Shanghai, P.R. China

6/29/08 "Spatio-temporal characteristics of exocytosis in astrocytes" in Session "Tripartite synapse and receptor mediated metabolism", 3rd International Society for Neurochemistry Special Neurochemistry

Conference/ 8th International Meeting for Brain Energy Metabolism-
"Neurodegeneration and Regeneration", Beijing, P.R. China.

4. Awards/Honors Received
None

5. Collaborations

Floyd, Candence - UAB
Grey, Michelle - UAB
Gross, Alecia - UAB
Lesort, Mathieu - UAB
Mike, Michael - UAB
Wilson, Scott - UAB

Ellis-Davies, Graham CR - Drexel University, Philadelphia, PA
Haddon, Robert C - University of California, Riverside, CA
Maduro, Morris - University of California, Riverside, CA
Mohideen, Umar - University of California, Riverside, CA
Mothet, Jean-Pierre - INSERM, Bordeaux, France
Schousboe, Arne - University of Copenhagen, Denmark
Zorec, Robert - University of Ljubljana, Slovenia

Robin Lester, Ph.D., Associate Professor

1. Summary of Scientific Achievements for 2008

Determined the mechanisms underlying permanent changes in neuronal excitability after withdrawal from nicotine. At early times following withdrawal we have characterized a novel form of plasticity in the hippocampal CA1 region driven by increased spontaneous activity originating in the dentate gyrus (paper in preparation). This appears to be a direct homeostatic adaptation in response to activation of the $\alpha 4\beta 2$ subtype of nicotinic receptor. During withdrawal we find that a second phase of increased CA1 excitability results from decreased K channel function in pyramidal cells.

2. Publications

Fonck, C., Nashmi, R., Salas, R., Zhou, C., Huang, Q., De Biasi, M., Lester, R.A.J. Lester, H.A. (2008). Demonstration of Functional $\alpha 4$ -Containing Nicotinic Receptors in the Medial Habenula. *Neuropharmacology* (in press).

3. Presentations

Dec 2007: Neuroscience Seminar Series, University of Tennessee, Memphis

Feb 2008: Department of Pharmacology, Southern Illinois University School of Medicine

Apr 2008: PM&R Grand Rounds, UAB

4. Awards/Honors Received

Nominated for the School of Medicine Argus Award for best lecturer in Neuroscience

5. Collaborations

Henry Lester (Caltech)

Michael Quick (USC)

Lucas Pozzo-Miller, Ph.D., Associate Professor

1. Summary of Scientific Achievements for 2008

Localized and brief application of BDNF to hippocampal slices increases quantal transmitter release onto CA1 pyramidal neurons via mobilization of Ca^{2+} from intracellular stores followed by Ca^{2+} influx. TRPC channels are required for the increase in mini frequency by BDNF. The increase in transmitter release has also been monitored by multiphoton imaging of FM1-43 in hippocampal slices, confirming with a direct approach that the BDNF effect is on vesicular fusion. Poster presented at the Gordon Conference on Synaptic Transmission (August 2004), platform presentation (slide) at 2004 Annual Society for Neuroscience Meeting, and poster at the 2007 Annual Society for Neuroscience Meeting. Manuscript in preparation.

Cell-autonomous expression of Rett syndrome-associated *MECP2* mutations cause dendritic spine loss in hippocampal CA1 and CA3 pyramidal neurons. Human RTT CA1 pyramidal neurons have fewer dendritic spines than non-MR individuals. Manuscript in preparation. Poster presented at the 2007 Annual Society for Neuroscience Meeting and the 8th and 9th Annual Rett Syndrome Symposium (2007 and 2008).

Hippocampal slices from *Mecp2*-null mice are hyperexcitable. Poster presented at the 9th Annual Rett Syndrome Symposium (2008).

Mossy fibers release BDNF onto CA3 pyramidal neurons and activate a TRPC3-mediated membrane current.

Endogenously released BDNF in cultured hippocampal slices plays a role in CA1 neuron dendritic spine maturation. The scavenger TrkB-IgG, as well as inhibitors of Trk and p75NTR signaling affect spine form in eYFP-transfected CA1 pyramidal neurons. Poster presented at the 2006 Annual Society for Neuroscience Meeting. Manuscript in preparation.

I_h modulates dendritic Ca^{2+} transients evoked by backpropagating action potentials in layer V pyramidal neurons of mouse prefrontal cortex. Poster presented at the 2003 Annual Society for Neuroscience Meeting. Manuscript in preparation.

2. Publications

1) Manuscripts and Abstracts

a) Accepted

1. Chapleau CA, ME Carlo, JL Larimore & L Pozzo-Miller (2008). The actions of BDNF on dendritic spine density and morphology in organotypic slice cultures depend on the presence of serum in culture media. *Journal of Neuroscience Methods* 169: 182-190.

2. Mathew SS, L Pozzo-Miller & JJ Hablitz (2008). Kainate modulates presynaptic GABA release from two vesicle pools. *Journal of Neuroscience* 28: 725-731.
3. Chapleau CA & L Pozzo-Miller (2008). Activity-dependent structural plasticity of dendritic spines. In: *Concise Learning and Memory: the Editor's Selection*, Byrne J (Ed.). Oxford, Elsevier.
4. Chapleau CA & L Pozzo-Miller (2008). Activity-dependent structural plasticity of dendritic spines. In: *Learning and Memory: a Comprehensive Reference*, Byrne J (Ed.). Oxford, Elsevier.
5. Amaral MD & L Pozzo-Miller (2007). BDNF induces dendritic calcium elevations associated with I_{BDNF} , a non-selective cationic current mediated by TRPC channels. *Journal of Neurophysiology* 98: 2476-2482.
6. Amaral MD & L Pozzo-Miller (2007). TRPC3 channels are necessary for brain-derived neurotrophic factor to activate a non-selective cationic current and to induce dendritic spine formation. *Journal of Neuroscience* 27: 5179-5189.
7. Hojjati MR, GM van Woerden, WJ Tyler, KP Giese, AJ Silva, L Pozzo-Miller & Y Elgersma (2007). Kinase activity is not required for αCaMKII -dependent presynaptic plasticity at hippocampal CA3-CA1 synapses. *Nature Neuroscience* 10: 1125-1127.
8. Moore CD, ER Thacker, J Larimore, D Gaston, A Underwood, B Kearns, S Patterson, T Jackson, C Chapleau, L Pozzo-Miller & A Theibert (2007). Centaurin alpha-1, a neuronal Arf GAP modulates dendritic differentiation. *Journal of Cell Science* 120: 2683-2693.
9. Amaral MD, CA Chapleau & L Pozzo-Miller (2007). Transient receptor potential channels as novel effectors of brain-derived neurotrophic factor signaling: Potential implications for Rett syndrome. *Pharmacology & Therapeutics* 113: 394-409.

b) Submitted

1. Larimore J, CA Chapleau, CD Moore, S Worth, I Rolle, Z Nie, L Pozzo-Miller & A Thiebert. The Arf1 GAP AGAP1/Centg2 regulates neuronal differentiation.

c) Published Abstracts

1. Chapleau CA, G Calfa, JM Rutherford, M Lane, JL Larimore, S Kudo, C Schanen, AK Percy & L Pozzo-Miller (2007). Cell-autonomous expression of Rett-associated *MECP2* mutations leads to dendritic spine pathologies in pyramidal hippocampal neurons. *Society for Neuroscience Abstracts* 54.11.
2. Amaral MD, SS Mathew, G Rumbaugh & L Pozzo-Miller (2007). BDNF causes action potential-independent vesicular release from presynaptic terminals labeled with FM1-43: multiphoton excitation microscopy in area CA1 of hippocampal slices. *Society for Neuroscience Abstracts* 443.8.
3. Larimore JL, C Chapleau, I Rolle, C Moore, S Worth, Z Nie, P

Randazzo, L Pozzo-Miller & A Theibert (2007). The Arf1 GAP Centaurin gamma-2/AGAP1 modulates neuronal differentiation. *American Society of Cell Biology Annual Meeting* 45.

4. Moore CD, S Worth, D Hill, J Larimore, C Chapleau, L Pozzo-Miller & A Theibert (2007). The ArfGAP Centaurin alpha-1 modulates neuronal differentiation through the regulation of Arf6. *American Society of Cell Biology Annual Meeting* 1268.

3. **Presentations**

Invited Speaker at the *Annual Rett Syndrome Symposium*, Chicago IL.

Invited Speaker at the *Rett Syndrome Clinical Trial Mini-Symposium*, Chicago IL.

Invited Speaker at the UCI Epilepsy Research Center Symposium "*Hot Topics in Epilepsy*", Newport Beach CA.

Center for Basic Neuroscience and Department of Psychiatry, University of Texas Southwestern Medical Center, Dallas TX.

Department of Physiology, University of Wisconsin-Madison, Madison, WI.

The Salomon Snyder Department of Neuroscience, John Hopkins University, Baltimore MD.

Invited Speaker at the "*Shared Neurobiology of Autism and Related Disorders*" meeting at University of Southern California, Los Angeles CA.

Department of Biology, University of Maryland, College Park MD.

Keynote Speaker, Microscopy Course, Instituto Ferreyra, Córdoba, Argentina.

Keynote Speaker, Annual South East Nerve Net Meeting, Wakulla Springs FL.

Department of Neurosurgery University of New Mexico, and The Mental Illness and Neuroscience Discovery (MIND) Institute, Albuquerque NM.

4. **Awards/Honors Received**

Invited Speaker at the University of California at Irvine Epilepsy Research Center Symposium "*Hot Topics in Epilepsy*", Newport Beach, CA.

Invited Speaker at the "*Shared Neurobiology of Autism and Related Disorders*" meeting at University of Southern California, Los Angeles, CA.

5. **External Collaborations**

None

Anne Theibert, Ph.D., Associate Professor

1. Summary of Scientific Achievements for 2008

My laboratory has shown that centaurin alpha-1, a candidate PI 3-kinase target and regulator of Arf6 GTPases, functions to control both dendritic and spine differentiation and secretory granule trafficking in neurons. Secretory granules traffic neuropeptides, neurotrophic factors and biogenic amines, as well as key plasma membrane protein and lipid components. Although a connection between secretory trafficking and differentiation has been previously proposed, our studies are the first to identify key proteins which may link these important neuronal activities.

Centaurin gamma-2 is another candidate PI 3-kinase target that regulates Arl1 GTPases. We demonstrated that centaurin gamma-2 functions as a negative regulator of dendritic differentiation that controls endosomal trafficking in neurons. As centaurin gamma-2 was also identified as a candidate autism susceptibility gene, our study identifies a potential mechanism whereby loss or mutation of centaurin gamma-2 activity could contribute to aberrant neuronal differentiation and brain development, which are thought to underlie neurodevelopmental disorders such as autism.

2. Publications

Manuscripts and chapters accepted, in press or published (give full reference and official status):

Moore, C.D., Thacker, E.E., Larimore, J., Gaston, D., Underwood, A., Kearns, B., Patterson, S.I., Jackson, T., Chapleau, C., Pozzo-Miller, L. & Theibert A. The neuronal Arf GAP centaurin alpha-1 modulates dendritic differentiation. *J. Cell Sci.* 120:2683-93, 2007.

Kahn, R.A., Bruford, E., Inoue, H., Logsdon, J.M. Jr, Nie, Z., Premont, R.T., Randazzo, P.A., Satake, M., Theibert, A.B., Zapp, M.L. & Cassel, D. Consensus nomenclature for the human ArfGAP domain-containing proteins. *J. Cell Biol.* 182:1039-44, 2008.

Although this information was not requested, I would like to provide it. I have submitted two senior author and 1 co-author manuscript:

Larimore, J., Chapleau, C., Moore, C., Worth, S., Rolle, I., Nie, S., Pozzo-Miller, L. & Theibert, A. The Arf1 GAP AGAP1/Ceng2 regulates neuronal differentiation. Submitted

Larimore, J., Ewell, S., Markwardt, S., Moore, C., Hermann-Gerdes, H., Faundez, V. and Theibert, A. The Arf GAP centaurin alpha-1/ADAP1 functions in secretory granule trafficking in neuronal cells. Submitted

Larimore, J., Chapleau, C., Kudo, S., Theibert, A., Percy, A. & Pozzo-Miller, L. Bdnf overexpression in hippocampal neurons prevents dendritic atrophy caused by Rett-associated MECP2 mutations. *Submitted*

3. Presentations

None

4. Awards/Honors Received

None

5. External Collaborations

None

Linda Overstreet-Wadiche, Ph.D., Assistant Professor

1. Summary of Scientific Achievements for 2008

We have found that brief neonatal seizures induced by hypoxia affect dentate neurogenesis in a manner similar to prolonged chemical-induced seizures. The SFN abstract for this project has been selected for inclusion in SFN 2008 media materials (lay-friendly summaries for media).

We have determined that the initial synaptic input to adult generated granule cells likely arises from a little-studied class of hippocampal interneuron that expresses NPY and NOS. Current studies are attempting to confirm this using paired recordings.

Most adult generated cells in the adult hippocampus undergo apoptosis during the weeks after cell birth rather than become functionally integrated into the neural network, and the fraction of cells that survive is modulated by experiences such as environmental enrichment. We have evidence that newborn neurons labeled in POMC-GFP transgenic mice are in a "critical period" for cell death/survival that will allow us to identify the factors that determine whether an individual cell survives or dies.

2. Publications

Markwardt S, Overstreet-Wadiche LS (2008) GABAergic signaling to adult generated neurons. *Journal of Physiology*, 586:3745-9.

Zhao C-S, Overstreet-Wadiche L (2008) Integration of adult generated neurons during epileptogenesis. *Epilepsia*, 49 s5:3-12.

3. Presentations

Feb 2008	Departmental seminar, Cell and Molecular Biology Department, Tulane University, New Orleans
Mar 2008	Departmental seminar, Biology Department, University of Texas at San Antonio, San Antonio
April 2008	Symposium GABA and Glutamate in Adult Neurogenesis, Experimental Biology 2008, San Diego

4. Awards/Honors Received

PI on UAB-Purdue Botanicals Pilot Grant (\$25,000) to study the effects of grape seed extract on adult neurogenesis.

Mentor for Dr. Chuansheng Zhao's Civitan Emerging Scholar Award (\$25,000) to study the short and long term consequences of neonatal seizures on neurogenesis.

Epilepsy Foundation grant to study seizure-induced neurogenesis (Year 2, \$50,000/year).

5. Collaborations

None

Gavin Rumbaugh, Ph.D., Assistant Professor

1. Summary of Scientific Achievements for 2008

We have made advances in the understanding of how actin is regulated at synapses. We have shown that actin - myosin dynamics underlie the stability of LTP at CA1 synapses. We also have preliminary evidence that actin - myosin contributes to an early stage of memory consolidation in hippocampus. This work is currently under peer review.

In a separate line of research, we have discovered that reduced expression of a key synaptic protein, SynGAP, results in a complex and interesting behavioral phenotype. This phenotype is similar to mouse models of major mental illness (i.e. schizophrenia) and provides evidence that abnormal synaptic plasticity contributes to neurological and cognitive defects that underlie mental illness. This work is also under peer-review.

2. Publications

Peer-reviewed original research

Heine M, Groc L, Frischknecht R, Béïque JC, Lounis B, Rumbaugh G, Hugarir RL, Cognet L, Choquet D (2008) Surface Mobility of Postsynaptic AMPARs Tunes Synaptic Transmission. *Science*. 320 (1): 201 - 205

Wu Y, Arai AC, Rumbaugh G, Srivastava AK, Turner G, Hayashi T, Suzuki E, Jiang Y, Zhang L, Rodriguez J, Boyle J, Tarpey P, Raymond FL, Nevelsteen J, Froyen G, Stratton M, Futreal A, Gecz J, Stevenson R, Schwartz CE, Valle D, Hugarir RL, Wang T. (2007) Mutations in ionotropic AMPA receptor 3 alter channel properties and are associated with moderate cognitive impairment in humans. *PNAS*. 104(46):18163-18168

Sia GM, Beïque JC, Rumbaugh G, Cho R, Worley PF, Hugarir RL. (2007) Interaction of the N-Terminal Domain of the AMPA Receptor GluR4 Subunit with the Neuronal Pentraxin NP1 Mediates GluR4 Synaptic Recruitment. *Neuron*. 55(1):87-102.

b. Review articles

Wilson S, Rumbaugh G (2008) Regulated protein degradation facilitates memory reconsolidation. *Cellscience Reviews* 4(4):31-35

3. Presentations

Molecular and Cellular Cognition Society (MCCS) Annual Meeting, Invited Speaker, Panel Presentation, November 2007
UAB, Department of Neurobiology, Seminar, Fall 2007

4. **Awards/Honors Received**
None

5. **Collaborations**
None

Jacques Wadiche, Ph.D., Assistant Professor**1. Summary of Scientific Achievements for 2008**

We have identified a mechanism that controls the synchronous release of concomitant release of synaptic vesicles from individual synapses. We are currently writing a manuscript describing this phenomenon and have begun to dissect its mechanistic properties.

We have characterized how the density of neuronal glutamate transporters restricts the activation of nearby glial receptors. We hypothesize that the expression of neuronal transporters controls the ensheathment of glial processes surrounding cerebellar synapses.

2. Publications

Tzingounis AV and Wadiche JI (2007). Glutamate transporters: confining runaway excitation by shaping synaptic transmission Nat Rev Neurosci. 12:935-47.

3. Presentations

None

4. Awards/Honors Received

None

5. External Collaborations

None

Scott Wilson, Ph.D., Assistant Professor

1. Summary of Scientific Achievements for 2008

Determined that Usp14 deficient mice suffer from motor endplate disease

Determined that loss of Usp14 results in a ubiquitin stress response in neurons and that restoration of ubiquitin levels in axJ mice prevents motor endplate disease.

Mapped a Usp14 modifier that protects Balb/c mice from premature death due to loss of Usp14.

2. Publications

Stephen Crimmins¹, Miriam Sutovsky², Ping-Chen Chung¹, Alexis Huffman¹, Crystal Wheeler¹, Deborah A. Swing³, Kevin Roth⁴, Julie Wilson¹, Peter Sutovsky^{3, 5} and Scott Wilson^{1, 6} Transgenic rescue of ataxia mice reveals a male-specific sterility defect. Accepted in Developmental Biology.

Walters, B.J.¹, Campbell, S.L.¹, Chen, P.C.¹, Taylor, A.P.², Schroeder, D.G.², Dobrunz, L.E.¹, Artavanis-Tsakonas, K.³, Ploegh, H.L.³, Wilson, J.A.¹, Cox, G.A.² and Wilson, S.M.^{1,4}. Differential effects of Usp14 and Uch-L1 on the ubiquitin proteasome system and synaptic activity. Accepted in Molecular and Cellular Neuroscience.

Wilson, S.M., and Rumbaugh, G. Regulated protein degradations facilitates memory reconsolidation. Cellscience Reviews (4);31-35 2008.

Submitted

Regulation of Synaptic structure by the ubiquitin C-terminal hydrolyase Uchl-1. Anna E. Cartier, Stevan N. Djakovic, Scott M. Wilson and Gentry N. Patrick. Neuron.

Corinna Lappe-Siefke¹, Sven Löbrich¹, Wulf Hevers², Michaela Schweizer¹, Jean-Marc Fritschy³, Jens Eilers², Scott M. Wilson⁴ and Matthias Kneussel^{1,5} Ax^J mutation of the ubiquitin-specific protease 14 gene alters *in vivo* GABA_A receptor $\alpha 1$ subunit surface expression and Purkinje cell function. Genes and Development.

3. Presentations

Emory Medical School, Department of Biochemistry. Ubiquitin stress results in neuromuscular junction disease in ataxia mice. February 2008.

Medical College of Georgia, Department of Developmental Neurobiology. Ubiquitin stress results in neuromuscular junction disease in ataxia mice. January 2008.

University of Alabama at Birmingham, Department of Physiology and Biophysics. December 2007.

Society for Neuroscience 2007, Ubiquitin proteasome pathway and human disease. Transgenic rescue of ataxia mice with neuronal expression of Usp14.

4. **Awards/Honors Received**
None

5. **Collaborations**
None

RECRUITMENT

CURRICULUM VITAE: Farah Domonique Lubin
 University of Alabama at Birmingham (UAB)
 Shelby Interdisciplinary Biomedical Research Building
 1825 University Boulevard
 Birmingham, AL 35294
 (205) 996-6084
 E-mail: flubin@nrc.uab.edu
 Citizenship: USA

MAJOR RESEARCH INTEREST

Epigenetic mechanisms of neural plasticity
 Epigenetic mechanisms mediating the effects of epilepsy
 Neurobiology of learning and memory

EDUCATION

- 1996-2001 Ph.D., Cell/Molecular Biology
 Binghamton University (SUNY), Binghamton, NY
 Advisor: Dennis W. McGee, Ph.D.
Dissertation Title: The Co-Regulatory Effect of Extracellular Matrix Proteins and Integrins with Interleukin-1 β on Cytokine Secretion by Epithelial Cells
- 1992-1996 BS, Major: Biology Minor: Chemistry, *summa cum laude* (Senior Honor Thesis)
 Alabama State University, Montgomery, AL

POSITIONS HELD

- 2009-Present Assistant Professor and Evelyn F. McKnight Brain Institute Investigator,
 Department of Neurobiology, University of Alabama-Birmingham, Birmingham, AL
- 2006-2008 Postdoctoral Fellow, Advisor: J. David Sweatt, Ph.D., Department of
 Neuroscience, Baylor College of Medicine, Houston, TX
 Department of Neurobiology, University of Alabama-Birmingham, Birmingham, AL
- 2002-2005 Postdoctoral Fellow, Cain Foundation Labs/Texas Children's Hospital, Advisor:
 Anne E. Anderson, M.D., Department of Pediatrics-Neurology, Baylor College
 of Medicine, Houston, TX
- 1996-2001 Research Assistant, Advisor: Dennis W. McGee, Ph.D., Mucosal Immunology
 Lab, (Clark Fellowship program), Binghamton University, Binghamton, NY
- 1995-1996 Research Assistant, Advisor: Eddie Moore, Ph.D., Molecular Biology Lab
 (MARC/NIH program), Alabama State University, Montgomery, AL
- Summer 1995 Research Assistant, Molecular Embryology Lab (MARC/NIH program),
 Memorial Sloan Kettering Cancer Center, New York, NY

AWARDS AND HONORS

- 2008-2011 NIMH/NIH Pathway to independence Award (K99/R00 MH082106)
- 2005-2007 NINDS/NIH Research Award (F32NS48811)
- 2004-2005 NINDS/NIH Microarray Supplemental Research Award (RO1NS39942)
- 2004-2005 AES/Milken Epilepsy Foundation Award
- 2002-2005 METPAC SFN Travel Fellowship Grant
- 2002 Gordon Conference Travel Award (Synaptic Transmission)
- 2002 UNCF-Merck Post-doctoral Science Research Fellowship (*alternate*)
- 2002-2003 NINDS Post-doctoral Supplemental Research Award (RO1NS39942)

2000	Robert L. Szymanski III memorial Travel Award
1998	Clifford D. Clark Fellowship Research Award
1996-2001	Clifford D. Clark Fellowship Academic Award
1993-1994	Minority Biomedical Research Services Award (MBRS; 2T34GM008167)
1994-1996	Minority Access to Research Careers Award (MARC; 5T35HL007801)

SOCIETY MEMBERSHIP

2002- Present	Society for Neuroscience
2002- Present	American Epilepsy Society
2002- Present	Women in Neuroscience
2005- Present	Molecular and Cellular Cognition Society
2005- Present	Comprehensive Neuroscience Center-UAB
2008- Present	American Physiological Society

AD HOC REVIEWER

Nature Neuroscience
 Neurobiology of Learning and Memory
 Journal of Neurochemistry
 Journal of Neuroscience
 Cell Science

TEACHING EXPERIENCE

2002-2007	Teaching: There are no formal teaching requirements during my postdoctoral training period. However, I have the opportunity to teach various techniques to rotating graduate students and junior post-docs in the lab.
2007	Co-Instructor: Science and Honor Technology Program-Mechanisms of Learning and Memory, University of Alabama, Alabama, AL
1998-1999	Teaching Assistant: Immunology, Binghamton University, Binghamton, NY
1995-1996	Teaching Assistant: Physics, Chemistry, Alabama State University, Montgomery, AL

UNIVERSITY SERVICES

2006-2008	Summer Program in Neuroscience (SPIN), University of Alabama-Birmingham, Birmingham, AL. SPIN is funded by the National Science Foundation Research Experience for Undergraduates (REU) program. Each summer, I provide motivated undergraduates who have demonstrated excellent scientific aptitude with the opportunity to experience independent research in the neurosciences.
2007	Alzheimer's Disease Research Center (ADRC) Harper Fellowship. University of Alabama-Birmingham, Birmingham, AL. I provided undergraduates, many on their way to medical school, the opportunity to experience basic science research for the first time in a laboratory setting.
2005-2006	Oral qualifying preparatory course, Baylor College of Medicine, Houston, TX. I provided first and secondary graduate students a forum by which they could develop critical reasoning skills through critical reading of the literature and methods for developing research plans and experimental design. All of these skills are instrumental in the preparation for their oral qualifying exams.

PUBLIC SERVICES

2008-Present	African-American Civic Empowerment Inaugural Fund. The purpose of this organization is to raise money to send young African-American adults from Alabama to national and regional public service and political trainings,
--------------	---

- conventions and other events so that we are better able to represent and benefit the State in all aspects of public service and politics.
- 2007-Present Faculty Women's Club. The UAB Faculty Women's Club helps create a sense of community among UAB women through programs to welcome newcomers, children's playgroups, intellectually diverse programs, interest groups, and service activities including our scholarship program for deserving women returning to college.
- 2007-Present International League Against Epilepsy (ILAE)-North American Commission initiative in Haiti. This is an effort of the North American Commission, born out of the ILAE, to increase epilepsy awareness in Haiti. A group of Haitian intellectuals called the Haitian League have organized to write grants and facilitate EEG monitoring of patients in rural parts of Haiti.

PUBLICATIONS

18. F. Lubin, T.L. Roth, and J.D. Sweatt. Site specific DNA methylation of the BDNF gene in memory formation. 2008, In Press *J. Neurosci.*
17. Y. Jiang, B. Langley, F.D. Lubin, W. Renthal, M.A. Wood, D.H. Yasui, A. Kumar, E.J. Nestler, S. Akbarian, A.C. Beckel-Mitchener. Epigenetics in the Nervous System. 2008, In Press *J. Neurosci.*
16. H.J. Ahn, C. Hernandez, J. Levenson, F. Lubin, H.C. Liou, and J.D. Sweatt. c-Rel, an NF- κ B Family Transcription Factor, is Required for Hippocampal Long-term Synaptic Plasticity and Memory Formation. 2008, *Learning and Memory* 11;15(7):539-49.
15. A.P. Nicholas*, F. Lubin*, P.J. Hallett, P. Vattam, A.R. Crossman, P. Ravenscroft, E. Bezard, S. Zhou, J.M. Brothie, J.D. Sweatt, and D.G. Standaert. Striatal Histone Post-Translational Modifications in MPTP Models of Levodopa-Induced Dyskinesia. *Co-First author. 2008, *J. Neurochem*, 106, 486-494.
14. Y.C. Lai, F. Lubin, Y. Ren, W.L Lee, A.E. Anderson. Nuclear factor-kappa B regulated transcriptomes in hippocampus during status epilepticus. 2007, *Epilepsia*, 48: 265-266.
13. F. Lubin and J.D. Sweatt. The I κ B kinase regulates chromatin structure during reconsolidation of conditioned fear memories. 2007, *Neuron*, 20; 55(6):942-57.
12. F. Lubin, Y. Ren, X. Xu, and A.E. Anderson. Nuclear Factor- κ B regulates seizure threshold and gene transcription following convulsant stimulation. 2007, *J. Neurochem*, 103 (4); 1381-1395.
11. M. Stulic, F. Lubin, P. O'Donnell, S. P. Tammarillo, and D. W. McGee. Effect of the α 3 β 1 integrin on the IL-1 stimulated activation of the c-Jun N-Terminal Kinase (JNK) in Caco-2 cells. 2007, *Cytokines*, 37(2):163-70.
10. J.M. Levenson, T. Roth, F. Lubin, C. Miller, I-Chia Huang, P. Desai, J.D. Sweatt. Evidence that (Cytosine-5) Methyltransferase regulates Synaptic plasticity in the CNS. 2006, *J. Biol. Chemistry*, 9;281(23):15763-73.
9. Y. Ren, L.F. Barnwell, J. Alexander, F. Lubin, P.J. Pfaffinger, J.P. Adelman, J.D. Sweatt, L. A. Schrader, A. E. Anderson. cAMP-dependent protein kinase phosphorylates small-conductance Ca²⁺-activated potassium channel, SK2. 2006, *J. Biol. Chemistry*, 28;281(17):11769-79.
8. L. F. Barnwell, X. Xu, F. Lubin, and A.E. Anderson. Activity-dependent alterations in kv4.2: A candidate role in epilepsy. 2005, *Epilepsia*, 46: 272-273.
7. F. Lubin, L. D. Johnston, J. D. Sweatt, and A.E. Anderson. Kainate mediates NF- κ B activation in hippocampus via PI3K and ERK. 2005, *Neuroscience*, 133(4):969-981.
6. F. Lubin, X. Xu, and A.E. Anderson. NF- κ B gene regulation in status epilepticus. 2005, *Epilepsia*, 46: 113-114.

5. G. Li, F. Lubin, and D.W. McGee. $\alpha 3\beta 1$ integrin induced suppression of the Caco-2 epithelial cell IL-1 signaling pathway leading to NF- κ B activation. 2004, Cellular Immunology, 231(1-2):30-9.
4. F. Lubin, V. Leung, and A.E. Anderson. Modulation of hippocampal NF- κ B transcriptional activity in the kainate model of epilepsy. 2004, Epilepsia, 45:10-10.
3. F. Lubin, M. Segal, and D. McGee. Regulation of epithelial cell cytokine responses by the $\alpha 3\beta 1$ integrin. 2003, Immunology, 108(2):204-10.
2. D. McGee, F. Lubin, and G. Li. Suppression of epithelial cell cytokine responses by the alpha 3 beta 1 integrin is mediated through suppressed NF-kappa B activation. 2001, Mol. Biol. Cell, 12:2520-2521.
1. F. Lubin, C. Goess, M. Segal, D. W. McGee. Differential effect on IL-6, IL-8, and MCP-1 secretion in intestinal epithelial cell lines by extracellular matrix proteins. 2000, FASEB 14 (6): A1200-A1200.

WRITTEN REPORTS ABOUT MY WORK

1. Nature Reviews Neuroscience p.816-817. Research highlights in Learning and Memory "Remodel to reconsolidate" November 2007:8 (11).
2. Cell p.197,199. Leading Edge, Neurobiology Select "A Frightful Change in Chromatin Behavior" October 19, 2007: 131 (2). Summary: Emerging roles for epigenetic modifications and chromatin remodeling in the nervous system provide the focal point for this issue's Neurobiology Select. Recent evidence shows that changes in chromatin structure are critical to the reconsolidation of fear memories. Other new papers characterize the regulation of neural stem cells by histone acetylation and establish roles for epigenetic modifications and chromatin remodeling in the formation of dendrites and synapses.
3. Neuroscience Gateway (Nature). October 2007. "Converging roads in a yellow wood". Featured Article: Lubin, F.D. & Sweatt, J.D. The I κ B kinase regulates chromatin structure during reconsolidation of conditioned fear memories. Neuron 55, 942-957 (2007).
4. UAB News The Kaleidoscope p.1,3. "Study eyes retrieval of memories, impact on brain, immune system". September 25, 2007: 42 (34).

MANUSCRIPTS SUBMITTED

1. T. L. Roth, F. Lubin, A. Funk, and J. D. Sweatt. Lasting epigenetic influence of early-life adversity on the BDNF gene. In review Biol. Psychiatry.
2. F. Lubin, D.L. Molfese, S. Artis, and J.D. Sweatt. Histone methylation at gene promoter regions during Memory Consolidation. In review Learning and Memory.
3. D.L. Molfese, J.D. Sweatt, and F. Lubin. Regulation of histone methylation during memory formation in the hippocampus. In review Neurobiol. of Learning and Memory

MANUSCRIPTS IN PREPARATION

1. F. Lubin, T.L. Roth, and J.D. Sweatt. Epigenetics: New Molecular Mechanisms for Memory Formation. Invited review in preparation to JPET.
2. F. Lubin and S. Nozell. NF- κ B in the nucleus: From form to function in the CNS. Invited review in preparation to Glia.

REVIEWS AND BOOK CHAPTERS

1. **F. Lubin**, E.D. Roth, J.D. Sweatt, and T.L. Roth. 2008. A novel approach to understanding neural plasticity: epigenetic regulation of the *BDNF* gene. Neural Pathways Research; Editor: Florian L. Pichler. Nova Science Publishers, Inc., NY.

INVITED PRESENTATIONS/LECTURES

2008. **F. Lubin**. Linking the epigenetic code of Gene regulation to Fear memory formation. Minisymposium. The Society for Neuroscience Annual Meeting, Washington, DC.
2008. **F. Lubin**. Epigenetic mechanisms in the functioning brain: Implications in memory formation and epilepsy. Center for Learning and Memory, Institute for Neuroscience. University of Texas at Austin, Austin, TX.
2008. **F. Lubin**. Epigenetic molecular mechanisms in adult behavior. University of Alabama-Birmingham, Birmingham, AL. Neurology Department, Schizophrenia meeting.
- 2007 **F. Lubin**. Linking the Epigenetic Code of Exon-Specific BDNF DNA Methylation to Fear Memory Formation. Molecular and Cellular Cognition Society Meeting, San Diego, CA.
- 2007 **F. Lubin**. Epigenetic mechanisms in memory formation. Science and Technology Honors Program, University of Alabama-Birmingham, Birmingham, AL.
- 2006 **F. Lubin** and J.D. Sweatt. NF- κ B Activation and Epigenetic Mechanisms in Memory Formation. University of Alabama-Birmingham, Birmingham, AL. Neurobiology departmental retreat.
- 2002 **F. Lubin**, L.D. Johnston, V.W. Leung, J.D. Sweatt, and A.E. Anderson. NF- κ B Activation Following Kainate-Treated Hippocampus. The Society for Neuroscience Annual Meeting, Orlando, FL.
- 1999 **F. Lubin**, J. Wong, and D.W. McGee. Extracellular matrix proteins and the $\alpha 3\beta 1$ integrin receptor modulate Caco-2 cell cytokine secretion. Binghamton University Fall Biological Symposium.
- 1996 **F. Lubin** and D.W. McGee. Regulation of intestinal epithelial cell cytokine secretion by ECM proteins. Binghamton University Fall Biological Symposium.

SELECTED RESEARCH ABSTRACTS

29. **F. Lubin**. Epigenetic Regulation of Genes in Seizure-induced Fear Memory Processing. Gordon Research Conference "Mechanisms in Epilepsy and neuronal synchronization." Maine August 2008.
28. D.L. Molfese, J.D. Sweatt, and **F. Lubin**. The molecular persistence of memory: Histone methylation, memory formation, and the molecular markers of extinction. The Society for Neuroscience Annual Meeting, Washington, DC. November 2008.
27. L. Pozzo-Miller, **F. Lubin**, S. Campbell, and G. Calfa. HDAC activity is required for BDNF to increase dendritic spine density and quantal neurotransmitter release onto CA1 pyramidal neurons. The Society for Neuroscience Annual Meeting, Washington, DC. November 2008.
26. D.L. Molfese, J.D. Sweatt, and **F. Lubin**. The molecular persistence of memory. 18th Annual Rush Record Neuroscience Forum, Baylor College of Medicine, Houston, TX. February 2008.
25. **F. Lubin**, T.L. Roth, and J.D. Sweatt. Linking the epigenetic code of exon-specific *BDNF* DNA methylation to fear memory formation. The Society for Neuroscience Annual Meeting, San Diego, CA. November 2007.
24. T.L. Roth, **F. Lubin**, A. Funk, J.D. Sweatt. The molecular scars of early stress: persisting changes in DNA methylation in a model of maternal maltreatment. The Society for Neuroscience Annual Meeting, San Diego, CA. November 2007.
23. D.L. Molfese, J.D. Sweatt, and **F. Lubin**. Regulation of histone methylation in the hippocampus during memory consolidation. The Society for Neuroscience Annual Meeting, San Diego, CA. November 2007.

22. D. L. Molfese, J.D. Sweatt, and **F. Lubin**. Regulation of histone methylation during memory formation in the hippocampus. 17th Annual Rush Record Neuroscience Forum, Baylor College of Medicine, Houston, TX. March 2007.
21. D.L. Molfese, J. Levenson, **F. Lubin**, and J.D. Sweatt. NF- κ B trafficking and DNA binding in long-term memory. The Society for Neuroscience Annual Meeting, Atlanta, GA. October 2006.
20. **F. Lubin** and J.D. Sweatt. Participation of the NF- κ B signaling pathway in histone regulation during long-term memory reconsolidation. The Society for Neuroscience Annual Meeting, Atlanta, GA. October 2006.
19. **F. Lubin**, J.D. Sweatt, and A.E. Anderson. Recruitment of NF- κ B to BDNF gene promoter regions in experimental temporal lobe epilepsy. Gordon Research Conference "Mechanisms in Epilepsy and neuronal synchronization." Maine August 2006.
18. **F. Lubin**, X. Xu, and A. E. Anderson. NF- κ B gene regulation triggered early by status epilepticus. The Society for Neuroscience Annual Meeting, Washington D.C. November 2005.
17. **F. Lubin**, X. Xu, and A.E. Anderson. NF- κ B gene regulation in status epilepticus. The American Epilepsy Society Annual Meeting, Washington D.C. December 2005.
16. D.W. McGee, M. Stulic, **F. Lubin**, P.M. O'Donnell, and B. Rafferty. Effect of activating the $\alpha 3 \beta 1$ integrin on IL-1 stimulated JNK signaling in Caco-2 cells. The Society for Mucosal Immunology's 12th International Congress of Mucosal Immunology, Boston, MA. June 2005.
15. **F. Lubin**, V. W. Leung, and A. E. Anderson. NF- κ B activation and gene regulation in the kainate epilepsy model. The Society for Neuroscience Annual Meeting, San Diego, CA. October 2004.
14. **F. Lubin**, V.W. Leung, L.D. Johnston, A. Varga, C.L. Lee and A.E. Anderson. Kainate-Mediated Transcriptional Activation in Hippocampus. The American Epilepsy Society Annual Meeting, Boston, MA. December 2003.
13. K.L. Williams, **F. D. Lubin**, V.W. Leung, M.W. Swank, A.E. Anderson. Proteomic Identification of a Novel Hippocampal MAPK Substrate, TOAD-64, in the Kainate Epilepsy Model. The Society for Neuroscience Annual Meeting, New Orleans, LA. November 2003.
12. **F. Lubin**, V.W. Leung, L.D. Johnston J.D. Sweatt, and A. E. Anderson. MAPK Activation and Transcriptional Regulation in the Kainate Model of Epilepsy. The Society for Neuroscience Annual Meeting, New Orleans, LA. November 2003.
11. **F. Lubin**, L.D. Johnston, J.D. Sweatt, and A.E. Anderson. Modulation of NF- κ B Activation in Rat Hippocampus. 6th Annual Pediatrics Fellow's Day, Baylor College of Medicine, Houston, TX, April 2003.
10. **F. Lubin**, L.D. Johnston, J.D. Sweatt, and A.E. Anderson. Modulation of NF- κ B Activation in Hippocampus. 13th Annual Rush Record Neuroscience Forum, Baylor College of Medicine, Houston, TX. March 2003.
9. **F. Lubin**, L.D. Johnston, V.W. Leung, and A.E. Anderson. Kainate Modulation of NF- κ B Activation in Rat Hippocampus. The American Epilepsy Society Annual Meeting, Seattle, WA, December 2002.
8. A.E. Anderson, **F. Lubin**, L.D. Johnston, V. Leung, M.W. Swank. Proteomic Analysis of Novel Hippocampal Protein Kinase Substrates in a Kainate Model of Epilepsy. The Society for Neuroscience Annual Meeting, Orlando, FL. November 2002.
7. **F. Lubin**, L.D. Johnston, V.W. Leung, J.D. Sweatt, and A.E. Anderson. Modulation of Hippocampal Transcriptional Activation: A Candidate Mechanism in epileptogenesis. 5th Annual Pediatrics Fellow's Day, Baylor College of Medicine, Houston, TX, April 2002.
6. **F. Lubin**, L. D. Johnston, V.W. Leung, J.D. Sweatt, and A.E. Anderson. Modulation of Hippocampal Transcriptional Activation: A Candidate Mechanism in the Kainate Model of

- Epilepsy. *12th Annual Rush Record Neuroscience Forum*, Baylor College of Medicine, Houston, TX. March 2002.
5. D.W. McGee, **F. Lubin** and G. Li. Suppression of epithelial cell cytokine secretion by the $\alpha 3\beta 1$ integrin is mediated through suppressed NF- κ B activation. *Cell Biology Annual Meeting*, Washington D.C. December 2001.
 4. D.W. McGee, and **F. Lubin**. A novel role for the $\alpha 3\beta 1$ integrin receptor in the regulation of cytokine secretion by epithelial cells. *AAI/CIS Joint Annual Meeting*, FL. April 2001.
 3. **F. Lubin**, C. Goess, M. Segal and D.W. McGee. Differential effect on IL-6, IL-8, and MCP-1 secretion in intestinal epithelial cell lines by extracellular matrix proteins. *Immunology 2000 AAI/CIS Joint Annual Meeting*, Seattle, WA. May 2000.
 2. D.W. McGee, **F. Lubin** and J. Wong. Extracellular Matrix Proteins and integrins modulate intestinal epithelial cell cytokine secretion. *Binghamton University Fall Biological Symposium*. November 1999.
 1. **F. Lubin**, and S. Singh. Evaluation of the Evolutionary Conservation of TRAFam/CD40bp/CRAF1. *American Society of Microbiology (ASM) Annual Meeting*, Washington D.C. Fall 1995.

RESEARCH PROJECTS AND FUNDING

Ongoing Research Support

Pathway to independence

K99/R00 MH082106-01 Lubin (PI)

NIH/NIMH

01/01/08-10/01/11

K99- \$90,000 for 1 year, R00- \$250,000/year

This proposal seeks to understand epigenetic mechanisms of gene regulation in the process of memory formation and storage (consolidation).

Status: Active.

Role: PI

Pending Research Grants

NARSAD Lubin (PI)

07/01/08-06/31/09

\$30,000/year

The Project is related to testing the hypothesis of a role for NF- κ B signaling in regulating chromatin structure in long-term changes in gene transcription and behavior.

Status: Pending Review.

Role: PI

Completed Research Projects

Postdoctoral NRSA

F32 NS048811-01A1 Lubin (PI)

NIH/NINDS

12/14/04-12/13/07

\$153,000 for 3 years

The overall goal of these studies is to further characterize the cellular and molecular mechanisms by which NF- κ B is activated in hippocampus and to determine whether NF- κ B contributes to altered gene expression in memory formation.

Role: PI

RO1NS39942-02 (Minority postdoctoral supplement)

Anderson (PI)

NIH/NINDS

04/01/02-04/30/04

\$164,455

The MAPK Cascade in Epilepsy

This research supplement proposal relates to the specific research goals and objectives of the parent grant. Using results from the parent grant, studies further evaluated the effects of MAPK inhibition and other potential downstream effectors, such as transcription factors, of MAPK in epilepsy.

Role: Co-Investigator

RO1NS39942-02 (Microarray supplement) Anderson (PI)

07/01/04-06/30/05
\$50,000

NIH/NINDS

The MAPK Cascade in Epilepsy

This research supplement proposal does not relate to the specific research goals and objectives of the parent grant. The goal of this supplement is to use DNA microarray analysis to profile CREB- and NF- κ B-responsive genes during epileptogenesis.

Role: Co-Investigator

AES/Milken Epilepsy Foundation Award Lubin (PI)

07/01/04-06/30/05
\$40,000

NF- κ B Activation in Epilepsy

These studies focus on cell signals that couple to specific NF- κ B-regulated gene changes in epilepsy. The overall goal is to elucidate mechanisms involved in the development of epilepsy and to identify potentially novel therapeutics targets.

Role: PI

MENTORED GRADUATE STUDENTS

As a postdoctoral fellow, I have the opportunity to co-mentor graduate students in the lab and contribute to the development and completion of their dissertation research.

Hyung Jin Ahn (PhD, 2007)	Neuroscience department, Baylor College of Medicine. Currently Postdoctoral Fellow at the University of Texas, Austin, TX. J. David Sweatt, Farah D. Lubin, Co-Mentors.
David L. Molfese (MS, 2003)	Neuroscience department, Baylor College of Medicine and Neurobiology Program, School of Medicine, UAB. Currently a Ph.D. candidate. J. David Sweatt, Farah D. Lubin, Co-Mentors.
Adam Funk (2007)	Cellular and Molecular Biology Program, UAB. Rotation student January-April 2007

MENTORED UNDERGRADUATE STUDENTS

Amanda Benton, Curriculum Biology, UAB. September 2007-December 2008.
 Dominik Rose, Curriculum Respiratory Therapy, UAB. December 2006-May 2008.
 Carmella Montgomery, Curriculum Biology, UAB. April 2007-May 2008.
 Rahel Lynes, Summer Program in Neuroscience, UAB. Oakwood College, Huntsville, AL. June-August 2007.
 Sonja Artis, Summer Program in Neuroscience, UAB. Oakwood College, Huntsville, AL. June-August 2006.
 Kelli Baalman, Summer Program in Neuroscience, UAB. Rockhurst University, Kansas City, MO. June-August 2006.
 Aswin Sundarakrishnan, Neuroscience department, Baylor College of Medicine. Drexel University. November 2005-April 2006.

REFERENCES

J. David Sweatt, Ph.D. Post-doctoral Mentor, Chair, Neurobiology Dept., University of Alabama at Birmingham, AL (205) 975-5196

E-mail: jsweatt@nrc.uab.edu

Anne E. Anderson, M.D. Post-doctoral Mentor, Dept. of Pediatrics-Neurology, Baylor College of Medicine Houston, TX (832) 824-3968

E-mail: annea@bcm.tmc.edu

Dennis W. McGee, Ph.D. Pre-doctoral Mentor, Dept. of Biological Sciences, Binghamton University Binghamton, NY (607) 777-2620

E-mail: dmcgee@binghamton.edu

John J. Hablitz, Ph.D. Research Mentor, Co-Chair, Professor Neurobiology Dept., University of Alabama at Birmingham, AL (205) 934-0742

E-mail: jhablitz@uab.edu

John W. Swann, Ph.D. Research Mentor, Director of Cain Foundation Labs, Dept. of Pediatric-Neurology, Baylor College of Medicine Houston, TX (832) 824-3968

E-mail: jswann@bcm.tmc.edu

Erik D. Roberson, M.D., Ph.D.

ASSISTANT PROFESSOR OF NEUROLOGY AND NEUROBIOLOGY
 VIRGINIA B. SPENCER SCHOLAR IN NEUROSCIENCE
 UNIVERSITY OF ALABAMA AT BIRMINGHAM
 1825 UNIVERSITY BOULEVARD, SHELBY 1106
 BIRMINGHAM, AL 35294-2182
 PHONE: (205) 996-9486
 FAX: (205) 934-2493
 eroberson@uab.edu

Education

- A.B.** in Molecular Biology with Highest Honors, 1990
Princeton University, Princeton, NJ
- Ph.D.** in Neuroscience (J. David Sweatt, Ph.D., mentor), 1997
Baylor College of Medicine, Houston, TX
- M.D.** with High Honors, 1999
Baylor College of Medicine, Houston, TX

Postgraduate Training

- 1999-00 **Intern**, Baylor College of Medicine, Houston, TX
- 2000-03 **Resident & Chief Resident in Neurology**
University of California, San Francisco
- 2003-05 **Clinical Fellow in Behavioral Neurology** with Bruce Miller, M.D.
University of California, San Francisco
- 2003-06 **Research Scientist** with Lennart Mucke, M.D.
Gladstone Institute of Neurological Disease, San Francisco, CA

Principal Positions Held

- 2003-05 **Clinical Instructor** of Neurology, UCSF
- 2003-06 **Research Scientist**, Gladstone Institute of Neurological Disease
- 2005-08 **Assistant Adjunct Professor** of Neurology, UCSF
- 2006-08 **Staff Scientist**, Gladstone Institute of Neurological Disease
- 2008- **Assistant Professor** of Neurology, UAB

Concurrent Appointments

- 2008- **Assistant Professor** of Neurobiology, UAB
- 2008- **Investigator**, McKnight Brain Institute, UAB

Honors & Awards

- Virginia B. Spenser Endowed Scholar in Neuroscience, 2008
- Kathryn Grupe Award for Excellence in Alzheimer's Disease Research, 2005
- S.D. Bechtel, Jr. Young Investigator Award, 2004
- Giannini Family Foundation Fellow, 2004
- UCSF Chief Resident in Neurology, 2002-2003
- Alpha Omega Alpha, 1999
- Life & Health Insurance Medical Research Fund Young Scientist Scholar, 1992-1997
- Baylor College of Medicine Dean's Award for Excellence, 1992-1997
- Baylor College of Medicine Presidential Scholar, 1990-1999

- NIH Medical Scientist Training Program fellowship, 1990–1999
- Phi Beta Kappa, 1990
- Valedictorian, Cedar Rapids Washington High School, 1986

Clinical Service

Clinical Activities

- UCSF Memory & Aging Center Clinic, 2003–2008
- Neurology Attending, San Francisco General Hospital inpatient service, ad hoc 2003–2005
- Neurology Attending, UCSF general neurology outpatient clinic, 2003–2004
- UAB Memory Disorders Clinic, 2008–

License & Certification

- California Medical Board, #A73759
- Alabama Board of Medical Examiners, #MD.29140
- American Board of Psychiatry and Neurology, #52944

Teaching and Mentoring

Formal Courses

- **Medical Neuroscience**, UAB (Robin Lester, director), 2008–
Small group sessions on clinical neuroscience for first-year medical students
- **Brain, Mind, & Behavior**, UCSF (Dan Lowenstein, director), 2005–2008
Small group sessions on neuroanatomy and clinical neuroscience for first-year medical students
- **Advances in Medical Science**, UCSF (Steve Finkbeiner, director), 2003–2005
Small group sessions on basic research in neurology for third-year medical students
- **Clinical Neurology**, UCSF, 2000–2008
Supervision of medical students and residents on rounds and in clinic
- **Medical Physiology**, BCM (Tom Poder, director), 1996
Weekly lectures for groups of 25 first-year medical students
- **Cellular Neurophysiology II**, BCM (Dan Johnston, director), 1993
Weekly problem sessions for first-year Neuroscience graduate students
- **Medical Neuroscience**, BCM (Bob Thalmann, director), 1992, 1997
Semiweekly lectures/labs for groups of 25 first-year medical students

Informal Teaching

Year	Activity	Contribution
2000–03	UCSF Neurology/Psychiatry 110	Supervised core medical students and interns/residents in Neurology, Psychiatry, Medicine, Neurosurgery
2002–03	UCSF Neurology CPC Series	Reorganized conference format with medical student participation; taught small groups of students in several sessions before each CPC
2002–03	UCSF Neurology Housestaff Conference	Planned curriculum and organized speakers; Developed new neuroanatomy module
2003–	UCSF Memory & Aging Center Clinic	Supervise students, interns, and residents rotating through behavioral neurology clinic
2005	UCSF MSTP Rounds	Prepared and co-presented interactive, case-based

Year	Activity	Contribution
		didactic session
2005–	UCSF Memory & Aging Center seminar series	Arrange basic- and disease-oriented neuroscience speakers as a regular part of seminar schedule
2007–	Medicine 160.04 Preceptorship	Mentor MSTP students in a clinical preceptorship during their graduate school training

Predoctoral Students Supervised or Mentored

Dates	Name	Program or school	Role	Current Position
2004	Nathanael Horton	Summer HS Student	Research co-supervisor	Brown University
2006	Charley Ma	Summer HS Student	Research co-supervisor	unchanged
2007	Carol Peebles	UCSF MSTP Student	Clinical preceptor	unchanged
2007	Meg Younger	UCSF Neuroscience Student	Research co-supervisor	unchanged

Professional Service

Service to Publications

2005	Member	<i>Annals of Neurology</i> Strategic Planning Committee
2006–	ad hoc reviewer	<i>Brain Research</i>
2006–	ad hoc reviewer	<i>Annals of Neurology</i> (8 manuscripts total)
2006–	ad hoc reviewer	<i>Psychiatric Times</i>
2007–	ad hoc reviewer	<i>Experimental Neurology</i>
2007–	ad hoc reviewer	<i>Advanced Drug Delivery Reviews</i>
2007–	ad hoc reviewer	<i>Neuropsychiatric Disease and Treatment</i>
2007–	ad hoc reviewer	<i>Neurochemical Research</i>
2007–	ad hoc reviewer	<i>BMC Pharmacology</i>
2007–	ad hoc reviewer	<i>Stroke</i>
2007–	ad hoc reviewer	<i>European Journal of Neurology</i>
2008–	ad hoc reviewer	<i>Journal of Cellular and Molecular Medicine</i>
2008–	ad hoc reviewer	<i>Archives of Neurology</i>

Invited Lectures

International

2006	5 th International Conference on the Frontotemporal Dementias
2007	Asian Brain Health Initiative Symposium, Beijing

National

2007	University of Texas Southwestern Medical Center Neuroscience Seminar
2007	University of Alabama Birmingham Neurobiology Seminar
2007	University of Michigan Neurology Grand Rounds
2008	University of North Carolina Neuroscience Center Seminar
2008	Emory University Department of Neurology Seminar
2008	Keystone Symposium on Alzheimer's Disease
2008	Washington University Alzheimer's Disease Research Center Symposium

Regional (last four years)

2005	Frontotemporal Dementia PPG External Scientific Advisory Board Meeting
2005	Gladstone Institutes Annual Retreat
2005	Bay Area Alzheimer's Disease Research Symposium
2006	Gladstone Institutes External Scientific Advisory Board Meeting

2006	UCSF Department of Neurology Robert A. Fishman Symposium
2006	Gladstone Institutes Advisory Council
2007	Gladstone Institutes "Science for Admin" Series
2007	Gladstone Institute of Neurological Disease Seminar Series (twice)
2007	UCSF Memory & Aging Center Seminar Series
2007	National Student Leadership Conference
2007	UCSF Department of Neurology Frontiers in Neurology and Neuroscience (Grand Rounds)
2008	Gladstone Institutes "Science for Admin" Series

University and Institute Service

2002-03	Chief Resident	UCSF Department of Neurology
2002-03	Member	UCSF Medical Staff Training Committee
2005-06	Member	Gladstone Diversity Leadership Team
2005-06	Member	Gladstone Student & Minority Outreach Committee
2007-08	Member	Gladstone Behavior Core Users' Committee

Government and Foundation Service

2004-06	Grant reviewer	John Douglas French Alzheimer's Foundation
2008-	Grant reviewer	Alzheimer Association

Public Service

1991-97	Member /Chair	Board of Education, Christ the Lord Lutheran Church & School
1998-99	Member	Church Council, Christ the Lord Lutheran Church & School
2001-08	Chairman	Board of Education, Gloria Dei Lutheran Church & School

Professional Memberships

1991-	Society for Neuroscience
2000-	American Academy of Neurology
2005-	Molecular and Cellular Cognition Society
2008-	International Society to Advance Alzheimer Research and Treatment

Research & Creative Activities**Research Funding***Current*

1. K08 NS054811.....	4/1/06-3/31/11
NIH/NINDS	
"Mechanisms for Tau Involvement in Alzheimer's Disease"	\$161,860 direct/yr 1
	\$809,300 direct/yr 1-5
2. Young Investigator Award.....	1/1/05-6/30/09
S.D. Bechtel, Jr.	
"The Role for Tau in Neurodegeneration"	\$33,333 direct/yr 1
	\$477,778 direct/yr 1-4
3. Investigator-initiated Award	1/1/08-12/31/09
Consortium for FTD Research (CFR)	
"Behavioral Abnormalities in Progranulin-deficient Mice"	\$36,554 direct/yr 1
	\$107,996 direct/yr 1-2

Completed

1. P50 AG023501	4/1/05-3/31/07
NIH/NIA/UCSF Alzheimer's Disease Research Center (pilot project subcontract)	\$27,778 direct/yr 1
"Mediation of A β -Induced Alzheimer Pathology by Nonfibrillary Tau"	\$27,778 direct/yr 1-2
2. Fellowship	4/1/04-3/31/06
Giannini Family Foundation	\$36,000 direct/yr 1

"Roles for Tau and Serotonin in Frontotemporal Dementia"

\$74,000 direct/yr 1-2

3. Young Scientist MD/PhD Scholarship

7/1/92-6/30/97

Life & Health Insurance Medical Research Fund

\$16,000 direct/yr 1

"Protein Kinase Activation Mediated by NMDA Receptor Occupation"

\$80,000 direct/yr 1-5

Patents

Number	Description
Pending	Methods and Compositions for Reducing Amyloid β Levels (Serial No. 60/859,380)
Pending	Agents That Reduce Neuronal Overexcitation (Serial No. 60/922,082)

Publications

Articles

1. Kadle, R., C. Suksang, **E.D. Roberson**, and R.E. Fellows. (1988). Identification of an insulin-like growth factor in astrocyte-conditioned medium. *Brain Res.* 460:60-67.
2. Sessoms, J.S., S.-J. Chen, D.M. Chetkovich, C.M. Powell, **E.D. Roberson**, J.D. Sweatt, and E. Klann. (1992). Ca^{2+} -induced persistent protein kinase C activation in rat hippocampal homogenates. *Second Messengers Phosphoproteins* 14:109-126.
3. **Roberson, E.D.**, and J.D. Sweatt. (1995). Regulation of adenylyl cyclase in LTP. *Behav. Brain Sci.* 18: 485-486.
4. **Roberson, E.D.**, and J.D. Sweatt. (1996). Transient activation of cyclic AMP-dependent protein kinase during long term potentiation. *J. Biol. Chem.* 271: 30436-30441.
5. **Roberson, E.D.**, J.D. English, and J.D. Sweatt. (1996). A biochemist's view of long-term potentiation. *Learn. Mem.* 3: 1-24.
6. Klann, E., **E.D. Roberson**, L.T. Knapp, and J.D. Sweatt. (1998). A role for superoxide in protein kinase C activation and induction of long-term potentiation. *J. Biol. Chem.* 273:4516-4522.
7. Matilla, T., **E.D. Roberson**, S. Banfi, J. Morales, D. Armstrong, E. Burrig, H.T. Orr, J.D. Sweatt, H.Y. Zoghbi, and M. Matzuk. (1998). Mice lacking ataxin-1 display learning deficits and decreased hippocampal paired-pulse facilitation. *J. Neurosci.* 18:5508-5516.
8. Sweatt, J.D., C.M. Atkins, J. Johnson, J.D. English, **E.D. Roberson**, S.-J. Chen, A. Newton, and E. Klann. (1998). Protected-site phosphorylation of protein kinase C in hippocampal long-term potentiation. *J. Neurochem.* 71:1075-1085.
9. **Roberson, E.D.**, J.D. English, J.P. Adams, J.C. Selcher, C. Kondratik, and J.D. Sweatt. (1999). the mitogen-activated protein kinase cascade couples PKA and PKC to cAMP response element binding protein phosphorylation in area CA1 of hippocampus. *J. Neurosci.* 19:4337-4348.
10. **Roberson, E.D.**, and J.D. Sweatt. (1999). A biochemical blueprint for long-term memory. *Learn. Mem.* 6:381-388.

11. Atkins, C.M., **E.D. Roberson**, and J.D. Sweatt. (1999). Cellular signaling roles of reactive oxygen species. *Recent Res. Devel. Neurochem.* 2:25–36.
12. Adams, J.P., **E.D. Roberson**, J.D. English, J.C. Selcher, and J.D. Sweatt. (2000). MAPK regulation of gene expression in the central nervous system. *Acta Neurobiol. Exp.* 60:377–394.
13. **Roberson, E.D.**, and J.D. Sweatt. (2001). Memory-forming chemical reactions. *Rev. Neurosci.* 12:41–50.
14. Nakamura, K., **E.D. Roberson**, and J.W. Tsao. (2004). Polyneuropathy following gastric bypass surgery. *Am. J. Med.* 115:679–680.
15. Johnson, J.K., J. Diehl, M.F. Mendez, J. Neuhaus, J.S. Shapira, M.S. Forman, D.J. Chute, **E.D. Roberson**, C. Pace-Savitsky, T.W. Chow, H.J. Rosen, H. Forstl, A. Kurz, and B.L. Miller. (2005). Frontotemporal lobar degeneration: Demographic characteristics among 353 patients. *Arch. Neurol.* 62:925–930.
16. **Roberson, E.D.**,[†] J.H. Hesse, K.R. Rose, H. Slama, K. Yaffe, M.S. Forman, C.A. Miller, J.Q. Trojanowski, J.H. Kramer, and B.L. Miller. (2005). Frontotemporal dementia progresses to death faster than Alzheimer's disease. *Neurology* 65:719–725. [[†] Corresponding author]
17. Mueller-Steiner, S., Y. Zhou, H. Arai, **E.D. Roberson**, X. Wang, G.-Q. Yu, L. Esposito, L. Mucke, and L. Gan. (2006). Anti-amyloidogenic and neuroprotective functions of cathepsin B: implications for Alzheimer's disease. *Neuron* 51:703–714.
18. **Roberson, E.D.**, and L. Mucke. (2006). 100 years and counting: Prospects for defeating Alzheimer's disease. *Science.* 314:781–784.
19. **Roberson, E.D.** (2006). Frontotemporal dementia. *Curr. Neurol. Neurosci. Reports.* 6:481–489.
20. **Roberson, E.D.**, K. Scarce-Levie, J.J. Palop, F. Yan, I. Cheng, T. Wu, H. Gerstein, G.-Q. Yu, and L. Mucke. (2007). Reducing endogenous tau ameliorates A β -induced deficits in an Alzheimer's disease mouse model. *Science* 316:750–754. [Commentary in *N. Engl. J. Med.* 357:933–5]
21. Palop, J.J., J. Chin, **E.D. Roberson**, J. Wang, M.T. Thwin, N. Bien-Ly, J. Yoo, K.O. Ho, G.-Q. Yu, A. Kreitzer, S. Finkbeiner, J.L. Noebels, and L. Mucke. (2007). Aberrant excitatory neuronal activity and compensatory remodeling of inhibitory hippocampal circuits in mouse models of Alzheimer's disease. *Neuron* 55:697–711.
22. Scarce-Levie, K., **E.D. Roberson**, H. Gerstein, V.S. Mandiyan, N. Shah, J.A. Cholfen, J.L.R. Rubenstein, and L. Mucke. (2008). Abnormal social behavior in mice lacking Fgf17. *Genes Brain Behav.* 7:344–354.
23. Meilandt, W.J., G.-Q. Yu, J. Chin, **E.D. Roberson**, J.J. Palop, T. Wu, K. Scarce-Levie, and L. Mucke. (2008). Enkephalin elevations contribute to neuronal and behavioral impairments in a transgenic mouse model of Alzheimer's disease. *J. Neurosci.* 28:5007–5017.

Articles in Preparation

24. **Roberson, E.D.**, W.J. Meilandt, J. Yao, and L. Mucke. Excitoprotective effect of tau reduction in hAPP mice: Gene expression microarray analysis.
25. **Roberson, E.D.**, A. Chung, and L. Mucke. MUSCULUS: An all-purpose tool for managing animal model colonies and tissue banks.

26. **Roberson, E.D.**, J. Yoo, J.L. Noebels, L. Mucke. Tau reduction prevents epileptiform activity in mouse models of Alzheimer disease.
27. Wacker, J.L., S.-Y. Huang, A.D. Steele, R. Aron, F. Giorgini, Q.V. Nguyen, **E.D. Roberson**, S. Lindquist, E. Masliah, and P.J. Muchowski. Loss of Hsp70 exacerbates pathogenesis but not levels of fibrillar aggregates in a mouse model of Huntington's disease.

Book Chapters

28. **Roberson, E.D.**, J.D. English, and J.D. Sweatt. (1996). Second messengers in LTP and LTD. In *Cortical Plasticity: LTP and LTD*, M. S. Fazeli and G. L. Collingridge, eds. (Oxford: BIOS Scientific Publishers, LTD), pp. 35-60.
29. Chin, J., **E.D. Roberson**, and L. Mucke. (2008). Molecular aspects of memory dysfunction in Alzheimer's disease. In *A Comprehensive Handbook of Learning and Memory: Molecular Mechanisms of Memory*, J.D. Sweatt, ed., J.H. Byrne, series ed. (London: Elsevier).
30. **Roberson, E.D.** Revisions to chapter on Neurodegeneration. In *Molecular Basis of Neuropharmacology: A Foundation for Clinical Neuroscience*, 2nd edition, by E.J. Nestler, S.E. Hyman, and R.C. Malenka. (New York: McGraw-Hill Companies, Inc.). In press.
31. **Roberson, E.D.**, and A. Kao. Animal models of dementia. In *The Behavioral Neurology of Dementia*, B.L. Miller and B.F. Boeve, eds. (Cambridge: Cambridge University Press). In press.

Book

Roberson, E.D. (Ed.) (planned 2009). *Alzheimer's Disease & Frontotemporal Dementia: Methods and Protocols*. (Totowa, NJ: Humana Press). In preparation.

Thesis and Dissertation

- Roberson, E.D.** (1990). Sequence-directed and protein-induced DNA bending at a locus involved in the E1A responsiveness of the adeno-associated virus P₅ promoter. Senior thesis, Princeton University.
- Roberson, E.D.** (1997). Roles for cyclic AMP-dependent protein kinase and superoxide in the induction of hippocampal long-term potentiation. Doctoral dissertation, Baylor College of Medicine.

Abstracts

1. Chetkovich, D.M., **E.D. Roberson**, and J.D. Sweatt. (1992). LTP-inducing tetanic stimulation causes an NMDA receptor-mediated increase in cAMP and a nitric oxide-mediated increase in cGMP in hippocampal area CA1. *Cold Spring Harbor Learn. Mem. Mtg. Abstr.*
2. **Roberson, E.D.**, and J.D. Sweatt. (1993). Cyclic AMP-dependent protein kinase is activated during the induction of long-term potentiation. *Soc. Neurosci. Abstr.* 19:1708.
3. Klann, E., **E.D. Roberson**, and R.M. Mack. (1995). Modulation of long-term potentiation by reactive oxygen species. *Soc. Neurosci. Abstr.* 21:1809.
4. **Roberson, E.D.**, and J.D. Sweatt. (1996). Cyclic AMP-dependent protein kinase is activated during hippocampal long-term potentiation. *Natl. Student Res. Forum Abstr.* 37:54.

5. **Roberson, E.D.**, and J.D. Sweatt. (1996). On the role of cyclic AMP-dependent protein kinase in hippocampal long-term potentiation. *Cold Spring Harbor Learn. Mem. Mtg. Abstr.*
6. Matilla, T., S. Banfi, D. Armstrong, E. Burright, **E.D. Roberson**, J.D. Sweatt, H.T. Orr, M. Matzuk, and H.Y. Zoghbi. (1996). Neurobehavioural and hippocampal abnormalities in spinocerebellar ataxia type I (*Sca1*) null mice. *Cold Spring Harbor Learn. Mem. Mtg. Abstr.*
7. Sweatt, J.D., C. Atkins, J. Johnson, J. English, **E. Roberson**, S.-J. Chen, A. Newton, and E. Klann. (1996). Increased PKC phosphorylation in hippocampal LTP. *Cold Spring Harbor Learn. Mem. Mtg. Abstr.*
8. Matilla, T., S. Banfi, N. Lu, D. Armstrong, E. Burright, **E.D. Roberson**, J.D. Sweatt, H.T. Orr, M. Matzuk, and H.Y. Zoghbi. (1996). Neurobehavioural and hippocampal abnormalities in spinocerebellar ataxia type I (*Sca1*) null mice. *Am. Soc. Hum. Genetics Abstr.*
9. **Roberson, E.D.**, J.D. English, and J.D. Sweatt. (1997). MAP kinase is activated by PKA or PKC and triggers CREB phosphorylation in hippocampal area CA1. *Soc. Neurosci. Abstr.* 23:1395.
10. Sweatt, J.D., C.M. Atkins, J. Johnson, J.D. English, **E.D. Roberson**, S.-J. Chen, A. Newton, and E. Klann. (1997). Protected-site phosphorylation of PKC in hippocampal LTP. *Soc. Neurosci. Abstr.* 23:1395.
11. Adams, J.P., **E.D. Roberson**, J.D. English, J.C. Selcher, and J.D. Sweatt. (1998). A critical role for MAP kinase in stimulus-transcription coupling in hippocampal area CA1. *Soc. Neurosci. Abstr.* 24:7.
12. **Roberson, E.D.**, J.D. English, J.P. Adams, J.C. Selcher, C. Atkins, and J.D. Sweatt. (1999). The mitogen-activated protein kinase cascade couples PKA and PKC to CREB phosphorylation in area CA1 of hippocampus. *J. Neurochem.* 73:S161.
13. Anderson, A.E., J.P. Adams, J.C. Selcher, **E.D. Roberson**, P.J. Pfaffinger, and J.D. Sweatt. (1999). MAPK, PKA, PKC, and CaMKII modulation and substrate phosphorylation in status epilepticus. *Soc. Neurosci. Abstr.* 25:541.
14. Anderson, A.E., J.P. Adams, J.C. Selcher, **E.D. Roberson**, P.J. Pfaffinger, and J.D. Sweatt. (1999). Modulation of signal transduction cascades and K^+ channel phosphorylation in the kainate model of status epilepticus. *Epilepsia* 40:21-22.
15. **Roberson, E.D.**, J.H. Hesse, K.R. Rose, K. Yaffe, J.H. Kramer, and B.L. Miller. (2004). Reduced survival in frontotemporal lobar degeneration. *Neurology* 62(S5):A158.
16. **Roberson, E.D.**, J.H. Hesse, K.R. Rose, H. Slama, K. Yaffe, M.S. Forman, C.A. Miller, J.Q. Trojanowski, J.H. Kramer, and B.L. Miller. (2004). Frontotemporal dementia progresses to death faster than Alzheimer's disease. FTD Satellite meeting at the 9th International Conference on Alzheimer's Disease and Related Disorders.
17. **Roberson, E.D.**, K. Searce-Levie, F. Yan, and L. Mucke. (2005). Tau reduction ameliorates behavioral and pathological abnormalities in APP transgenic mice. *Annals of Neurology* 58(S9):S12-13.
18. **Roberson, E.D.**, K. Searce-Levie, F. Yan, G.-Q. Yu, and L. Mucke. (2005). Tau reduction ameliorates behavioral and pathological abnormalities in APP transgenic mice. Program No. 208.20. 2005 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience. Online.

19. Mueller-Stainer, S., Y. Zhou, J. Chen, **E.D. Roberson**, G.-Q. Yu, X. Wang, L. Esposito, L. Mucke, and L. Gan. (2005). Genetic ablation of Cathepsin B has neuroprotective effects in APP-FAD transgenic mice. Program No. 662.12. *2005 Abstract Viewer/Itinerary Planner*. Washington, DC: Society for Neuroscience. Online.
20. **Roberson, E.D.**, K. Searce-Levie, F. Yan, G.-Q. Yu, and L. Mucke. (2006). Reducing tau prevents A β -induced cognitive impairment in a mouse model of Alzheimer disease. *Neurology* 66(S2):A280.
21. **Roberson, E.D.**, K. Searce-Levie, F. Yan, G.-Q. Yu, and L. Mucke. (2006). Reducing endogenous tau prevents APP/A β -induced deficits in a mouse model of Alzheimer's disease. *Alzheimer's & Dementia* 2:S38.
22. Gan, L., S. Mueller-Stainer, Y. Zhou, H. Arai, **E.D. Roberson**, J. Chen, X. Wang, G.-Q. Yu, L. Esposito, L. Mucke. (2006). Anti-amyloidogenic and neuroprotective functions of cathepsin B: implications for Alzheimer's disease. *Alzheimer's & Dementia* 2:S88.
23. **Roberson, E.D.**, K. Searce-Levie, F. Yan, G.-Q. Yu, and L. Mucke. (2006). Reducing tau prevents A β -induced premature mortality and cognitive deficits despite amyloid plaques and neuritic dystrophy. *Annals of Neurology* 60(S3):S6-7.
24. **Roberson, E.D.**, K. Searce-Levie, J.J. Palop, F. Yan, I. Cheng, T. Wu, H. Gerstein, G.-Q. Yu, and L. Mucke. (2007). Tau reduction increases resistance to excitotoxins and network dysfunction. *Annals of Neurology* 62(S11):S50. [Selected for walking tour.]
25. Palop, J.J., J. Chin, **E.D. Roberson**, J. Wang, M.T. Thwin, N. Bien-Ly, J. Yoo, K.O. Ho, G.-Q. Yu, A. Kreitzer, S. Finkbeiner, J.L. Noebels, and L. Mucke. (2007). Spontaneous non-convulsive seizure activity and compensatory hippocampal inhibition in mouse models of Alzheimer's disease. *Annals of Neurology* 62(5):547.
26. Searce-Levie, K., **E.D. Roberson**, H. Gerstein, J. Cholfin, J.L.R. Rubenstein, and L. Mucke. (2007). Abnormal social behavior in mice lacking Fgf17. Program No. 644.15. *2007 Abstract Viewer/Itinerary Planner*. Washington, DC: Society for Neuroscience. Online.
27. **Roberson, E.D.**, K. Searce-Levie, J.J. Palop, F. Yan, I. Cheng, T. Wu, H. Gerstein, G.-Q. Yu, and L. Mucke. (2007). Reducing endogenous tau increases resistance to A β and excitotoxins. Program No. 888.19. *2007 Abstract Viewer/Itinerary Planner*. Washington, DC: Society for Neuroscience. Online.
28. Palop, J.J., J. Chin, **E.D. Roberson**, J. Wang, M. Thwin, N. Bien-Ly, J. Yoo, G.-Q. Yu, A. Kreitzer, S. Finkbeiner, J.L. Noebels, and L. Mucke. (2007). Aberrant excitatory neuronal activity and compensatory remodeling of inhibitory hippocampal circuits in mouse models of Alzheimer's disease. Program No. 888.20. *2007 Abstract Viewer/Itinerary Planner*. Washington, DC: Society for Neuroscience. Online.
29. **Roberson, E.D.**, W.J. Meilandt, J. Yao, J. Yoo, J.L. Noebels, and L. Mucke. (2008). Tau reduction prevents epileptiform activity in a mouse model of Alzheimer's disease: Gene expression microarray analysis. *Alzheimer's & Dementia* 4:T224.

Kristina M. Visscher

Harvard University
Cognitive Neuroscience Lab
William James Hall
33 Kirkland Street
Cambridge, MA 02138

visscher@nmr.mgh.harvard.edu
www.brandeis.edu/~visscher

EDUCATION AND CURRENT POSITION

- Assistant Professor, University of Alabama, at Birmingham, AL (to begin April, 2009)
- Postdoctoral Researcher, Harvard University, Cambridge, MA (2008-present)
Postdoctoral advisor: Dr. Randy L. Buckner
- Postdoctoral Researcher, Brandeis University, Waltham, MA (2004-2008)
Postdoctoral advisor: Dr. Robert Sekuler
- Ph.D., Neuroscience, Washington University, St. Louis, MO (2004)
Thesis advisor: Dr. Steven E. Petersen
- B.A., Physics, Cum Laude, Carleton College, Northfield, MN (1998)

AWARDS

- NIH Training Fellow, Neurobiology: Genes, Channels and Behavior
Brandeis University. (2004-2006)
- Selected for and attended Neuroinformatics Summer School
Woods Hole Marine Biological Laboratory. (2006)
- Spencer T. and Ann W. Olin Fellow for Excellence in Biomedical Research
Washington University. (2004)
- O'Leary Prize for Outstanding Research in Neuroscience, Finalist
Washington University. (2004)
- Selected for and attended Complex Systems Summer School
Santa Fe Institute for Complex Systems. (2003)
- NIH Systems Training Grant Fellow
Washington University. (1999-2002)
- National Science Foundation Research Experience for Undergraduates Fellow
University of Oregon. (1997)
- National Science Foundation Research Experience for Undergraduates Fellow
University of Alabama. (1996)

INVITED TALKS

- Pulitzer Foundation for the Arts, St. Louis, Missouri. (October, 2008)
 Art and Perception: A conversation about Dan Flavin's work, Constructed Light.
- University of Alabama, Birmingham (April, 2008)
 Background neural activity alters the way we perceive and remember.
- Smith College (February, 2008)
 Background neural activity alters the way we perceive and remember.
- University of Michigan (January, 2008)
 Comparing apples to apples: Executive functions operate similarly on analogous inputs from different sensory modalities.
- Wellesley College (December, 2007)
 Background activity alters the way we perceive and remember.
- Rhodes College (January, 2007)
 Comparing apples to apples: auditory and visual short-term memory behave similarly.

SERVICE AND MENTORSHIP

- Mentor Direct supervisor to graduate, undergraduate and advanced high school students. Each student performed original research and gave presentations about it. (2001-2008)
- Board Member Young Scientist Program. YSP is an umbrella organization of many graduate student-run science outreach organizations at Washington University. The board organizes them and distributes funds. (2000-2004)
- Referee For the journals Cerebral Cortex, NeuroImage and Brain Research.

PROFESSIONAL MEMBERSHIPS

- Cognitive Neuroscience Society
 Society for Neuroscience

RESEARCH EXPERIENCE

- Functional Magnetic Resonance Imaging**
 Examination of the timecourses of functional connections among areas in the human brain.
 Harvard University, with Dr. Randy Buckner. (2008-present)
- Psychophysics, Computational Models of Memory, and EEG**
 Psychophysical comparison of memory for sounds and visual images using well-matched stimuli.
 Effects of ignoring and attention on memory and EEG.
 Brandeis University, with Dr. Robert Sekuler. (2004-2008)

Functional Magnetic Resonance Imaging

Exploring task-level control: Functional MRI of sustained neural activity.
Washington University, with Dr. Steven E. Petersen.

Thesis committee: Dr. Lawrence Snyder, Dr. Marcus Raichle, Dr. Randy Buckner, and Dr. Gordon Shulman. (2000-2004)

Functional magnetic resonance imaging of language processing in children and comparison with adults.

Washington University, with Dr. Steven E. Petersen and Dr. Bradley L. Schlaggar. (1999-2000)

Electrophysiology

Role of the parietal cortex in the processing of visual spatial information.
With Dr. Lawrence Snyder. (2000)

Electrophysiology of the vestibular system.

Washington University, with Dr. Dora Angelaki. (2000)

Computational Modeling

Computer modeling of arrays of retinal ganglion cells.

Washington University, with Dr. David Van Essen and Dr. Charles Anderson. (1999)

Physics and Chemistry

Computer modeling of polymer motion through a small pore, applications to electrophoresis.

University of Oregon, with Dr. Jeff Cina, Chemical Physics Institute. (1997)

Electrochemistry of dopamine.

University of Alabama, with Dr. Yeong-Taik Kim, Chemistry Department. (1996)

Computer modeling of small molecules.

University of Alabama, with Dr. David Nikles, Chemistry Department. (1995)

TEACHING EXPERIENCE

Head Instructor **Brandeis University.** (2005)
Behavioral Neuroscience.

Colloquium Advisor **Brandeis University.** (2006)
Autism and Human Developmental Disorders.

Team Head **Washington University Neuroscience Teaching Team.** (2000-2004)
Organized outings to St. Louis schools.
Interactive demonstrations to teach kids about the brain.

Guest Lecturer **Brandeis University.** (2005)
Lectures on functional neuroimaging for the Cognitive Neuroscience course.

Teaching Assistant **Washington University.** (2000)
Cellular and Molecular Neuroscience.

- Teacher
- Carleton College.** (1996-1998)
 Introduction to Physics with and without Calculus.
 Physics of Instrumentation (pre-med).
 Revolutions in Physics.
 Atomic and Nuclear Physics.
- Science Museum of Minnesota,** St. Paul, MN. (1998)
Lewis and Clark Summer School, St. Louis, MO. (1999)
 Science outreach classes of my own design including Chemistry,
 "Incredible Inflatable Structures" and "How to take apart a VCR."

INFORMAL SCIENCE EDUCATION

- Museum Interpreter **St. Louis Science Center.** (2004)
 Helped design hands-on visitor activities.
 Gave interactive demonstrations at the exhibit "The Brain."
- City Museum,** St. Louis, MO. (1999-2002)
 Created projects for visitors to this innovative hands-on museum.
 Helped run the museum on occasional weekends.
- Volunteer **Brain Awareness Week and International Brain Bee,** Boston, MA.
 (2005-present)
- Outreach Created short Physics documentary for Discover Magazine competition.
 (2007)

PUBLICATIONS

- Visscher, K.M.,** Kahana, M.J., Sekuler, R. (in press). Trial-to-trial carry-over in auditory short-term memory. *Journal of Experimental Psychology: Learning, Memory & Cognition*.
- Visscher, K.M.,** Kaplan, E., Kahana, M.J., Sekuler, R. (2007). Auditory short-term memory behaves like visual short-term memory. *PLoS Biology* 5(3).
- Palmer, E.D., **Visscher, K.M.,** Kang, H.C., Burgund, E.D., Buckner, R.L., Petersen, S.E. (2008). Defining task-block-related signals using fMRI: I. Structure of a task-level control system. *Submitted*.
- Visscher, K.M.,** Palmer, E.D., Kang, H.C., Burgund, E.D., Buckner, R.L., Petersen, S.E. (2008). Defining task-block-related signals using fMRI: II. Implementing task-level control. *Submitted*.
- Dosenbach, N.U.F., **Visscher, K.M.,** Palmer, E.D., Miezin, F.M., Wenger, K.K., Kang, H.C., Burgund, E.D., Grimes, A.L., Schlaggar, B.L., Petersen, S.E. (2006). A core system for the implementation of task sets. *Neuron*, 50(5):799-812.
- Weissman, D.H., Roberts, K.C., **Visscher, K.M.,** Woldorff, M.G. (2006). Zoning out: The neural bases of momentary lapses in attention. *Nature Neuroscience*, 9(7): 971-8.
- Wenger, K.K, **Visscher, K.M.,** Miezin, F.M., Petersen, S.E., Schlaggar, B.L. (2004). Comparison of sustained and transient activity in children and adults using a mixed blocked/event-related fMRI design. *NeuroImage*, 22(2): 975-85.

Visscher, K.M., Miezin, F. M., Kelly, J., Buckner, R.L., Donaldson, D.I., McAvoy, M., Bhalodia, V., Petersen, S. E. (2003). Mixed blocked/event-related designs can correctly separate transient and sustained activity in fMRI. *NeuroImage*, 19: 1694-708.

Visscher, K.M., Viets, E., Snyder, L. (2003). Effects of training on memory-guided saccade performance. *Vision Research*, 43: 2061-71.

Schlaggar, B. L., Brown, T.T., Lugar, H.M., Visscher, K.M., Miezin, F.M., Petersen, S.E. (2002). Functional neuroanatomical differences between adults and children in the processing of single words. *Science* 296, 1476-1479.

ABSTRACTS

Visscher, K.M., Sekuler, R. (2008). Pre-stimulus neural activity predicts success in ignoring. *Computational and Systems Neuroscience Conference Abstracts*.

Visscher, K.M., Sekuler, R. (2007). EEG correlates of intentional ignoring. *Society for Neuroscience Abstracts*.

Visscher, K.M., Kaplan, E., Kahana, M.J., Sekuler, R. (2006). Visual and auditory short-term memory are highly similar when examined with comparable stimuli and identical tasks: Comparing apples to apples. *Society for Neuroscience Abstracts*.

Visscher, K.M., Kahana, M.J., Sekuler, R. (2006). Short-term memory for spectrally and temporally complex sounds: Comparing apples to apples. *Cognitive Neuroscience Society Abstracts*.

Dosenbach, N.U.F., Visscher, K.M., Miezin, F.M., Palmer, E.D., Wenger, K.K., Kang, H.C., Grimes, A.L., Burgund, E.D., Schlaggar, B.L., Petersen, S.E. (2005). Mixed blocked/event-related fMRI suggests that anterior cingulate/medial superior frontal cortex and anterior insula form a core network for the instantiation and maintenance of task set. *Society for Neuroscience Abstracts*.

Weissman, D.H., Roberts, K.C., Visscher, K.M., Woldorff, M.G. (2005). The neural correlates of momentary lapses in attention. *Society for Neuroscience Abstracts*.

Visscher, K.M., Palmer, E.D., Kang, H.C., Dosenbach, N.U.F., , Petersen, S.E. (2004). Potential control processes common to a range of tasks: Sustained, task-related fMRI signals examined across 10 tasks. *Society for Neuroscience Abstracts*.

Visscher, K.M., Eder, K.E., Miezin, F.M., Petersen, S.E. (2004) Differentiating task-general control activity from task-specific control activity. *Cognitive Neuroscience Society Abstracts*.

Visscher, K.M., Palmer, E. D., Burgund, E. D., Kang, H. C., Miezin, F. M., Lyon, J. K., Buckner, R. L. , Petersen, S. E. (2003). Sustained, block-related activity compared across four tasks shows both common and task-modulated responses. *Cognitive Neuroscience Society Abstracts*.

Wenger, K.K., Visscher, K.M., Miezin, F.M., Petersen, S.E., , Schlaggar, B.L. (2003). Mixed block/event-related designs separate transient and sustained activity in fMRI in children. *Society for Neuroscience Abstracts*.

Visscher, K.M., Miezin, F. M., Lugar, H. M., Bhalodia, V., Kelly, J., Donaldson, D. I., Buckner, R. L. , Petersen, S. E. (2002). A mixed block/event-related paradigm can correctly separate transient and sustained activity in fMRI. *Cognitive Neuroscience Society Abstracts*.

- Visscher, K.M., Breneman, M., Miezin, F. M., Buckner, R. L. , Petersen, S. E. (2002). Semantic vs. physical judgments: a mixed block/event-related analysis. *Society for Neuroscience Abstracts*.
- Petersen, S. E., Visscher, K.M., Miezin, F. M., Kelly, J. , Buckner, R. L. (2002). Potential limitations on the use of mixed block/event-related designs. *Society for Neuroscience Abstracts*.
- Kelly, J. E., Visscher, K.M., McAvoy, M., Petersen, S. E. , Buckner, R. L. (2002). Bay Zero simulation explores methodology of mixed blocked/evented-related functional MRI experiments. *Organization for Human Brain Mapping Abstracts*.
- Schlaggar, B. L., Brandling-Bennett, E., Visscher, K.M., Brown, T. T., Palmer, E. D., Miezin, F. M., Snyder, A. Z., Kelley, W. M. , Petersen, S. E. (2000). FMRI in adults performing lexical tasks designed for school age children demonstrates expected patterns of activation. *Society for Neuroscience Abstracts*.

FACULTY BIOSKETECHES

PROFESSORS

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 J. David Sweatt, PhD		POSITION TITLE	
eRA COMMONS USER NAME JSWEATT		Professor and Chairman	
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as</i>			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of South Alabama Mobile, AL	BS	1981	Chemistry
Vanderbilt University Nashville, TN	Ph.D.	1986	Pharmacology (Advisor—Lee Limbird)

Professional Experience

1986 Post-doc, Laboratory of Dr. Peter Reed, Dept. of Pharmacology, Vanderbilt University
 1986 – 1989 Post-doc, Laboratory of Dr. Eric Kandel, HHMI, Columbia University
 1989 – 2006 Assistant-Associate-Full Professor, Department of Neuroscience, Baylor College of Medicine
 joint appointments in Molecular Physiology and Biophysics, and Molecular and Human Genetics
 1998 – 2005 Co-Director, then Director, Neuroscience Graduate Program, Baylor College of Medicine
 1998 – 2005 Director, Mouse Synaptic Plasticity Core, MRRC, Baylor Coll. Med.
 2006-present Professor and Evelyn F. McKnight Chairman, Department of Neurobiology,
 University of Alabama, Birmingham, School of Medicine
 2006-present Director, McKnight Brain Institute, University of Alabama, Birmingham, School of Medicine
 2006-present Professor, Departments of Psychology, Physiology and Biophysics, and Genetics, University of
 Alabama, Birmingham
 2006-present Member, Civitan International Research Center, University of Alabama, Birmingham, School of
 Medicine
 2006-present Senior Scientist, Center for Glial Biology in Medicine, University of Alabama, Birmingham,
 School of Medicine
 2006-present Senior Scientist and Associate Director, UAB Center for Aging, University of Alabama,
 Birmingham
 2006-present Adjunct Professor, Departments of Neuroscience and Molecular Physiology, Baylor College of
 Medicine

Honors and Awards

Rotary Clubs International CART Award, 2008; NARSAD Distinguished Investigator Award, 2007; Evelyn
 McKnight Endowed Chair, UAB School of Medicine, 2006-present; NIMH Board of Scientific Counselors, 2006-
 2010; Reviewing Editor, Hippocampus, 2006 – present; President, Molecular and Cellular Cognition Society,
 2006-present; Associate Editor, Physiological Reviews, 2005-2008; Associate Editor, Neurobiology of Learning
 and Memory, 2004-present; Associate Editor, Journal of Neuroscience, 2004-present; Editorial Board,
 Neurobiology of Learning and Memory, 2003; Editorial Board, Hippocampus, 2002-2006; Councilor, Molecular
 and Cellular Cognition Society, 2002-present; ACNP Memorial Travel Award, 2000; Texas Advanced
 Technology Program Award, 1999; NARSAD Independent Investigator Award, 1998; Marc Dresden Award for
 Excellence in Graduate Education, 1993; Mc Knight Scholar Award, 1990; Klingenstein Fellowship Award,
 1990; Graham Hoyle Fellowship, 1989; American Federation for Aging Research Award, 1989; College
 Presidential Scholarship, U. of South Alabama, 1978.

Bibliography: (from a total of 170 published papers)

1. Kennedy, T.E., Gawinowicz, M.A., Barzilai, A., Kandel, E.R., and Sweatt, J.D. (1988) Sequencing of proteins from two-dimensional gels using in situ digestion and transfer to PVDF membranes: Application to proteins associated with sensitization in Aplysia. Proc. Natl. Acad. Sci. USA 85:7008-7012.

2. Kennedy, T.E., Wager-Smith, K.A., Barzilai, A., Kandel, E.R., and Sweatt, J.D. (1988) Sequencing proteins from acrylamide gels. *Nature* 336:499-500.
3. Sweatt, J.D. and Kandel, E.R. (1989) Persistent and transcriptionally-dependent increase in protein phosphorylation upon long-term facilitation of *Aplysia* sensory neurons. *Nature*, 339:51-54, 1989.
4. Barzilai, A., Kennedy, T.E., Sweatt, J.D., and Kandel, E.R. (1989) Serotonin modulates total protein synthesis and initiates a sequential alteration in the expression of specific proteins during long-term facilitation in the sensory neurons of *Aplysia*. *Neuron*, 2:1577-1586, 1989.
5. Sweatt, J.D., Volterra, A., Edmonds, B., Karl, K., Siegelbaum, S.A., and Kandel, E.R. (1989) FMRFamide reverses protein phosphorylation produced by 5-HT and cyclic AMP in *Aplysia* sensory neurons. *Nature*, 342:275-278.
6. Bergold, P.J., Sweatt, J.D., Winicov, I., Weiss, K., Kandel, E.R., and Schwartz, J.H. (1990) Protein synthesized during acquisition of long-term facilitation leads to persistent loss of regulatory subunits of the A-kinase in *Aplysia* sensory neurons. *Proc. Nat. Acad. Sci., USA* 87: 3787-3789.
7. Chetkovich, D., Gray, R., Johnston, D., and Sweatt, J.D. (1991) NMDA-receptor activation increases cAMP levels and voltage-gated Ca^{++} channel activity in area CA1 of hippocampus. *Proc. Nat. Acad. Sci., USA* 88:6467-6471.
8. Klann, E., Chen, S.-J., and Sweatt, J.D. (1991) Persistent protein kinase activation in the maintenance phase of long-term potentiation. *J. Biol. Chem.* 266:24253-24256.
9. Kennedy, T.E., Kuhl, D., Barzilai, A., Sweatt, J.D., and Kandel, E.R. (1992) Long-term sensitization training in *Aplysia* leads to an increase in calreticulin, a major presynaptic calcium-binding protein. *Neuron* 9:1013-1024.
10. Chetkovich, D.M. and Sweatt, J.D. (1993) Hippocampal NMDA receptors couple to adenylyl cyclase via calcium/calmodulin. *J. Neurochemistry* 61, 1933-1942.
11. Powell, C.M., Johnston, D., and Sweatt, J.D. (1994) Autonomously active protein kinase C in the maintenance phase of NMDA receptor independent LTP. *J. Biol. Chem.* 269:27958-27963.
12. English, J.D. and Sweatt, J.D. (1996) Activation of p42 mitogen-activated protein kinase in hippocampal long term potentiation. *J. Biol. Chem.* 271:24329-24332.
13. Roberson, E.D. and Sweatt, J.D. Transient activation of cyclic AMP-dependent protein kinase during hippocampal long-term potentiation. (1996) *J. Biol. Chem.* 271:30436-30441.
14. English, J.D. and Sweatt, J.D. (1997) A Requirement for the Mitogen-activated Protein Kinase Cascade in Hippocampal Long-term Potentiation. *J. Biol. Chem.* 272:19103-19106.
15. Klann, E., Roberson, E.D., Knapp, L.T. and Sweatt, J.D. (1998) A role for superoxide in protein kinase C activation and induction of long-term potentiation. *J. Biol. Chem.* 273: 4516-4522.
16. Jiang, Y., Armstrong, D., Albrecht, U., Atkins, C.M., Noebels, J., Eichele, G., Sweatt, J.D., and Beaudet, A.L. (1998) Mutation of the Angelman E3 ubiquitin ligase in mice causes increased cytoplasmic p53 and deficits of contextual learning and long-term potentiation. *Neuron* 21:799-811.
17. Atkins, C.M., Selcher, J.C., Petraitis, J.J., Trzaskos, J.M., and Sweatt, J.D. (1998) The MAP kinase cascade is required for mammalian associative learning. *Nature Neuroscience* 1:602-609.
18. Roberson, E.D.*, English*, J.D., Adams, J.P., Selcher, J.C., Kondratieff, C. and Sweatt, J.D. (1999) The mitogen-activated protein kinase cascade couples PKA and PKC to CREB phosphorylation in area CA1 of hippocampus. * denotes equal contributions. *J. Neuroscience* 19: 4337-4348.
19. Atkins, C.M. and Sweatt, J.D. (1999) Reactive oxygen species mediate activity dependent neuron-glia signaling in output fibers of the hippocampus. *J. Neuroscience* 19: 7241-7248.
20. Selcher, J., Atkins, C.M., Trzaskos, J.M., Paylor, R., and Sweatt, J.D. (1999) A necessity for MAP kinase activation in mammalian spatial learning. *Learning & Memory* 6:478-490.
21. Weeber, E., Atkins, C., Selcher, J., A. Varga, B. Mirnikjoo, R. Paylor, M. Leitges and Sweatt, J.D. (2000) A Role for the Beta Isoform of PKC in Amygdala-dependent Fear Conditioning. *J. Neuroscience* 20:5906-5914.
22. Adams, P., Anderson, A., Dineley, K., Cook, R., Pfaffinger, P.J., and Sweatt, J.D. (2000) Potassium channels are a target of the MAP kinase cascade. *J. Neurochemistry* 75: 2277-2287.
23. Schafe, G.E., Atkins, C.M., Swank, M.W., Bauer, E.P., Sweatt, J.D. and LeDoux, J.E. (2000) Activation of ERK/MAP kinase in the amygdala is required for memory consolidation of Pavlovian fear conditioning. *J. Neuroscience* 20: 8177-8187.
24. Sweatt, J.D. (2001) The neuronal MAP kinase cascade: a biochemical signal integration system subserving synaptic plasticity and memory. *Journal of Neurochemistry* 76:1-11.
25. Sweatt, J.D. (2001) Proto-oncogenes subserve memory formation in the adult CNS. *Neuron* 31:671-674.

26. Dineley, K.T., Westerman, M., Bui, D., Bell, K., Ashe, K.H., and Sweatt, J.D. (2001) Beta-amyloid activates the mitogen-activated protein kinase cascade through hippocampal alpha7 nicotinic acetylcholine receptors: in vitro and in vivo mechanisms related to Alzheimer's Disease. *J. Neuroscience* 21:4125-33.
27. Swank, M.W. and Sweatt, J.D. (2001) Increased histone- and lysine acetyltransferase activity and biphasic activation of the ERK/RSK cascade in insular cortex during novel taste learning. *J. Neuroscience* 21: 3383-3391.
28. Levenson, J., Weeber, E., Selcher, J., Kategaya, L.S., Antzoulatos, E., Sweatt, J.D., and Eskin, A. (2002) Long-term potentiation and contextual fear conditioning increase neuronal glutamate uptake. *Nature Neuroscience* 5:155-61.
29. Weeber, E.J., Levy, M., Sampson, M.J., Anfous, D., Armstrong, D., Brown, S.E., Sweatt, J.D., and Craigen, W.J. (2002) A role for mitochondrial porins and the permeability transition pore in learning and synaptic plasticity. *J. Biol Chem* 277:18891-7.
30. Dineley, K., Xia, X., Bui, D., Sweatt, J.D., and Zheng, H. (2002) Accelerated plaque accumulation, associative learning deficits, and up-regulation of alpha7 nicotinic receptor protein in transgenic mice co-expressing mutant human presenilin 1 and amyloid precursor protein. *J. Biol Chem* 277:22768-80.
31. Dineley, K.T., Bell, K.A., Bui, D., and Sweatt, J.D. (2002) Beta-amyloid peptide1-42 activates alpha7 nicotinic acetylcholine receptors expressed in *Xenopus* oocytes. *J. Biol Chem* 277:25056-61.
32. Watase K, Weeber EJ, Xu B, Antalffy B, Nellis A, Yuva-Paylor L, Armstrong D, Sweatt JD, Orr HT, Paylor RL and Zoghbi HY. (2002) A long CAG tract in the mouse Sca1 locus replicates human SCA1 and reveals the impact of mutant protein solubility on selective neuronal vulnerability. *Neuron* 34:905-19.
33. Schrader, L.A., Anderson, A.E., Mayne, A., Gutierrez, C., Pfaffinger, P.J., and Sweatt, J.D. PKA modulation of Kv4.2-encoded A-type potassium channels requires formation of a supramolecular complex. *J. Neuroscience*, 22(23):10123-33.
34. Weeber, E.J. and Sweatt, J.D. (2002) Molecular Neurobiology of Human Cognition. *Neuron* 33: 845-848.
35. Hendricks, T.J., Fyodorov, D.V., Wegman, L.J., Lelutiu, N.B., Pehek, E.A., Yamamoto, B., Silver, J., Weeber, E.J., Sweatt, J.D., and Deneris, E.S. (2003) Disruption of early serotonin neuron development in mice lacking the Pet-1 ETS gene is followed by abnormal aggression and anxiety-like behavior. *Neuron* 37:233-44.
36. Yoo, S-Y., Pennesi, M.E., Weeber, E.J., Xu, B., Antalffy, B., Chen, S., Wu, S., Sweatt, J.D., and Zoghbi, H.Y. (2003) SCA7 knockout mice reproduce features of human SCA7 and reveal that mutant ataxin-7 gradually accumulates in neurons and interferes with presynaptic functions. *Neuron* 37:383-401.
37. Weeber, E.J., Jiang, Y-H., Varga, A., Carrasquillo, Y., Brown, S.E., Christian, J.M., Mirnikjoo, B., Elgersma, Y., Silva, A., Beaudet, A.L., and Sweatt, J.D. (2003) Derangements of hippocampal CaMKII in a mouse model for Angelman Mental Retardation Syndrome. *J. Neuroscience* 23:2634-44.
38. Levy, M., Faas, G., Saggau, P., Craigen, W.J., and Sweatt, J.D. (2003) Mitochondrial regulation of synaptic plasticity in the hippocampus. *J. Biol Chem* 278:17727-34.
39. Morozov, A., Muzzio, I.A., Bourthouladze, R., Van-Strien, N., Lapidus, K., Yin, D.Q., Winder, D.G., Adams, J.P., Sweatt, J.D., and Kandel, E.R. (2003) Rap1 couples cAMP signaling to a distinct pool of p42/44MAPK regulating excitability, synaptic plasticity, learning and memory. *Neuron* 39(2):309-25.
40. Varga, A.W.*, Yuan, L.*, Anderson, A.E., Schrader, L.S., Wu, G-Y., Gatchel, J.R., Johnston, D., and Sweatt, J.D. *equal contributions. (2004) CaMKII modulates Kv4.2 channel expression and upregulates neuronal A-type potassium currents. *J. Neurosci* 24:3643-54.
41. Levenson, J.M., Choi, S., Ahn, H-J., Lee, S-Y., Cao, Y.A., Worley, K., and Sweatt, J.D. (2004) A bioinformatics analysis of memory consolidation reveals involvement of the transcription factor c-Rel. *J. Neuroscience* 24: 3933-3943.
42. Levenson, J.M., O'Riordan, K., Brown, K.D., Trinh, M.A., Molfese, D., and Sweatt, J.D. (2004) Regulation of histone acetylation during memory formation in the hippocampus. *J. Biological Chemistry* 279:40545-59.
43. Birnbaum, S.G., Yuan, P.X., Wang, M., Vijayraghavan, S., Bloom, A.K., Davis, D.J., Gobeski, K.T., Sweatt, J.D., Manji, H.K. and Arnsten, A. (2004) Protein Kinase C overactivity impairs prefrontal cortical regulation of working memory. *Science*, 306:882-4.
44. Levenson, J.M. and Sweatt, J.D. (2005) Epigenetic mechanisms in memory formation. *Nature Reviews Neuroscience* 6:108-115.
45. Beffert, U., Weeber, E. J., Duradas, A., Qiu, S., Masiulis, I, Sweatt, J. D., Li, W., Adelmann, G., Frotscher, M., Hammer, R.E., and Herz, J. (2005) Modulation of synaptic plasticity and memory by reelin involves differential splicing of the lipoprotein receptor ApoER2. *Neuron* 47:567-79.
46. Schrader, L.A., Birnbaum, S.G., Nadin, B.M., Ren, Y., Bui, D., Anderson, A.E. and Sweatt, J.D. (2006) ERK/MAPK regulates the Kv4.2 potassium channel by direct phosphorylation of the pore-forming subunit. *American Journal of Physiology – Cell Physiology* 290:C852-61.

47. Moretti, P., Levenson, J.M., Battaglia, F., Atkinson, R., Teague, R., Antalffy, B., Armstrong, D., Arancio, O., Sweatt, J.D. and Zoghbi, H.Y. (2006) Synaptic plasticity and learning and memory are impaired in a mouse model of Rett syndrome. *J. Neuroscience* 26:319-27.
48. Chan, C-S, Weeber, E.J., Zong, L., Kaminski, M., Fuchs, E., Sweatt, J.D., and Davis, R.L (2006) β 1-integrins are required for hippocampal synaptic transmission, synaptic plasticity and working memory. *J. Neuroscience* 26:223-32.
49. Beffert, U., Durudas, A., Weeber, E.J., Stolt, P.C., Giehl, K.M., Sweatt, J.D., Hammer, R.E., and Herz, J. (2006) Functional dissection of reelin signaling by site-directed disruption of dab1 adaptor binding to Apoer2: distinct roles in development and synaptic plasticity. *J. Neuroscience* 26:2041-52.
50. Levenson, J.M., Roth, T.L., Lubin, F.D., Miller, C.A., Huang, I., Desai, P., Malone, L., and Sweatt, J.D. (2006) Evidence that DNA (Cytosine-5) Methyltransferase regulates synaptic plasticity in the hippocampus. *J. Biol. Chemistry*, 281:15763-73.
51. Shalin, S.C., Hernandez, C.M., Dougherty, M.K., Morrison, D.K., and Sweatt, J.D. (2006) Kinase suppressor of Ras1 compartmentalizes hippocampal signal transduction and subserves synaptic plasticity and memory formation. *Neuron*. 50:765-79.
52. Chwang, W.B., O'Riordan K.J., Levenson, J.M., and Sweatt, J.D. (2006) ERK/MAPK regulates hippocampal histone phosphorylation following contextual fear conditioning. *Learn Mem.* 13:322-8.
53. Chen, X., Yuan, L.L., Zhao, C., Birnbaum, S.G., Frick, A., Jung, W.E., Schwarz, T.L., Sweatt, J.D., and Johnston, D. (2006) Deletion of Kv4.2 gene eliminates dendritic A-type K⁺ current and enhances induction of long-term potentiation in hippocampal CA1 pyramidal neurons. *J. Neuroscience*, 26:12143-51.
54. Miller, C.A., Sweatt, J.D. Covalent modification of DNA regulates memory formation. (2007) *Neuron* 53:857-69.
55. Kim, S.Y., Levenson, J., Korsmeyer, S., Sweatt, J.D., and Schumacher, A. (2007) Development regulation of EED complex composition governs a switch in global histone modifications in brain. *J. Biological Chemistry* 282:9962-72.
56. Miller, C.A., Campbell, S., and Sweatt, J.D. DNA methylation and histone acetylation work in concert to regulate memory formation and synaptic plasticity. (2007) *Neurobiology of Learning and Memory* 89:599-603.
57. Lubin, F.D., and Sweatt, J.D. (2007) The I κ B kinase regulates chromatin structure during reconsolidation of conditioned fear memories. *Neuron* 55:942-57.
58. Chwang, W.B., Arthur, J.S., Schumacher, A., and Sweatt, J.D. (2007) The nuclear kinase mitogen- and stress-activated protein kinase 1 regulates hippocampal chromatin remodeling in memory formation. *J. Neuroscience* 27:12732-42.
59. Samuels, I.S., Karlo, J.C., Faruzzi, A.N., Pickering, K., Herrup, K., Sweatt, J.D., Saitta, S.C., and Landreth, G.E. (2008) Deletion of ERK2 Mitogen-Activated Protein Kinase Identifies Its Key Roles in Cortical Neurogenesis and Cognitive Function. *J. Neurosci.* 28 6983-6995.
60. Ahn, H.J., Hernandez, C.M., Levenson, J.M., Lubin, F.D., Liou, H.C., and Sweatt, J.D. (2008) c-Rel, an NF-kappaB family transcription factor, is required for hippocampal long-term synaptic plasticity and memory formation. *Learn Mem.* 15:539-49.

Research Projects Ongoing or Completed During the Last 3 Years:

R01 AG31722 (D. Sweatt, PI)	
NINDS - "Trophic Interaction of Nerve and Muscle"	08/01/07 – 04/01/12
Alzheimer's Disease Research 13660 (D. Sweatt, PI)	
American Health Assistance Foundation "Alpha7 Nicotinic receptors and MAP Kinase in AD Models"	04/01/02 – 05/31/06
Project 2: PPG – Regulation of Neuronal Excitability (D. Johnston, PI; D Sweatt, PI Proj 2)	
NINDS	
"Molecular mechanisms for modulation of hippocampal neuron potassium channels"	
R01 MH57014 (D Sweatt PI)	12/01/98 – 05/31/08
"Biochemical Mechanisms for Long-term Potentiation"	12/01/95 – 2/28/10
P30 NS057098-01 (K. Roth, PI)	
"Alabama Neuroscience Blueprint Core Center"	09/04/06 – 06/30/11
"Cellular Physiology Core"- D. Sweatt, Director	
NARSAD Distinguished Investigator Award (D. Sweatt PI)	
"DNA Methylation in the Adult Nervous System."	
Rotary International CART Research Grant (D. Sweatt, PI)	05/01/07 – 03/31/08
	6/1/2008 – 5/31/2009

Hablitz, John J.

Program Director/Principal Investigator (Last, First, Middle):

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 John J. Hablitz, Ph.D.		POSITION TITLE Professor	
eRA COMMONS USER NAME hablitz			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
State University of New York, Plattsburgh	B.A.	1968	Psychology
University of Houston, Houston, Texas	M.A.	1970	Psychology
University of Houston, Houston, Texas	Ph.D.	1972	Psychology
Baylor College of Medicine, Houston, Texas	Postdoc	1972-73	Neurophysiology

A. Positions and Honors.**Positions and Employment**

1974-1983 Assistant Professor of Physiology and Neurology, Baylor College of Medicine
 1978-1979 Visiting Scientist, Institute of Neurophysiology, University of Oslo, Oslo, Norway
 1983-1988 Assoc Professor of Neurology, Physiology and Biophysics, Baylor College of Medicine
 1984-1985 Visiting Scientist, Dept. of Neurophysiology, Max-Planck Institute for Psychiatry, Munich
 1989-Pres Professor of Physiology and Biophysics, University of Alabama at Birmingham
 1989-1996 Senior Scientist, Neurobiology Research Center, University of Alabama at Birmingham
 1996-Pres Professor of Neurobiology, University of Alabama at Birmingham
 1997-2001 Chairman, Graduate Neuroscience Training Program, Univ. of Alabama at Birmingham

Professional Memberships

Society for Neuroscience
 American Epilepsy Society
 American Physiological Society

Honors

1987-1991 Member, Neurological Sciences 2 Study Section, NIH
 1989 Javits Neuroscience Investigator Award
 2000-2003 Member, VA Merit Review Neurobiology Panel D
 2003-2007 Member, Neurobiology of Learning and Memory Study Section, NIH

Selected Peer-Reviewed Publications (in chronological order).

(Publications selected from 118 peer-reviewed publications)
 Hablitz JJ, Braud WG. Adrenalin, sodium amobarbital, and the Kamin effect in the albino rat. *Learn Motiv* 1972;3:51-58.
 Hablitz JJ. Operant conditioning and slow potential changes from monkey cortex. *Electroen Clin Neuro* 1973;34:399-408.
 Hablitz JJ. Spontaneous ictal-like discharges and sustained potential shifts in the developing rat neocortex. *J Neurophysiol* 1987;58:1052-1065.
 Hablitz JJ, Heinemann U. Alterations in the microenvironment during epileptogenesis in the immature neocortex. *Dev Brain Res* 1989;46:243-252.
 Sutor B, Hablitz JJ. Excitatory postsynaptic potentials in rat neocortical neurons in vitro. I. Electrophysiological evidence for two distinct EPSPs. *J Neurophysiol* 1989;61:607-620.

- Sutor B, Hablitz JJ. Excitatory postsynaptic potentials in rat neocortical neurons in vitro. II. Involvement of N-methyl-D-aspartate receptors in the generation of EPSPs. *J Neurophysiol* 1989;61:621-634.
- Sutor B, Hablitz JJ. Cholinergic modulation of epileptiform activity in the developing rat neocortex. *Dev Brain Res* 1989;46:155-160.
- Sutor B, Hablitz JJ. Long-term potentiation in frontal cortex: Role of NMDA-modulated polysynaptic excitatory pathways. *Neurosci Lett* 1989;97:111-117.
- Hablitz JJ, Sutor B. Excitatory postsynaptic potentials in rat neocortical neurons in vitro. III. Effects of a quinoxalinedione non-NMDA receptor antagonist. *J Neurophysiol* 1990;64:1282-90.
- Lee WL, Hablitz JJ. Initiation and maintenance of epileptiform activity by excitatory amino acid receptors in the disinhibited rat neocortex. *J Neurophysiol* 1991;65:87-95.
- Lee WL, Hablitz JJ. Excitatory synaptic involvement in epileptiform bursting in the immature rat neocortex. *J Neurophysiol* 1991;67:1894-1901.
- Zhou FM, Hablitz JJ. Zinc enhances GABAergic transmission in rat neocortical neurons. *J Neurophysiol* 1993;70:1264-1269.
- Burgard E, Hablitz JJ. NMDA receptor-mediated components of miniature excitatory synaptic currents in developing rat neocortex. *J Neurophysiol* 1993;70:1841-1852.
- Burke JP, Hablitz JJ. Presynaptic depression of synaptic transmission mediated by activation of metabotropic glutamate receptors in rat neocortex. *J Neurosci* 1994;14:5120-5130.
- Andreassen M, Hablitz JJ. Paired-pulse facilitation in the dentate gyrus: A patch clamp study in rat hippocampus *in vitro*. *J Neurophysiol* 1994;72:326-336.
- Sutor B., Hablitz JJ, Rucker F, ten Burggencate G. Spread of epileptiform activity in the immature rat neocortex monitored using voltage-sensitive dyes. *J Neurophysiol* 1995;72:1756-1768.
- Zhou FM, Hablitz JJ. Postnatal development of the membrane properties of layer I neurons. *J Neurosci* 1996;16:1131-1139.
- Zhou FM, Hablitz JJ. Layer I neurons of rat neocortex. I. Action potential and repetitive firing properties. *J Neurophysiol* 1996;76:651-667.
- Zhou FM, Hablitz JJ. Layer I neurons of rat neocortex. II. Voltage-dependent outward currents. *J Neurophysiol* 1996;76:668-682.
- Zhou FM, Hablitz JJ. Morphological properties of rat neocortical layer I neurons examined using intracellular staining. *J Comp Neurol* 1996;376:198-213.
- Burke JP, Hablitz JJ. Activation of G-proteins by neocortical metabotropic receptors reduces spike frequency adaptation. *Neuroscience* 1996;75:123-131.
- Zhou F, Hablitz JJ. Rapid kinetics and inward rectification of miniature EPSCs in layer I neurons of rat neocortex. *J Neurophysiol* 1997;77:2416-2426.
- Zhou F, Hablitz JJ. Metabotropic glutamate receptor enhancement of spontaneous IPSCs in neocortical interneurons. *J Neurophysiol* 1997;78:2287-2295.
- Chu ZG, Hablitz JJ. Activation of group I mGluRs increases spontaneous IPSC frequency in rat neocortex. *J Neurophysiol* 1998;80:621-627.
- DeFazio T, Hablitz JJ. Zinc and Zolpidem modulate mIPSCs in rat neocortical pyramidal neurons. *J Neurophysiol* 1998;80:1670-1677.
- Zhou FM, Hablitz JJ. Dopamine modulation of membrane and synaptic properties of interneurons in rat cerebral cortex. *J Neurophysiol* 1999;81:967-976.
- DeFazio RA, Hablitz JJ. Reduction of zolpidem sensitivity in a freeze lesion model of neocortical dysgenesis. *J Neurophysiol* 1999;81: 404-407.
- DeFazio RA, Hablitz JJ. Alterations in NMDA receptors in a rat model of cortical dysplasia. *J Neurophysiol* 2000;83:315-321.
- Swann JW, Hablitz JJ. Cellular abnormalities and synaptic plasticity in seizure disorders of the immature nervous system. *Ment Retard Dev D R* 2000;6:258-267.

Hablitz, John J.

Program Director/Principal Investigator (Last, First, Middle):

- DeFazio RA, Keros S, Quick MW, Hablitz JJ. Potassium-coupled chloride cotransport controls intracellular chloride in rat neocortical pyramidal neurons. *J Neurosci* 2000;20:8068-76.
- Chu Z, Hablitz JJ. Quisqualate induces an inward current via mGluR activation in neocortical pyramidal neurons. *Brain Res* 2000; 879:88-92
- Chu Z, Hablitz JJ. Nicotinic acetylcholine receptor-mediated synaptic potentials in rat neocortex. *Brain Res* 2000;887:399-405.
- Gonzalez-Islas C, Hablitz JJ. Dopamine inhibition of evoked IPSCs in rat prefrontal cortex. *J Neurophysiol* 2001;86:2911-2918.
- Chu Z, Hablitz JJ. GABA_B receptor-mediated heterosynaptic depression of excitatory synaptic transmission in rat frontal neocortex. *Brain Res* 2003;959:39-49.
- Gonzalez-Islas C, Hablitz JJ. Dopamine enhances EPSCs in layer II-III pyramidal neurons in rat prefrontal cortex. *J Neurosci* 2003;23:867-875.
- Keros S, Hablitz JJ. Ectopic action potential generation in cortical interneurons during synchronized GABA responses. *Neuroscience* 2005;131:833-842.
- DeFazio RA, Hablitz JJ. Horizontal spread of activity in neocortical inhibitory networks. *Dev Brain Res* 2005;157:83-92.
- Campbell S, Hablitz JJ. Modification of epileptiform discharges in neocortical neurons following glutamate uptake inhibition. *Epilepsia* 2005;46 (Suppl. 5):1-5.
- Keros S, Hablitz JJ. Subtype-specific GABA transporter antagonists synergistically modulate phasic and tonic GABA_A conductances in rat neocortex. *J Neurophysiol* 2005;94:2073-2085.
- Wu JP, Hablitz JJ. Cooperative activation of D1 and D2 dopamine receptors enhances a hyperpolarization-activated inward current in layer I interneurons. *J Neurosci* 2005;25:6322-28.
- Olsen M, Higashimori H, Campbell S, Hablitz J, Sontheimer H. Functional expression of Kir4.1 channels in spinal cord astrocytes. *Glia* 2006;53:516-528.
- Bandyopadhyay S, Sutor B, Hablitz JJ. Endogenous acetylcholine enhances synchronized interneuron activity in rat neocortex. *J Neurophysiol* 2006;95:1908-1916.
- Bandyopadhyay S, Hablitz JJ. NR2B antagonists restrict spatiotemporal spread of activity in a rat model of cortical dysplasia. *Epilepsy Res* 2006;72:127-139.
- Bandyopadhyay S, Hablitz JJ. Dopaminergic modulation of local network activity in rat prefrontal cortex. *J Neurophysiol* 2007;97:4120-4128.
- Campbell SA, Mathew SS, Hablitz JJ. Pre- and postsynaptic effects of kainate on layer II/III pyramidal cells in rat neocortex. *Neuropharmacology* 2007;53:37-47.
- Mathew SS, Pozzo-Miller L, Hablitz JJ. Kainate modulates presynaptic GABA release from two vesicle pools. *J Neurosci* (In Press).

C. Research Support

Ongoing Research Support

Title: Neocortical Epilepsy During Development Principal Investigator: John J. Hablitz, Ph.D.
 Agency: NIH/NINDS Type: RO1 NS22373 Period: 04/01/86-05/31/12
 Goals: The grant examines the role of glutamate transporters in neocortical epilepsy. There is no overlap with the current proposal.

Title: UAB Neuroscience Core Center Principal Investigator: John J. Hablitz, Ph.D.
 Agency: NIH/NINDS Type: P30 NS47466 Period: 07/01/05-06/30/10
 Goals: This grant provides multiple cores for NINDS funded investigators.

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 Harald W. Sontheimer, Ph.D.		POSITION TITLE Professor	
eRA COMMONS USER NAME (credential, e.g., agency login) hsontheimer			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of Ulm, FRG	BS	1982	Biology/Physics (BA)
University of Ulm, FRG	MS	1986	Neurobiology (MS)
University of Heidelberg, FRG	PhD	1989	Neuroscience

A. Positions and Honors.**Positions and Employment**

1989-1991 Postdoctoral Associate, Depart. of Neurology, Yale University, New Haven, Connecticut
 1991-1994 Assistant Professor, Depart. of Neurology, Yale University, New Haven, Connecticut
 1992-1994 Assistant Professor of Neurobiology, Yale University, New Haven, Connecticut
 1994-1996 Assistant Professor, Physiology and Biophysics, University of Alabama at Birmingham
 1994-1996 Assistant Professor, Cell Biology, University of Alabama at Birmingham (UAB)
 1996-1997 Assistant Professor, Neurobiology, University of Alabama at Birmingham
 1997-2000 Associate Professor, Neurobiology, Cell Biology, and Physiology & Biophysics, UAB
 2000-present Professor, Neurobiology, Cell Biology, and Physiology & Biophysics, UAB
 2002-present Director, Cellular & Molecular Biology Graduate Program, UAB
 2005-present Director, Civitan International Research Center, UAB
 2006-present Director, UAB Center for Glial Biology in Medicine

Professional Memberships and Honors

1989 Ph.D. degree awarded with highest honors, summa cum laude
 1992 Winter Conference on Brain Research Fellowship
 1993 Dean's Young Faculty Award
 1997 Organizer & Chair of Society for Neurosciences Symposium, New Orleans, LA
 1998 Keynote Speaker, Advances in Ion Channel Research Symposium, San Francisco, CA
 1999 Keynote Speaker, Am. Associate for the Advancement of Science Conference, Anaheim, CA
 2002 Keynote Speaker, 127th Annual Meeting of the American Neurological Association, New York.
 2004 McNulty Civitan Scientist Award
 2004 Keynote Speaker, Glioma Conference, Berlin Germany
 2004 American Epilepsy Society, Symposium speaker, "Astrocytes and Epileptogenesis"
 2005 Soc. Neuroscience Symposium Chair, Role of Astrocytes in Epilepsy
 2002-2007 NDGB study section, regular member
 2006-2010 Soc. Neurosci. Program Committee

B. Selected Peer-Reviewed Publications (partial list from 114 total in chronological order).

Bordey, A. and Sontheimer, H. Properties of human glial cells associated with epileptic seizure foci *in situ*. Epilepsy Res., 32: 285-302 (1998). PMID: 9761328
 L. Soroceanu, Gillespie, G.Y., Khazaeli, M.B., Sontheimer, H. Use of Chlorotoxin for targeting of primary brain tumors. Cancer Res., 58:4871-4879 (1998). PMID: 9809993
 Soroceanu, L., Manning, T., and Sontheimer H. Modulation of glioma cell migration and invasion using Cl⁻ and K⁺ ion channel blockers. J. Neurosci. 19:5942-5954 (1999). PMID: 10407033
 Ye, Z.-C. and Sontheimer, H. Glioma cells release excitotoxic concentrations of glutamate. Cancer Res., 59: 4383-4391 (1999). PMID: 10485487
 Bordey, A. and Sontheimer, H. Differential inhibition of glial K⁺ currents by 4-AP.. J. Neurophysiol., 82: 3476-3487 (1999). PMID: 10601476

- Ye., Z.-C., Rothstein, J.D., and Sontheimer, H. Compromised glutamate transport in human glioma cells: Mislocalization of sodium-dependent glutamate transport and enhanced activity of cystine-glutamate exchange. J. Neurosci., 19:10767-10777 (1999). PMID: 10594060
- Ransom, C. B., Ransom, B. R., and Sontheimer, H. Activity-dependent extracellular K^+ accumulation in rat optic nerve: the role of glial and axonal Na^+ pumps. J. Physiol., 522.3:427-442 (2000). PMCID: 2269766
- Manning, Jr., T.J., Parker, J.C., and Sontheimer, H. The role of Lysophosphatidic acid and Rho in glioma cell motility. Cell Motility and the Cytoskeleton, 45:185-199 (2000). PMID: 10706774
- MacFarlane, S., and Sontheimer, H. Changes in ion channel expression accompany cell cycle progression of spinal cord astrocytes. GLIA, 30:39-48 (2000). PMID: 10696143
- Bordey, A., and Sontheimer, H. Ion channel expression by astrocytes in situ: a comparison of different CNS regions. GLIA, 30:27-38 (2000). PMID: 10696142
- Bordey, A., Sontheimer, H., and Trouslard, J. Muscarinic activation of BK channels induces membrane oscillations in glioma cells and leads to inhibition of cell migration. J. Membrane Biol., 176: 31-40 (2000). PMID: 10882426
- MacFarlane S., and Sontheimer, H. Modulation of Kv1.5 currents by Src tyrosine phosphorylation: potential role in the differentiation of astrocytes. J. Neurosci., 20: 5245-5253 (2000). PMID: 10884308
- Soroceanu, L., Manning, T.J., and Sontheimer, H. Reduced expression of connexin-43 and functional gap junction coupling correlates with malignancy grade of human gliomas. GLIA, 33:107-117 (2001). PMID: 11180508
- Ransom, C.B., and Sontheimer, H. BK channels in human glioma cells. J. Neurophysiol., 85:790-803 (2001). PMID: 11160513
- Bordey, A., Lyons, S.A., Hablitz, J.J., and Sontheimer, H. Electrophysiological characteristics of reactive astrocytes in experimental cortical dysplasia. J. Neurophysiol., 85:1719-1731 (2001). PMID: 11287494
- Smitherman K.A., and Sontheimer, H. Inhibition of glial Na^+ and K^+ currents by tamoxifen. J. Membrane Biol., 181: 125-135 (2001). PMID: 11420599
- Ransom, C.B., O'Neal, J. and Sontheimer, H. Volume-activated Chloride currents contribute to the resting conductance and invasive migration of human glioma cells. J. Neurosci., 21: 7674-7683 (2001). PMID: 11567057
- Ye, Z.-C., Ransom, B.R., and Sontheimer, H. (1R,3S)-1-Aminocyclopentane- 1,3-dicarboxylic acid (RS-ACPD) reduces intracellular glutamate levels in astrocytes. J. Neurochem., 79: 1-12 (2001). PMID: 11723168
- Liu, X., Reinhart, P. H., and Sontheimer, H., Cloning and characterization of gBK, a novel isoform of BK channels expressed in human glioma cells. J. Neurosci., 22(5):1840-1849 (2002). PMID: 11880513
- Ransom B.R., Liu, X., and Sontheimer H. BK channels in human glioma cells have enhanced calcium sensitivity. GLIA, 38:281-291 (2002). PMID: 12007141
- Deshane, J., Garner, C.C., and Sontheimer, H. Chlorotoxin inhibits glioma cell invasion via matrix metalloproteinase 2 (MMP-2). J. Biol. Chemistry, 278: 4135-4144 (2003). PMID: 12454020
- Parkerson, K. A. and Sontheimer, H. Contribution of Chloride Channels to Volume Regulation of Cortical Astrocytes. Am. J. Physiol. Cell Physiol. 284: C1460-C1466 (2003). PMID: 12606317
- Olsen, M.L., Schade, S., Lyons, S.A., Amaral, M.D., and Sontheimer, H. Expression of voltage-gated chloride channels in human glioma cells. J. Neurosci., 23: 5572-5582 (2003). PMID: 12843258
- Ritch, P.S., Carroll, S.L., and Sontheimer, H. Neuregulin-1 enhances motility and migration of human astrocytic glioma cells. J. Biol. Chem., 278: 20971-20978 (2003). PMID: 12600989
- Sontheimer, H. Malignant Glioma: Perverting Glutamate and Ion Homeostasis for Selective Advantage. Trends in Neuroscience, 26: 543-549 (2003). PMID: 14522147
- Olsen M.L. and Sontheimer, H. Mislocalization of K_{ir} Channels in Malignant Glia. GLIA 46:63-73 (2004). PMCID: 2548404
- Parkerson, K. A. and Sontheimer, H. Biophysical and pharmacological characterization of hypotonically-activated chloride currents in cortical astrocytes. GLIA, 46: 419-436 (2004). PMCID: 2548408
- Sontheimer, H. Ion channels and amino acid transporters support the growth and invasion of primary brain tumors. Molecular Neurobiology, 19: 61-72 (2004). PMCID: 2548410
- Weaver, A.K., Liu, X., and Sontheimer, H. Role for Calcium-activated Potassium Channels (BK) in Growth Control of Human Malignant Glioma Cells. J. Neurosci. Res., 15;78(2):224-34 (2004). PMCID: 2561220

- Ernest, N.-J., Van Duyn, L., Weaver, A.K., and Sontheimer, H. The Relative Contribution of Chloride Channels and Transporters to Regulatory Volume Decrease in Human Glioma Cells. Am. J. Physiology, 288: C1451-60 (2005). PMID: 2548409
- Ritch, P.S., Carroll, S.L., and Sontheimer, H. Neuregulin-1 enhances survival of human glioma cells. GLIA, 51:217-28 (2005). PMID: 2548407
- Chung W. J., Gillespie, G.Y., Hamza, H., and Sontheimer, H. Inhibition of cystine uptake arrests the growth of primary brain tumors. J. Neurosci., 25(31):7101-10 (2005). PMID: 16079392
- Olsen, M.L., Higashimori, H., Campell, S., Hablitz, J.J. and Sontheimer, H. Molecular identification of inwardly rectifying K⁺ channels in spinal cord astrocytes. GLIA, 53:516-528 (2006). PMID: 2553202
- McFerrin M. and Sontheimer, H. A role for ion channels in glioma cell invasion; Neuron Glia Biology, 2:39-49 (2006). PMID: 1389710
- Weaver, A.K., Bomben, V.C., & Sontheimer, H. Expression and function of Calcium-activated potassium channels in human glioma cells. GLIA 54: 223-233 (2006). PMID: 2562223
- MacVicar, B.A., Kimelberg, H.K. and Sontheimer, H. Anion channels in astrocytes: biophysics, pharmacology and function. GLIA, 54: 747-757 (2006) (review)
- Ernest, N.-J., and Sontheimer, H. Extracellular glutamine is a critical modulator for regulatory volume increase in human glioma cells. Brain Research, 1144:231-8 (2007). PMID: 1899165
- McCoy, E. and Sontheimer, H. Water channel expression and function in normal and malignant glial cells. GLIA, 55(10):1034-43 (2007). PMID: 2561225
- Habela, C.W. and Sontheimer, H. Cytoplasmic volume condensation is an integral part of mitosis. Cell Cycle 6:1613-1620 (2007). PMID: 2042484
- Lyons, S.A., Chung, W.J., Weaver, A.K., Ogunrinu, T. and Sontheimer H. Autocrine glutamate signaling promotes glioma cell invasion. Cancer Research, 67:9463-9471 (2007). PMID: 2045073
- Olsen, M.L., Campell, S.L., and Sontheimer, H. Differential distribution of Kir4.1 in spinal cord astrocytes suggests regional differences in K⁺ homeostasis. J. Neurophysiol., 98:786-93 (2007). PMID: 2040512
- Higashimori, H. and Sontheimer, H. Role of Kir4.1 Channels in Growth Control of Glia. GLIA, 55: 1668-1679 (2007). PMID: 2040118
- Weaver, A.K., Olsen, M.L., McFerrin, M.B. and Sontheimer, H. BK Channels are Coupled to IP3-receptors via Lipid Rafts: a Novel Mechanism for Coupling [Ca²⁺]_i to Channel Activation, J. Biol. Chem., 282:31558-68 (2007). PMID: 2227909
- Bomben, V. and Sontheimer H., Inhibition of transient receptor potential canonical (TRPC) channels impairs cytokinesis in human malignant gliomas. Cell Proliferation, 41:98-121 (2008). PMID: 18211288.
- Ernest, N.-J., Habela, C.W. and Sontheimer, H. Cytoplasmic condensation is both necessary and sufficient to induce apoptotic cell death. J. Cell Sci., 121:290-297 (2008). PMID: 18198188
- Sontheimer, H., An unexpected role for ion channels in brain tumor metastasis. Exp Biol Med., 233:779-791 (2008). PMID: 18445774
- Sontheimer, H., A role for glutamate in growth and invasion of primary brain tumors. J Neurochem. 105:287-95 (2008). PMID: 18284616
- Olsen M. and Sontheimer, H. Functional implications for Kir4.1 channels in glial biology: From K⁺ buffering to cell differentiation. J Neurochem, 107:589-601 (2008) PMID: 18691387
- Habela, C.W., Olsen, M.L., Sontheimer, H. CIC3 is a critical regulator of the cell cycle in normal and malignant glial cells. J Neurosci. 28:9205-17. (2008). PMID: 18784301

C. Research Support

Ongoing Research Support

R01NS052634 Sontheimer (PI)

NIH/NINDS

7/01/2005-4/30/2009

Amino-acid Transport and the Biology of Human Gliomas

This project examines the hypothesis that tumor cells utilize glutamate as an autocrine signal that enhances their invasion. We speculate that glutamate being released via a cystine transporter acts as an autocrine or paracrine signal.

Role: Principal Investigator

No overlap

R01NS31234 Sontheimer (PI)

3/10/94-11/30/2011

NIH/NINDS

Properties and Function of Glia Ion Channels

This grant examines the role of potassium channels in astrocytes with the goal of ascribing defined cell biological roles to molecularly identifiable K^+ channels. A major objective is to characterize changes in Ca^{2+} activated K^+ channels that are involved in cell proliferation during development and after reactive gliosis.

Role: Principal Investigator

No overlap

R01NS36692-A2 Sontheimer (PI)

8/01/97-3/31/2013

NIH/NINDS

Role of Chloride Channels in Glia and Glioma Migration

This grant is the proposal in hand, for which we are hereby seeking competitive renewal. It is currently in no-cost extension. For the past 8 years we have examined the role of Cl^- channels in glioma biology. These results from the previous cycle suggest that Cl^- channels are involved in cell shrinkage as cells invade and have led to the introduction of chlorotoxin, a putative Cl^- channel inhibitor into clinical trials.

Role: Principal Investigator

No overlap

T32GM008111

Sontheimer (PI)

7/1/04-6/30/2012

NIH NIGMS

Title: Predoctoral Training in Cell and Molecular Biology

Goals: The objective of the Cellular and Molecular Biology (CMB) Training Program is to provide high quality training to prepare outstanding individuals for careers in research and teaching. This is the proposal for which continued funding is sought.

Role: Principle Investigator

Training grant, no overlap

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 Brenner, Michael		POSITION TITLE Professor	
eRA COMMONS USER NAME Michaelb			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Harvard College, Cambridge, MA	BS	1961-65	Biochemistry
Univ. California-Berkeley, Berkeley, CA	PhD	1965-70	Biochemistry
Univ. California San Diego, LaJolla, CA	Postdoc	1970-71	Developmental Biology

A. Positions and Honors.**Positions and Employment**

1972-76 Assistant Professor of Biology, Harvard University
 1976-79 Associate Professor of Biology, Harvard University
 1979-80 Visiting Assistant Professor, Department of Biology, Boston College
 1980-84 Associate Professor of Biochemistry, Temple University Medical School
 1984 Principal Research Scientist, Genex Corporation
 1985-87 Research Scientist, Laboratory of Dr. Jun-ichi Tomizawa, NIDDK, NIH
 1987-92 Research Scientist, Laboratory of Dr. Ernst Freese, NINDS, NIH
 1992-98 Research Scientist, Laboratory of Dr. John Hallenbeck, NINDS, NIH
 1998-2007 Associate Professor, Department of Neurobiology, University of Alabama at Birmingham
 2007-present Professor, Department of Neurobiology, University of Alabama at Birmingham

Honors

1965-66 Churchill Foundation Fellowship, Churchill College, Cambridge, England (organic chemistry)
 1993 National Institutes of Health Award of Merit
 1999 Grupo Carso Award: biennial award by the Fundación Mexicana para la Salud (Mexican Foundation for Health) for best research paper on organ and tissue transplantation
 2000 Moore Award for best paper on clinico-pathologic correlation, annual meeting of the American Academy of Neuropathology
 2002 Outstanding poster award, Gordon Conference on Intermediate Filaments
 2003 Outstanding poster award (selected for an oral presentation), American Society of Neurochemistry annual meeting
 2005 Paper in Annals of Neurology selected for special commentary

Federal Government Review Panels

Invited Participant, NCI/MMHCC Neuro-Oncology Model Forum, NY, NY, November, 2000
 Adhoc Reviewer, National Research Council COBASE visiting scientist program, November 2001.
 Member NIH Special Emphasis Panel ZNS1 SRB-A Study Section, June 2002
 Member NIH DBD (formerly BDCN5) Study Section, October 2002 to June 2006; adhoc February 2007

B. Selected peer-reviewed publications (in chronological order).

(Publications selected from 86 peer-reviewed publications)

- 2002 Li, R., Messing, A., Goldman, J.E. and BRENNER, M. GFAP Mutations in Alexander Disease, *Int. J. Dev. Neurosci.* 20:259-268.
- 2003 Messing, A. and BRENNER, M. Alexander disease: GFAP mutations unify young and old. *Lancet Neurol.* 2:75.
- 2003 Johnson, A.B. and BRENNER, M. Alexander Disease: Clinical, Pathological and Genetic Features. *J. Child Neurol.* 18:625-632.
- 2004 Lupien, C., BRENNER, M., Guérin, S.L., and Salesse, C. Expression of glial fibrillary acidic protein in primary cultures of human Müller cells. *Exp. Eye Res.* 79:423-429.
- 2004 Thyagarajan, D., Chataway, T., Li, R., Gai, W.P., BRENNER, M. Dominantly-inherited adult-onset leukodystrophy with palatal tremor caused by a mutation in the glial fibrillary acidic protein gene. *Mov. Disord.* 19:1244-1248..
- 2004 Su, M., Hu, H., Lee, Y., d'Azzo, A., Messing, A. and BRENNER, M. Expression specificity of GFAP transgenes. *Neurochem. Res.* 29:2075-2093..
- 2005 Van der Knaap, M.S., Salomons, G.S., Li, R., Franzoni, E., Gutiérrez-Solana, L.G., Smit, L.M.E., Robinson, R., Ferrie, C.D., Cree, B., Reddy, A., Thomas, N., Banwell, B., Barkhof, F., Jakobs, C., Johnson, A., Messing, A. and BRENNER, M. Unusual variants of Alexander disease. *Annals Neurol.* 57(3):327-338.
- 2005 Li, R., Johnson, A.B., Salomons, G.S., Goldman, J.E., Naidu, S., Quinlan, R., Cree, B., Ruyle, S.Z., Banwell, B., D'Hooghe, M., Siebert, J.R., Rolf, C.M., Cox, H., Reddy, A., Gutiérrez-Solana, L.G., Collins, A., Weller, R.O., Jakobs, C., Messing, A., Van der Knaap, M.S., and BRENNER, M. GFAP mutations in infantile, juvenile and adult forms of Alexander disease. *Annals Neurol.* 57(3):310-326.
- 2005 Hsiao, V.C., Rujin, T., Long, H., Perng, M.D., BRENNER, M., Quinlan, R. and Goldman, J.E. Alexander disease mutation of GFAP causes filament disorganization and decreased solubility of GFAP protein. *J. Cell Science* 118:2057-2065.
- 2006 Li, R., Salomons, G.S., Johnson, A., Van der Knaap, Boespflug-Tanguy, O., Rodriguez, D., Gorospe, J.R., Messing, A. and BRENNER, M. Propensity for paternal inheritance of de novo mutations in Alexander disease. *Hum. Genet.* 119:137-44.
- 2006 de Leeuw, B., Su, M., ter Horst, M., Iwata, S., Rodijk, M., Hoebe, R.C., Messing, A., Smitt, P.S. and BRENNER, M. Increased glia-specific transgene expression with GFAP promoters containing multiple enhancer elements. *J. Neurosci. Res.* 83:744-753.
- 2006 Lee, Y., Su, M., Messing, A. and BRENNER, M. Astrocyte heterogeneity revealed by expression of a GFAP-lacZ transgene. *Glia* 53:677-687.
- 2006 Der Perng, M.D., Su, M., Wen, S.F., Li, R., Gibbon, T., Prescott, A.R., BRENNER, M. and Quinlan, R.A. The Alexander disease-causing GFAP mutant, R416W, accumulates into Rosenthal fibers by a pathway involving filament aggregation and the association of α B-crystallin and HSP27. *Am. J. Hum. Gen.* 79:197-213.
- 2007 Quinlan, R., BRENNER, M., Goldman, J.E. and Messing, A. GFAP and its role in Alexander disease. *Exp. Cell Res.* 313:2077-2087.
- 2008 Howard, K.L., Hall, D.A., Moon, M., Agarwal, P., Newman, E., and BRENNER, M. Adult-Onset Alexander Disease with Progressive Ataxia and Palatal Tremor. *Mov. Disord.* 23:118-122..
- 2008 Lee, Y., Su, M., Messing, A., Su, M. and BRENNER, M. (2008) GFAP promoter elements required for region-specific and astrocyte-specific expression. *Glia* 56: 481-493.
- 2008 BRENNER, M., Goldman, J.E., Quinlan, R. and Messing, A. "Alexander disease and astrocytes," an invited chapter for the book "Astrocytes in (patho)physiology of the nervous system," Pappas, V. and Haydon, P., eds., Springer, Boston, MA (in press).
- 2008 Liu, B., Wang, S., BRENNER, M., Paton, J.F., and Kasparov, S. (2008) Enhancement of cell-specific transgene expression from a Tet-Off regulatory system using a transcriptional amplification strategy in the rat brain. *J. Gene Med.* 10:583-592.
- 2009 Dotti, M.T., Buccoliero, R., Lee, A., Gorospe, J.R., Flint, D., Galluzzi, P., Bianchi, S., D'Eramo, C., Naidu, S., Federico, A. and BRENNER, M. "An infantile case of Alexander disease unusual for its MRI features and a GFAP allele carrying both the p.Arg79His mutation and the p.Glu223Gln coding variant. *J. Neurol* (in press)."

C. Research Support**Ongoing Research Support**RO1NS39055 Brenner (PI)
NIH NINDS

7/1/99-2/28/11

Analyses & Applications of GFAP Transcription

This project studies the function of astrocytes by analyzing the transcriptional regulation of the gene encoding glial fibrillary acidic protein (GFAP), an astrocyte-specific protein, and also seeks to develop more effective astrocyte-specific expression cassettes.

P01NS42803 Messing (PI); Brenner (Co-PI)
NIH NINDS

3/15/02-2/28/07 (in a no cost extension)

Alexander Disease: Cellular and Molecular Mechanisms

This is a part of a program project administered by Dr. Albee Messing (University of Wisconsin Madison). This project investigates the involvement of GFAP mutations in Alexander disease through genetic analysis of patient DNA, and study of the properties of mutant GFAP protein in cell free polymerization assays, cultured cells and transgenic mice. My role is as PI of one of the projects, "Mutations and Biochemistry of GFAP in Alexander Disease," in which we are analyzing putative patients for GFAP mutations and studying the biochemical and physiological properties of the mutant GFAP. A competitive renewal application with a score of 120 and recommended for funding by Council is pending.

P30HD38985 Percy (PI) Brenner (Core B Co-Director)
NIH NICHD

08/01/00-06/30/13

UAB Mental Retardation Research Center; Core B: Recombinant Technologies Core

This Core provides state-of-the-art technical and personnel support for MRRC researchers interested in the genetic manipulation of cells, tissues and animals, including knock out of endogenous genes and expression of transgenes. I supervise the personnel running the Core and make policy decisions.

NIH Roth (PI) Brenner (Core B Co-Director)

8/1/06 - 7/30/11

Alabama Neuroscience Blueprint Core Center; Core B: Molecular Engineering Core

The "Alabama Neuroscience Blueprint Core Center" at the UAB provides new interdisciplinary research core services to Neuroscience Blueprint Institute and Center funded investigators at UAB and participating institutions including Auburn University, University of South Alabama, Southern Research Institute, Tulane University, and Louisiana State University. The Molecular Engineering Core (Core B) assists with the generation of targeting cassettes for the production of both transgenic and knockout animals and with their genotyping.

PENDING (Note: Both of these grants have been recommended for funding by NIH Council)P01NS42803 Messing (PI)
NIH NINDS

8/01/08-7/31/13

Alexander Disease: Cellular and Molecular Mechanisms

(This application is a competitive renewal for the P01 project described above. It has been recommended for funding by Council.)

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 David G. Standaert		POSITION TITLE John and Juanelle Strain Professor of Neurology	
eRA COMMONS USER NAME DGSTANDAERT			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Harvard University, Cambridge, MA	A.B.	1982	Biochemistry
Washington University, St. Louis, MO	M.D., Ph.D.	1988	Medicine, Pharmacology
Jewish Hospital, St. Louis, MO	Intern	1988-1989	Internal Medicine
University of Pennsylvania, Philadelphia, PA	Resident	1989-1992	Neurology
Massachusetts General Hospital	Fellow	1992-1995	Movement Disorders

A. Positions and Honors.

- 1982 Graduated magna cum laude from Harvard University
 1988 Irwin Levy Prize in Neurology and Neurological Surgery
 1991 Sam Zeritsky Resident's Research Award in Neurology
 1992-1995 Research and Clinical Fellow, Neurology Service, Massachusetts General Hospital, Boston, MA
 1992-1995 American Academy of Neurology Research Fellowship Award in Neuropharmacology
 1992-1995 Howard Hughes Medical Institute Postdoctoral Research Fellowship for Physicians
 1995-2001 Assistant Professor of Neurology, Harvard Medical School, Boston, MA
 1996-1999 Cotzias Fellowship, American Parkinson's Disease Association
 2001-2006 Associate Professor of Neurology, Harvard Medical School, Boston, MA
 2003-2008 Scientific Advisory Board, Dystonia Medical Research Foundation
 2003-2008 Chairperson, Standards Committee, Parkinson Study Group
 2004-2006 Associate Director, Movement Disorders Unit, Massachusetts General Hospital
 2004-2008 Initial Review Group NSD-B, National Institutes of Health, regular member
 2005-2006 Chair, Partners Human Research Committee (IRB), MGH Panel A
 2005-2006 Director, MGH/MIT Morris Udall Center of Excellence in PD Research
 2006 Chair, ZNS1, NIH Udall Centers Review Panel
 2007 "Best Doctors in America"
 2001-present Scientific Advisory Board, American Parkinson Disease Association
 2005-present Scientific Advisory Board, Michael J. Fox Foundation
 2005-present Handling Editor, Journal of Neurochemistry
 2006-present Professor of Neurology, Neurobiology, and Cell Biology, University of Alabama at Birmingham (UAB)
 2006-present Director, Center for Neurodegeneration and Experimental Therapeutics, UAB
 2006-present Director, Division of Movement Disorders, Dept of Neurology (UAB)
 2007-present Vice Chair, Department of Neurology, UAB
 2008-present Director, Comprehensive Neuroscience Center, UAB

B. Selected peer-reviewed publications (in chronological order, selected from >100).

- Dunah AW, Wang Y, Yasuda RP, Kameyama K, Haganir RL, Wolfe BB, Standaert DG. Alterations in subunit expression, composition, and phosphorylation of striatal N-methyl-D-aspartate glutamate receptors in a rat 6-hydroxydopamine model of Parkinson's disease. *Mol Pharmacol* 2000; 57:342-352. PMID: 10648644
 Kuppenbender KD, Standaert DG, Feuerstein TJ, Penney JB Jr, Young AB, Landwehrmeyer GB. Expression of NMDA receptor subunit mRNAs in neurochemically identified projection and interneurons in the human striatum. *J Comp Neurol* 2000; 419:407-421. PMID: 10742712
 Dunah AW, Standaert DG. Dopamine D1 receptor-dependent trafficking of striatal NMDA glutamate receptors to the postsynaptic membrane. *J Neurosci* 2001; 21:5546-5558. PMID: 11466426

- Augood SJ, Hollingsworth ZH, Albers DS, Yang L, Leung J-C, Muller B, Klein C, Breakefield XO, Standaert DG. Dopamine transmission in DYT1 dystonia: a biochemical and autoradiographical study. *Neurology* 2002; 59:445-448. PMID: 2177384
- Dunah AW, Jeong H, Griffin A, Kim Y-M, Standaert DG, Hersch SM, Mouradian MM, Young AB, Tanese N, Krainc D. Sp1 and TAFII130 transcriptional activity disrupted in early Huntington's disease. *Science* 2002; 296:2238-2243. PMID: 11988536
- Augood SJ, Keller-McGandy CE, Siriani A, Hewett J, Ramesh V, Sapp E, DiFiglia M, Breakefield XO, Standaert DG. Distribution and ultrastructural localization of torsinA immunoreactivity in the human brain. *Brain Res* 2003; 986:12-21. PMID: 12965225
- Dunah AW, Standaert DG. Subcellular segregation of distinct heteromeric NMDA glutamate receptors in the striatum. *J Neurochem* 2003; 85:935-943. PMID 2716425
- Dunah AW, Sirianni AC, Fienberg AA, Bastia E, Schwarzschild MA, Standaert DG. Dopamine D1-dependent trafficking of striatal N-methyl-D-aspartate glutamate receptors requires Fyn protein tyrosine kinase but not DARPP-32. *Mol Pharmacol* 2004; 65:121-129. PMID: 14722243
- Hallett PJ, Standaert DG. Rationale for and use of NMDA receptor antagonists in Parkinson's disease. *Pharmacol Ther* 2004; 102:155-174. PMID: 15163596
- Standaert DG. Applications of laser capture microdissection in the study of neurodegenerative disease. *Arch Neurol* 2005; 62:203-205. PMID: 15710848
- Hallett PJ, Dunah AW, Ravenscroft P, Zhou S, Bezard E, Crossman AR, Brotchie JM, Standaert DG. Alterations of striatal NMDA receptor subunits associated with the development of dyskinesia in the MPTP-lesioned primate model of Parkinson's disease. *Neuropharmacology* 2005; 48:503-516. PMID: 15755478
- Zucker B, Luthi-Carter R, Kama JA, Dunah AW, Stern EA, Fox JH, Standaert DG, Young AB, Augood SJ. Transcriptional dysregulation in striatal projection- and interneurons in a mouse model of Huntington's disease: Neuronal selectivity and potential neuroprotective role of HAP1. *Hum Mol Genet* 2005; 14:179-189. PMID 15548548
- Cantuti-Castelvetri I, Klucken J, Ingelsson M, Ramasamy K, McLean PJ, Frosch MP, Hyman BT, Standaert DG. Alpha-synuclein and chaperones in dementia with Lewy bodies. *J Neuropathol Exp Neurol* 2005; 64:1058-1066. PMID: 16319716
- Cantuti-Castelvetri I, Lin MT, Zheng K, Keller-McGandy CE, Betensky RA, Johns DR, Beal MF, Standaert DG, Simon DK. Somatic mitochondrial DNA mutations in single neurons and glia. *Neurobiol Aging* 2005; 26:1343-1355. PMID: 16243605
- Hallett PJ, Dunah AW, Ravenscroft P, Zhou S, Bezard E, Crossman AR, Brotchie JM, Standaert DG. Alterations of striatal NMDA receptor subunits associated with the development of dyskinesia in the MPTP-lesioned primate model of Parkinson's disease. *Neuropharmacology* 2005; 48:503-516. PMID: 15755478
- Miller DW, Johnson JM, Solano SM, Hollingsworth ZR, Standaert DG, Young AB. Absence of alpha-synuclein mRNA expression in normal and multiple system atrophy oligodendroglia. *J Neural Transm* 2005; 112:1613-1624. PMID: 16284907
- Sharma N, Baxter MG, Petravic J, Bagg DC, Schienda A, Standaert DG, Breakefield XO. Impaired motor learning in mice expressing torsinA with the DYT1 dystonia mutation. *J Neurosci* 2005; 25:5351-5355. PMID: 15930383
- Hallett PJ, Spoelgen R, Hyman BT, Standaert DG, Dunah AW. Dopamine D1 activation potentiates striatal NMDA receptors by tyrosine phosphorylation-dependent subunit trafficking. *J Neurosci*. 2006 Apr 26;26(17):4690-700. PMID: 16641250
- Ingelsson M, Ramasamy K, Cantuti-Castelvetri I, Skoglund L, Matsui T, Orne J, Kowa H, Raju S, Vanderburg CR, Augustinack JC, de Silva R, Lees AJ, Lannfelt L, Growdon JH, Frosch MP, Standaert DG, Irizarry MC, Hyman BT. No alteration in tau exon 10 alternative splicing in tangle-bearing neurons of the Alzheimer's disease brain. *Acta Neuropathol (Berl)*. 2006 Oct;112(4):439-49. PMID: 16802167
- Sadri-Vakili G, Menon AS, Farrell LA, Keller-McGandy CE, Cantuti-Castelvetri I, Standaert DG, Augood SJ, Yohrling GJ, Cha JH. Huntingtin inclusions do not down-regulate specific genes in the R6/2 Huntington's disease mouse. *Eur J Neurosci*. 2006 Jun;23(12):3171-5. PMID: 16820007
- Pisani A, Martella G, Tscherter A, Bonsi P, Sharma N, Bernardi G, Standaert DG. Altered responses to dopaminergic D2 receptor activation and N-type calcium currents in striatal cholinergic interneurons in a mouse model of DYT1 dystonia. *Neurobiol Dis*. 2006 Nov;24(2):318-25. PMID: 16934985

- Scherzer CR, Eklund AC, Morse LJ, Liao Z, Locascio JJ, Fefer D, Schwarzschild MA, Schlossmacher MG, Hauser MA, Vance JM, Sudarsky LR, Standaert DG, Growdon JH, Jensen RV, Gullans SR. Molecular markers of early Parkinson's disease based on gene expression in blood. *Proc Natl Acad Sci U S A*. 2007 Jan 16;104(3):955-60. PMID: 17215369
- St Martin JL, Klucken J, Outeiro TF, Nguyen P, Keller-McGandy C, Cantuti-Castelvetri I, Grammatopoulos TN, Standaert DG, Hyman BT, McLean PJ. Dopaminergic neuron loss and up-regulation of chaperone protein mRNA induced by targeted over-expression of alpha-synuclein in mouse substantia nigra. *J Neurochem*. 2007 Mar;100(6):1449-57. PMID: 17241127
- Cantuti-Castelvetri C, Keller-McGandy C, Bouzou B, Asteris G, Clark TW, Frosch MP, Standaert DG. Effects of Gender on Nigral Gene Expression in Parkinson Disease. *Neurobiology of Disease*. 2007, Jun; 26(3):606-14. PMID: 17412603
- Outeiro TF, Grammatopoulos TN, Altmann S, Amore A, Standaert DF, Hyman BT, Kazantsev AG. Pharmacological inhibition of PARP-1 reduces alpha-synuclein- and MPP (+)-induced cytotoxicity in Parkinson's disease. *Biochem Biophys Res Commun*. 2007 Jun 8; 357(3): 596-602. PMID: 17449015
- Balcioglu A, Kim MO, Sharma N, Cha JH, Breakefield XO, Standaert DG. Dopamine release is impaired in a mouse model of DYT1 dystonia. *J Neurochem*. 2007 Jul 11;102 (3) 783-788. PMID: 17550429
- Grammatopoulos TN, Outeiro TF, Hyman BT, Standaert DG. Angiotensin II protects against alpha-synuclein toxicity and reduces protein aggregation in vitro. *Biochem Biophys Res Commun*. 2007 Nov 23;363(3):846-51. PMID: 17900533
- Lewis TB, Standaert DG. Design of clinical trials of gene therapy in Parkinson disease. *Exp Neurol*. 2008 Jan; 209(1): 41-7. PMID: 17920590
- Yacoubian TA, Cantuti-Castelvetri I, Bouzou B, Asteris G, McLean PJ, Hyman BT, Standaert DG. Transcriptional dysregulation in a transgenic model of Parkinson disease. *Neurobiol Dis*. 2008 Mar;29(3):515-28. PMID: 18191405
- Breakefield XO, Blood AJ, Li Y, Hallett M, Hanson PI, Standaert DG. The pathophysiological basis of dystonias. *Nat Rev Neurosci*. 2008 Mar; 9(3): 222-34. PMID: 18285800
- Nicholas AP, Lubin FD, Hallett PJ, Vattam P, Ravenscroft P, Bezard E, Zhou S, Fox SH, Brotchie JM, David Sweatt J, Standaert DG. Striatal Histone Modifications in Models of Levodopa-Induced Dyskinesia. *J. Neurochem*. 2008 Jul; 106(1):486-94. PMID: 18410512.
- Raju DV, Ahern TH, Shah DJ, Wright TM, Standaert DG, Hall RA, Smith Y. Differential synaptic plasticity of the corticostriatal and thalamostriatal systems in an MPTP-treated monkey model of parkinsonism. *Eur J Neurosci*. 2008 Apr; 27(7):1647-58. PMID: 18380666 [PubMed-in process].
- Hallett PJ, Collins TL, Standaert DG, Dunah AW. Biochemical Fractionation of brain tissue for studies of receptor distribution and trafficking. *Curr Protoc Neurosci*. 2008 Jan;Chapter 1:Unit 1.16. PMID: 18428670
- Yacoubian TA, Standaert DG. Targets for neuroprotection in Parkinson's disease. *Biochem Biophys Acta*. 2008 Oct 1 [Epub ahead of print] PMID: 18930814

C. Research Support.

ONGOING

1-R01-AG024040-01A2 Litvan (PI)

07/01/06-06/30/10

NIH/NIH

Genetic and Environmental Risk Factors for PSP

To collect DNA from patients with PSP to study genetic and environmental risk factors.

Role: Site Principal Investigator

APDA, Standaert (PI)

09/01/06-08/31/13

American Parkinson's Disease Association

APDA Advanced Center for Parkinson's Research

The APDA advanced center supports pilot and investigational projects in Parkinson's disease

Role: Principal Investigator

2-P01-NS37409-05A2, Breakefield (PI)

01/15/99-03/31/09

NIH/NINDS

To study the biology of DYT1 using genetically engineered mouse models.

Role: Principal Investigator (Project 1)

MJFF, Standaert (PI) 06/30/07-06/29/09
 Michael J. Fox Foundation
 Validation of VPS41, a Protein Involved in Lysosomal Trafficking, as a Target for Parkinson's Disease Therapy
 To study the role of VPS41 in Parkinson's Disease.
 Role: Principle Investigator

MJFF Critical Challenges West (PI) 12/15/07-12/14/08
 Michael J. Fox Foundation
 Viral Delivery of LRRK2 to Mouse Dopaminergic Neurons Using High-Capacity Viral Vectors
 This grant seeks to address whether LRRK2-mediated toxicity is kinase dependent *in vivo*.
 Role: Co-Investigator

The Bachmann Strauss Dystonia & Parkinson Foundation Inc, Standaert (PI)
 BSDF 01/01/08-12/31/08
 Cholinergic-Neuron Specific Inactivation of the Dyt1 Gene in Mice
 To study the effect of the DYT1 mutation in cholinergic cells.
 Role: Principle Investigator

MJFF Therapeutics Development Program Standaert (PI) 9/1/08-8/31/09
 MJFF
 Validation of TorsinA as a Target for PD Therapy in Mammalian Models
 Role: Principle Investigator

COMPLETED (Last Three Years)

R01-NS34361-09, Standaert (PI) 07/01/96-06/30/06
 NIH/NINDS
 NMDA Receptors: Regulation of Basal Ganglia Function
 The goal was to determine the mechanisms responsible for changes in NMDA receptors in models of parkinsonism.
 Role: Principal Investigator

P50-NS38372-07, Standaert (Program Director, PI Proj 1) 07/01/04-06/30/06
 NIH/NINDS
 MGH/MIT Morris Udall Center of Excellence in PD Research
 The goal of the project was to examine alterations in gene expression in Parkinson disease and animal models of PD
 Role: Program Director, Principal Investigator (Project 4)

R01-AG13617, Young (PI) 08/15/95-07/31/05
 NIH
 Metabotropic Glutamate Receptors in Neurodegeneration
 The goals are the employ pharmacological and anatomical methods to study the role of metabotropic glutamate receptors in neurodegenerative process.
 Role: Investigator

R21-NS045410, Bonato (PI) 08/15/03-07/31/08
 NIH/NINDS
 Data Mining to Identify Motor Fluctuations in Parkinson's disease
 The purpose of this project is to develop data mining and artificial intelligence systems to recognize there presence and severity of motor fluctuations in patients with Parkinson's disease.
 Role: Co-Principle Investigator

ASSOCIATE PROFESSORS

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 Lynn E. Dobrunz, Ph.D.		POSITION TITLE Associate Professor of Neurobiology	
eRA COMMONS USER NAME dobrunz			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing,</i>			
INSTITUTION AND LOCATION	DEGREE (if appl)	YEAR(s)	FIELD OF STUDY
Harvard University, Cambridge MA	S.B.	1984-1988	Engineering Science and Bioengineering
The Johns Hopkins University School of Medicine, Baltimore, MD	Ph.D.	1988-1994	Biomedical Engineering
The Salk Institute for Biological Studies, La Jolla, CA	Postdoctoral Fellow	1994-1999	Molecular Neurobiology

A. Positions and Honors**Positions and Employment**

- 1999-present Assistant Professor, Department of Neurobiology, University of Alabama at Birmingham, Birmingham, AL.
- 2002-present Secondary appointment, UAB Department of Physiology and Biophysics
- 2005-present UAB Center for Aging
- 2006-present UAB Civitan International Research Center
- 2006-present UAB Comprehensive Neurosciences Center

Other Experience and Professional Memberships

Society for Neuroscience, Women in Neuroscience

Honors

- Ford Foundation Summer Research Award, 1987
- Magna Cum Laude, Harvard University, 1988
- Phi Beta Kappa, 1988
- National Science Foundation Award for Creativity in Engineering, 1988-1987
- Able Wolman Fellowship, 1988-1989
- Howard Hughes Medical Institute Career Development Award, 1999-2000

B. Peer-Reviewed Publications (in chronological order)

1. Frangioni, J.V., T.S. Kwan-Gett, **L.E. Dobrunz**, & T.A. McMahon. 1987. The mechanism of low frequency sound production in muscle. *Biophys. J.* 51: 775-783
2. **Dobrunz, L.E.**, D.G. Pelletier, & T.A. McMahon. 1992. Muscle stiffness measured under conditions simulating natural sound production. *Biophys. J.* 58:557-565.
3. **Dobrunz, L.E.** & M.R. Berman. 1994. Effect of temperature on Ca^{2+} -dependent and mechanical modulators of relaxation. *J Mol Cell Cardiol.* 26:243-250.
4. **Dobrunz, L.E.**, P.H. Backx, & D.T. Yue. 1995. Steady-state $[Ca^{2+}]_i$ -force relationship in intact twitching cardiac muscle: direct evidence for modulation by isoproterenol and EMD 53998. *Biophys. J.* 69: 189-201.
5. **Dobrunz, L.E.** & C.F. Stevens. 1997. Heterogeneity of release probability, facilitation and depletion at central synapses. *Neuron* 18:995-1008.
6. Zador, A.M. & **L.E. Dobrunz**. 1997. Dynamic synapses in the cortex. *Neuron* 19:1-4.

7. **Dobrunz, L.E., E.P. Huang, & C.F. Stevens.** 1997. Very short-term plasticity in hippocampal synapses. Proc. Natl. Acad. Sci. USA 94:14843-14847.
8. **Dobrunz, L.E.** 1998. Long-term potentiation and the computational synapse. Proc. Natl. Acad. Sci. USA 95:4086-4088.
9. **Dobrunz, L.E. & C.F. Stevens.** 1999. Response of hippocampal synapses to natural stimulus patterns. Neuron 22:157-166.
10. **Dobrunz, L.E. & C.C. Garner.** 2002. Priming Plasticity. Nature 415:277-278.
11. **Dobrunz, L.E.** 2002. Release Probability is Regulated by the Size of the Readily Releasable Vesicle Pool at Excitatory Synapses in Hippocampus. Intl. J. Dev. Neurosci. 20:225-236.
12. **Scheiderer, C.L., L.E. Dobrunz, & L.L. McMahon.** 2003. A Novel Form of Long-Term Depression in Rat Hippocampus Induced by Activation of $\alpha 1$ Adrenergic Receptors, J. Neurophysiol., 91:1071-1077.
13. **Sun, H.Y, S.A. Lyons, & L.E. Dobrunz.** 2005. Mechanisms of target-cell specific short-term plasticity at Schaffer collateral synapses onto interneurons vs. pyramidal cells in juvenile rats. J Physiol, 568:815-840.
14. **deKay, J.G., T.C. Chang, N. Mills, Speed, H.E. & L.E. Dobrunz.** 2006. Responses of Excitatory Hippocampal Synapses to Natural Stimulus Patterns Reveal a Decrease in Short-term Facilitation and Increase in Short-term Depression During Postnatal Development. Hippocampus, 16:66-79.
15. **Scheiderer, C.L., K. Kolasa, M. Ward, D. Parsons, L.E. Harrell, L.E. Dobrunz, & L.L. McMahon.** 2006. Sympathetic sprouting drives hippocampal cholinergic reinnervation that prevents loss of a muscarinic receptor-dependent long-term depression at CA3-CA1 synapses, J. Neurosci 26:3745-3756.
16. **McCutchen, E., C.L. Scheiderer, L.E. Dobrunz, & L.L. McMahon.** 2006. Coexistence of Muscarinic Long-Term Depression with Electrically Induced Long-Term Potentiation and Depression at CA3-CA1 Synapses, J. Neurophysiol. 96:3114-3121.
17. **Crimmins, S., Jin, Y., Wheeler, C., Huffman, A.K., Chapman, C., Dobrunz, L.E., Levey, A., Roth, K.A., Wilson, J.A., & Wilson, S.M.** 2006. Transgenic rescue of *ataxia* mice with neuronal-specific expression of *Usp14*, J. Neurosci., 26: 11423-11431.
18. **Sun, H.Y. & L.E. Dobrunz.** 2006. Presynaptic Kainate Receptor Activation is a Novel Mechanism for Target-Cell Specific Short-Term Plasticity at Schaffer Collateral Synapses, J. Neurosci 26:10796-10807.

C. Research Support

Ongoing Research Support

Title: "Frequency Dependence of Excitatory Synaptic Transmission"

Principal Investigator: Lynn E. Dobrunz, Ph.D.

Agency: NIH NIMH

Type: R01 MH065328

Period: 12/1/02-11/31/07

Role: PI

Goals: This project compares short-term plasticity and the frequency dependence of excitatory synaptic transmission between glutamatergic synapses onto hippocampal CA1 pyramidal cells and s. radiatum interneurons.

Title: "REU Site: Research Experience for Undergraduates in Neuroscience at UAB"

Principal Investigator: Lynn E. Dobrunz, Ph.D.

Agency: NSF

Type: REU Site Grant

Period: 6/1/05 – 5/31/08

Role: PI

Goals: This project provides money for a summer undergraduate research program in neuroscience.

Title: "Muscarinic Receptor Induced LTD in Rat Hippocampus"

Principal Investigator: Lori L. McMahon, Ph.D.

Agency: NIH NIA

Type: R01 AG021612

Period: 1/1/04 – 12/31/08

Role: Co-Investigator

Goals: This project investigates a novel form of synaptic long-term depression induced by the M1 subtype of muscarinic acetylcholine receptors in rat hippocampus.

Pending Research Support

Title: Developmental Changes in Excitatory Synapses in Hippocampus

Principal Investigator: Lynn E. Dobrunz, Ph.D.

Agency: NIH NICHD

Type: R03

Role: PI

Goals: The goal of this grant is investigate the changes that occur in presynaptic function at temporoammonic synapses onto CA1 pyramidal cells in early postnatal development.

Priority score from 11/1/06 submission = 124, 2.3 percentile.

Title: A novel system to study postsynaptic molecules that affect presynaptic function

Principal Investigator: Lynn E. Dobrunz, Ph.D.

Agency: NIH NIMH

Type: R21

Role: PI

Priority score from 11/1/06 submission = 176. NIMH does not give percentiles for R21s.

Title: "Frequency Dependence of Excitatory Synaptic Transmission"

Principal Investigator: Lynn E. Dobrunz, Ph.D.

Agency: NIH NIMH

Type: R01 MH065328

Period: 12/1/07-11/31/12

Role: PI

Goals: This project compares short-term plasticity and the frequency dependence of excitatory synaptic transmission between glutamatergic synapses onto hippocampal CA1 pyramidal cells and s. radiatum interneurons.

Completed Research Support

Title: Howard Hughes Medical Institute Career Development Award

Principal Investigator: Lynn Dobrunz, Ph.D.

Agency: Howard Hughes/UAB

Type: Development

Period: 9/1/99-8/31/00

Goals: The development award provided start-up funds for the purchase of equipment for Dr. Dobrunz new laboratory.

Title: Alzheimer's Research Center

Principal Investigator: Lindy Harrell, M.D., Ph.D.

Agency: NIH NIA

Type: RO1 AG16582-03

Period: 4/1/99 – 3/31/04

Pilot Project II: "Cholinergic Modulation of Hippocampal Synaptic Plasticity: Potential Therapeutic Targets in Alzheimer's Disease"

Lori L. McMahon, Project Leader

Project Period: 4/1/01-3/31/02

Role: Co-PI

Goals: The goal of this pilot grant was to investigate long-term depression in hippocampus caused by activation of muscarinic acetylcholine receptors. Dr. Dobrunz was Co-PI along with Dr. McMahon.

Title: "Modulation of Glutamate Synapses in Neonatal Cortex"

Principal Investigator: Michael J. Friedlander, Ph.D.

Agency: NIH NICHD

Period: 6/14/00-05/31/05

Type: PO1 HD38760

Project II: "Developmental Changes in Presynaptic Function at Glutamatergic Synapses in Hippocampus"

Lynn E. Dobrunz, Ph.D. - Project Leader

Project Period: 6/14/00 - 5/31/03

Role: Project Leader

Goals: This program project analyzed glutamatergic synaptic transmission in the neonatal cerebral cortex. The goal of this Project II was to study the effects of developmental regulation on presynaptic function in neonatal hippocampus.

Title: "Metabotropic Glutamate Receptors in Aged Hippocampus"

Principal Investigator: Lynn E. Dobrunz, Ph.D.

Agency: UAB Center for Aging

Period: 4/1/05 - 3/31/06

Type: Intramural Pilot Research Grant

Role: PI

Goals: The goal of this project was to examine alterations in mGluR receptor expression and function in aged hippocampus

Title: "Role of Usp14 in the Development of the Nervous System"

Principal Investigator: Scott M. Wilson, Ph.D.

Agency: March of Dimes

Period: 02/01/2004-01/31/2006

Role: Co-Investigator

Goals: The goal of this project was to enable us to uncover new processes that rely on ubiquitin-signaling and to determine how alterations in these pathways can lead to neurological disease.

Title: "Developmental Regulation of Short-term Plasticity at Schaffer Collateral Synapses in Hippocampus"

Principal Investigator: Huayu Sun, M.D., Ph.D.

Agency: UAB Civitan International Research Center

Period: 10/1/05 - 9/30/06

Type: Emerging Scholars Award

Sponsor: Lynn E. Dobrunz, Ph.D.

Goals: The goal of this project was to examine changes in short-term plasticity at excitatory Schaffer collateral synapses during early postnatal development.

Title: "Changes in Group I mGluR effects on hippocampal synaptic plasticity in aging"

Principal Investigator: Lynn E. Dobrunz, Ph.D.

Agency: UAB Evelyn F. McKnight Brain Institute

Period: 3/1/05 - 2/28/07

Type: Intramural Pilot Research Grant

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 Robin A. J. Lester, Ph.D.		POSITION TITLE Associate Professor	
eRA COMMONS USER NAME (credential, e.g., agency login) LESTER			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of Bristol, England	BSc	1984	Pharmacology
University of Bristol, England	PhD	1988	Pharmacology

A. Positions and Honors.**Positions and Employment**

1988-91 Postdoctoral Fellow (Dr. Craig E. Jahr), Vollum Institute, Oregon Health Sciences University
 1992-93 Research Assistant Professor, Molecular Physiology & Biophysics, Baylor College of Medicine
 1993-1995 Research Assistant Professor, Division of Neuroscience, Baylor College of Medicine
 1995-1996 Associate Scientist, Neurobiology Research Center, University of Alabama at Birmingham
 1995-present Assistant Professor, Physiology and Biophysics, University of Alabama at Birmingham
 1996-2001 Assistant Professor, Neurobiology, University of Alabama at Birmingham
 2001-present Associate Professor, Neurobiology, University of Alabama at Birmingham

Other Experience and Professional Memberships

1999-present NIH NIDA-K study section (ad hoc)
 2000-present NIH MDCN-4 study section (member 2000 - 2004)
 2001-2005 Tobacco-Related Disease Research Program study section

Honors

Executive Editorial Board: Neuropharmacology

B. Selected Peer-Reviewed Publications (in chronological order).

Herron CE, Lester RAJ, Coan EJ and Collingridge GL (1986) Frequency-dependent involvement of NMDA receptors in the hippocampus: a novel synaptic mechanism. *Nature* 322:265-268.
 Collingridge GL, Herron CE and Lester RAJ (1988) Synaptic activation of N-methyl-D-aspartate receptors in the Schaffer collateral-commissural pathway of rat hippocampus. *J Physiol* 399:283-300.
 Collingridge GL, Herron CE and Lester RAJ (1988) Frequency-dependent N-methyl-D-aspartate receptor-mediated synaptic transmission in rat hippocampus. *J Physiol* 399:301-312.
 Davies SN, Lester RAJ, Reymann KG and Collingridge GL (1989) Temporally distinct pre- and postsynaptic mechanisms maintain long-term potentiation. *Nature* 338:500-503.
 Lester RAJ, Quarum ML, Partker JD, Weber E and Jahr CE (1989) Interaction of 6-cyano-7-nitroquinoxaline-2,3-dione with the N-methyl-D-aspartate receptor-associated glycine binding site. *Mol Pharmacol* 35:565-570.
 Lester RAJ and Jahr CE (1990) Quisqualate receptor-mediated depression of calcium currents in hippocampal neurons. *Neuron* 4:741-749.

- Lester RAJ, Clements JD, Westbrook GL and Jahr CE (1990) Channel kinetics determine the time course of NMDA receptor-mediated synaptic currents. Nature 346:565-567.
- Lester RAJ and Jahr CE (1992). Behavior of NMDA channels depends on agonist affinity. J Neurosci 12:635-643.
- Clements JD, Lester RAJ, Tong G, Jahr CE and Westbrook GL (1992) Time course of glutamate in the synaptic cleft. Science 258:1498-1501.
- Lester RAJ, Tong G and Jahr CE (1993) Interaction between the glutamate and glycine binding sites of the NMDA receptor. J Neurosci 13:1088-1096.
- Lester RAJ, and Dani JA (1994) Time-dependent changes in central nicotinic acetylcholine channel kinetics in outside-out patches. Neuropharmacol 33:27-34.
- Lester RAJ. and Dani, JA (1995) Acetylcholine receptor desensitization induced by nicotine in rat medial habenula neurons. J. Neurophysiol. 74:195-206.
- Fenster CP, Rains MF, Noerager B, Quick MW, and Lester RAJ. (1997) Influence of subunit composition on desensitization of nicotinic receptors at low concentrations of nicotine. J Neurosci 17:5747-5759.
- Fenster CP, Beckman ML, Parker JC, Sheffield EB, Whitworth TL, Quick MW and Lester RAJ (1999) Regulation of $\alpha 4\beta 2$ nicotinic receptor desensitization by calcium and protein kinase C. Mol Pharmacol 55:432-443.
- Quick MW, Ceballos RM, Kasten M, McIntosh MJ and Lester RAJ (1999) $\alpha 3\beta 4$ subunit-containing nicotinic acetylcholine receptors dominate function in medial habenula neurons. Neuropharmacol 38:769-783.
- Fenster CP, Whitworth T, Quick MW and Lester RAJ (1999) Upregulation of surface $\alpha 4\beta 2$ nicotinic receptors is initiated by receptor desensitization following chronic exposure to nicotine. J Neurosci. 19:4804-4814.
- Zhai R, Olias G, Chung WJ, Lester, RAJ, tom Dieck S, Lanfnaese K, Kreutz MR, Kindler S, Gundelfinger ED, Garner C. (2000) Temporal appearance of the presynaptic cytomatrix protein Bassoon during synaptogenesis. Cell. Molec. Neurobiol. 15:417-428.
- Sheffield EB, Quick MW and Lester RAJ (2000) Nicotinic acetylcholine receptor subunit mRNA expression and channel function in medial habenula neurons. Neuropharmacol. 39:2591-2603.
- Hicks JH, Dani JA, and Lester RAJ (2000) Regulation of the sensitivity of acetylcholine receptors to nicotine in rat habenula neurons. J. Physiol. 529: 579-597.
- Covernton PJO and Lester RAJ. (2002) Prolonged stimulation of presynaptic nicotinic acetylcholine receptors in the rat interpeduncular nucleus has differential effects on transmitter release. Int. J. Dev. Neurosci. 20: 247-258.
- Parker JC, Sarkar D, Quick MW and Lester RAJ (2003) Interactions of atropine with heterologously expressed and native $\alpha 3$ subunit-containing nicotinic acetylcholine receptors. Br. J. Pharmacol. 138: 801-810.
- Cho CH, Song W, Leitzell K, Teo E, Meleth AD, Quick MW and Lester RAJ (2005) Rapid upregulation of $\alpha 7$ nicotinic acetylcholine receptors by tyrosine dephosphorylation. J. Neurosci. 25:3712-3723.
- Li L, Cao D, Kim H, Lester R and Fukuchi K (2006) Simvastatin Enhances Learning and Memory Independent of Amyloid Load in Mice. Ann. Neurol. 60:729-739.
- Guo X and Lester RAJ (2007) Ca^{2+} Flux and Signaling Implications via Nicotinic Acetylcholine Receptors in Rat Medial Habenula. J. Neurophysiol. 97:83-92.
- Guo X and Lester RAJ (2007) Regulation of Nicotinic Acetylcholine Receptor Desensitization by Ca^{2+} . J. Neurophysiol. 97:93-101.
- Fonck C, Nashmi R, Salas R, Zhou C, Huang Q, De Biasi M, Lester RAJ & Lester HA (2008) Demonstration of Functional $\alpha 4$ -Containing Nicotinic Receptors in the Medial Habenula. Neuropharmacol. (In press).

C. Other Support**Active support**

RO1 DA 11940-02 Lester (PI)

07/15/98 – 03/31/09

NIH-NIDA

Subunit-Specific Regulation of Nicotinic Receptors

The major aims of this project are to understand the links between nicotinic acetylcholine receptor subunit composition and the short and long-term functional regulation by both biochemical mechanisms and chronic nicotine. These studies will be carried out in heterologous expression systems and are directed at characterizing cellular events underlying nicotine addiction.

Completed

RO1 NS 31669-06A2 Lester (PI)

04/01/94-02/28/06

NINDS

Central Nicotinic Channel Kinetics and Synaptic Function

The goals of this project are to characterize the properties of native nicotinic acetylcholine receptor channels in neurons in order to understand the physiological function of nicotinic synaptic transmission in the CNS.

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 Lori McMahon, Ph.D.		POSITION TITLE Associate Professor	
eRA COMMONS USER NAME LORIMCMAHON			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Southern Illinois University, Edwardsville, IL	B.A.	1983-1987	Biology/Chemistry
St. Louis Health Science Ctr, St. Louis, MO	Ph.D.	1987-1993	Neuropharmacology
Dept. of Pharmacological & Physiological Science			
Duke University, Durham NC	Postdoc	1993-1998	Neurophysiology
Department of Neurobiology			

A. Positions and Honors. List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

Employment

1987-1993 Graduate Assistant, Saint Louis University
 1993-1998 Research Associate, Duke University
 1998-present Assistant Professor, UAB Department of Physiology & Biophysics
 1998-present Secondary Appointment, UAB Department of Neurobiology
 2002-present Assistant Scientist, UAB Alzheimer's Disease Research Center
 2006-present Associate Professor w/ tenure, UAB Dept of Physiology & Bio
 2006-present Associate Scientist, Civitan International Research Center

Honors

1983-1987 Presidential Scholarship, Southern Illinois University
 1987 Ella Ott Weissman Award in Biological Sciences
 1987-1988 Saint Louis University Predoctoral Fellowship
 1988-1992 NIH Institutional Neuropharmacology Training Grant, Saint Louis Univ.
 1992-1993 Saint Louis University Predoctoral Fellowship
 1994-1995 NIH Institutional Postdoctoral Fellowship, Duke University
 1995-1998 NIH NRSA Individual Postdoctoral Training Grant, Duke University
 New Investigator Award, Epilepsy Foundation
 1999 Glaxo-Wellcome Travel Award
 2000-2002 Junior Investigator Award, American Heart Association
 2002 Ad Hoc Reviewer, NIH Study Section, MDCN 3
 2002-present American Physiological Society Awards Committee
 2002-present Editorial Board, Journal of Neurophysiology
 2004-2005 Ad hoc member of NIH Study Section, Molecular Neuropharmacology
 2005-2008 Permanent Member, NIH Study Section, Molecular Neuropharmacology

2006-present Director, Neuroscience Graduate Program
 2006-present Co-Director, Synaptic Plasticity Core Facility

B. Selected peer-reviewed publications or manuscripts in press:

1. Howlett AC, Champion-Dorrow TM, **McMahon LL**, Westlake TM. (1991) The cannabinoid receptor: biochemical and cellular properties in neuroblastoma cells. *Pharm. Biochem. and Behav.* 40: 565-569.
2. Chiappinelli VA, Wolf KM, Feng C, Yum L, **McMahon LL**. (1993) Different responses to opioid measured in terminals and somas of Edinger-Westphal neurons. *Neurosci.* 57:425-432.
3. **McMahon LL**, Yoon K.-W., Chiappinelli VA. (1994) Electrophysiological evidence for presynaptic nicotinic receptors in the avian ventral lateral geniculate nucleus. *J. Neurophys.* 71:826-829.
4. **McMahon LL**, Yoon K.-W., Chiappinelli VA. (1994) Nicotinic receptor activation facilitates GABAergic neurotransmission in the avian lateral spiriform nucleus. *Neurosci.* 59:689-698.
5. **McMahon LL**, Kauer JA. (1997) Hippocampal interneurons express a novel form of synaptic plasticity. *Neuron*, 18:295-305.
6. **McMahon LL**, Kauer JA. (1997) Hippocampal interneurons are excited by serotonin-gated ion channels. *J. Neurophys.*, 78:2493-2502.
7. Kauer JA, **McMahon LL**. (1997) Depressing transmission in GABAergic hippocampal neurons. *Molecular Psychiatry*, 2:434-436.
8. **McMahon LL**, Williams JH, Kauer JA. (1998) Functionally distinct groups of interneurons identified during rhythmic oscillations in hippocampus. *J. Neurosci.* 18:5640-5651.
9. Chattipakorn SC, **McMahon LL**. (2002) Pharmacological characterization of glycine-gated chloride currents recorded in rat hippocampal slices. *J. Neurophys.* 87:1515-1525.
10. Chattipakorn SC, **McMahon LL** (2003) Strychnine-sensitive glycine receptors depress hyperexcitability in rat dentate gyrus. *J. Neurophys.* 89, 1339-1342.
11. Jovov, BJ, Tousson A, **McMahon LL**, Benos DJ (2003) Immunolocalization of acid sensing ion channel 2a in rat cerebellum. *Histochem. Cell Biol.*, 119:437-446.
12. Scheiderer CL, Dobrunz LE, **McMahon LL**. (2004) A novel form of long-term synaptic depression in rat hippocampus induced by activation of α_1 adrenergic receptors. *J. Neurophys.* 91:1071-1077
13. Shaughnessy L, Chamblin B, **McMahon LL**, Nair A, Thomas MB, Wakefield J, Koentgen F, and Ramabhadran R. (2004) Novel Approaches to models of Alzheimer's Disease Pathology for Drug Screening and Development. *J. Molec. Neurosci.* 24:23-32.
14. Smith CC and **McMahon LL** (2005) Estrogen-Induced Increase in LTP Magnitude Occurs Only When the Ratio of NMDA Transmission to AMPA Transmission is increased. *J. Neurosci.* 25, 7780-7791.
15. Song W, Chattipakorn SC, **McMahon LL** (2006) Glycine-gated Chloride Channels Depress Synaptic Transmission in Rat Hippocampus. *J. Neurophys.*, 95, 2366-2379.
16. Scheiderer CL, McCutchen E., Thacher EE., Kolasa K, Ward MK, Parsons D, Harrell LE, Dobrunz LE, **McMahon LL** (2006). Sympathetic Sprouting Drives Hippocampal Cholinergic Reinnervation That Prevents Loss of a Muscarinic

- Receptor-Dependent Long-Term Depression at CA3-CA1 Synapses. J. Neurosci., 26, 3745-56.
17. Smith CC and **McMahon LL** (2006) Estradiol-Induced Increase in the Magnitude of Long-Term Potentiation is Prevented by Blocking NR2B Containing Receptors. J. Neurosci., 26, 8517-22.
 18. McCutchen E, Scheiderer CL, Dobrunz LE, and **McMahon LL** (2006) Coexistence of Muscarinic Long-Term Depression with Electrically Induced Long-Term Potentiation and Depression at CA3-CA1 Synapses. J. Neurophys., 96(6):3114-21.
 19. Scheiderer CL, McCutchen E., Thacker EE., Dobrunz LE, **McMahon LL** (2007) Coactivation of M1 muscarinic and $\alpha 1$ adrenergic receptors stimulates ERK1/2 and induces long-term depression at CA3-CA1 synapses in rat hippocampus. J. Neurosci. In Revision.
 20. McCoy PA and **McMahon LL** (2007) Muscarinic Receptor Dependent Long Term Depression in Rat Visual Cortex is PKC independent but Requires ERK1/2 Activation and Protein Synthesis. In Revision.

C. Research Support. List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and responsibilities of principal investigator identified above.

Current

NIH NINDS R01 NS41382 (L.L. McMahon, PI)

12/01/01 - 11/30/07

(no cost extension)

"Glycine-gated chloride channels and hippocampal excitability"

The major goal of this project is to elucidate, using electrophysiological recording techniques, the functional role of glycine gated chloride channels in providing inhibition in hippocampus and suppressing seizure activity. A second goal is to determine the synaptic versus extrasynaptic location of glycine receptors and the source of glycine in hippocampus.

NIH NIA R01 AG2161201 (L.L. McMahon, PI)

01/01/04-12/31/08

"Muscarinic receptor induced LTD in rat hippocampus"

The major goal of this project is to characterize two forms of long-term depression mediated via activation of muscarinic M1 receptors and adrenergic $\alpha 1$ receptors and to determine the effects of hippocampal cholinergic denervation and sympathetic sprouting on the expression of these plasticities.

Evelyn F. McKnight Research Award (L.L. McMahon, PI)

03/01/05-02/28/07

"Estrogen and Hippocampal Plasticity in Young Adult and Aged Rats"

The major goal of this project is to determine how estradiol modulates hippocampal spine density, ionotropic glutamate receptor function and long-term synaptic plasticity in area CA1 of female hippocampus. A major focus is to identify hormone-dependent mechanisms that are altered or lost by the aging process.

NRSA 1 F31 NS056835
Individual Graduate Student Award
2007-2009

PI: Portia A McCoy (score: 7.6%)
Sponsor: Lori L. McMahon
Title: Cholinergic Dependent Plasticity in Visual Cortex

Recently Completed

NRSA 1 F32 MH071085
Individual Graduate Student Award

2004-2006

PI: Caroline Smith (score: 10.6%),
Sponsor: Lori L. McMahon, PhD
Title: Estrogen modulates hippocampal morphology and plasticity

NIH NRSA 1F31 NS45469-01
Individual Graduate Student Award

2002-2004

PI: Cary Scheiderer (score: 10.2%)
Sponsor: Lori L. McMahon, PhD
Title: Muscarinic LTD Modulation by Cholinergic Denervation

RO1 AG16582-03 Pilot Project #1 (L. L. McMahon, PI) 04/01/01-03/31/02
NIH

"Cholinergic modulation of hippocampal synaptic plasticity: potential therapeutic targets in Alzheimer's Disease."

The major goal of this project is to examine the cellular mechanism underlying a novel form of long-term depression of excitatory transmission in hippocampus that involves activation of muscarinic cholinergic receptors.

American Heart Association (L. L. McMahon, PI) 07/01/00 - 06/30/02
"Activation of glycine-gated chloride channels by taurine is a potential neuroprotective mechanism against cell death".

The major goal of this project is to determine the mechanism underlying taurine's potential neuroprotective role in preventing cell death and the involvement of glycine receptors.

New Investigator Award (L.L. McMahon, PI) 07/01/99-06/30/00
American Epilepsy Foundation
"Glycine: An important inhibitory neurotransmitter controlling hippocampal excitability."

The major goal of this project is to examine the developmental expression of glycine-gated chloride channels in hippocampus and determine what role these receptors play in controlling hyperexcitability and seizure activity.

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 Vladimir Parpura		POSITION TITLE Assoc Professor	
eRA COMMONS USER NAME vparpura			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of Zagreb, Croatia	M.D.	1989	Medicine
Iowa State University, Ames, IA	Ph.D.	1993	Zoology/Neuroscience
Iowa State University, Ames, IA	Postdoc.	1994	Neuroscience
Mayo Clinic, Rochester, MN	Postdoc.	1996	Physiology & Biophysics

A. Positions and Honors.**Positions:**

- 09/86-12/89 Research assistant in biochemistry. Gangliosides in patients suffering from cancer. Dept. of Chemistry & Biochemistry, University of Zagreb (Drs. I. Kracun and C. Cosovic)
- 09/86-12/89 Research assistant in clinical immunology. *Parietaria officinalis*-induced allergy. Dept. of Physiology & Immunology, Dept. of Internal Medicine, University of Zagreb (Drs. M. Marusic and S. Cvitanovic)
- 01/90-07/90 Research assistant in neurophysiology. Slow excitatory potentials in rat spinal dorsal horn *in vitro*. Dept. of Veterinary Physiology & Pharmacology, Iowa State University, Ames, IA (Dr. M. Randic)
- 08/90-12/93 Research assistant in departmental research. Atomic force microscopy of living cells. Glia-neuron signaling. Dept. of Zoology & Genetics, Iowa State University, Ames, IA (Dr. P.G. Haydon)
- 01/94-11/94 Postdoctoral research associate. Glia-neuron signaling. Dept. of Zoology & Genetics, Iowa State University, Ames, IA (Dr. P.G. Haydon)
- 09-10/94 Visiting postdoctoral research associate. Dept. of Pharmacology and Cell Biology, Yale University Medical School, New Haven, CT (Dr. R Jahn)
- 12/94-11/96 Postdoctoral research fellow. Dept. of Physiology & Biophysics, Mayo Clinic, Rochester, MN (Dr. J.M. Fernandez)
- 01/96- 07/02 Visiting scientist, Cornell Nanofabrication Facility, Knight Laboratory, Cornell University, Ithaca, NY
- 12/96-6/00 Affiliate Assistant Professor. Dept. of Zoology & Genetics, Iowa State University, Ames, IA
- 07/00-6/05 Assistant Professor. Dept. of Cell Biology & Neuroscience, University of California, Riverside, CA
- 07/05-6/07 Associate Professor (with tenure). Dept. of Cell Biology & Neuroscience, University of California, Riverside, CA
- 07/07-present Associate Professor (with tenure). Dept. of Neurobiology, University of Alabama, Birmingham, AL.

Honors:

- 1988 Rector's Award, University of Zagreb
- 1988 Nikola Tesla's Award, Yugoslav Academy of Sciences and Arts
- 1990-1992 Premium for Academic Excellence (PACE) Award, Iowa State University
- 1993 Research Excellence Award, Iowa State University
- 1993 Organizer of the 2nd Annual Neuroscience Meeting at ISU, Iowa State University
- 1995-1996 Research Fellow, Mayo Foundation
- 1998 Short Term Fellowship, Human Frontier Science Program Organization (HFSP), "Dopamine-induced morphological changes of spines and dendrites"
- 2003 Winter Conference on Brain Research Travel Fellow
- 2004 Institute for Complex Adaptive Matter Senior Fellow

B. Selected peer-reviewed publications (in chronological order).

(Publications selected from 56 peer-reviewed journal publications)

1. Parpura, V., Basarsky, T.A., Liu, F., Jeftinija, K., Jeftinija, S., Haydon, P. G. (1994). Glutamate-mediated astrocyte-neuron signalling. *Nature* 369: 744-747.
2. Basarsky, T.A., Parpura, V., Haydon, P. G. (1994). Hippocampal synaptogenesis in cell culture: Developmental time course of synapse formation, calcium influx and synaptic protein distribution. *J. Neurosci.* 14: 6402-6411.
3. Parpura, V., Liu, F., Brethorst, S., Jeftinija, K., Jeftinija, S., Haydon, P.G. (1995). \square -latrotoxin stimulates glutamate release from cortical astrocytes. *FEBS Lett.* 360: 266-270.
4. Parpura, V., Liu, F., Jeftinija, K., Haydon, P.G., Jeftinija, S. (1995). Neuroligand-evoked calcium-dependent release of excitatory amino acids from Schwann cells. *J. Neurosci.* 15: 5831-5839.
5. Tan, W., Parpura, V., Haydon, P.G., Yeung, E.S. (1995). Imaging neurotransmitter in living cells based on native fluorescence detection. *Anal. Chem.* 67: 2575-2579.
6. Parpura, V., Fang, Y., Basarsky, T. A., Jahn, R., Haydon, P.G. (1995). Expression of synaptobrevin II, cellubrevin and syntaxin in cultured astrocytes. *FEBS Lett.* 377:489-492.
7. Parpura, V., Basarsky, T.A., Haydon, P.G. (1996). Astrocyte-neuron signalling. In: Excitatory amino acids and the cerebral cortex (Conti, F., Hicks, T.P., eds). MIT Press/ Bradford Books, Cambridge, MA pp 167-174.
8. Parpura, V., Fernanadez, J.M. (1997). Nanofabricated carbon detector (NACAD). In: Cornell Nanofabrication Facility 1996- 1997 research accomplishments. Cornell University, Ithaca, NY pp 24-25.
9. Araque, A., Parpura, V., Sanzgiri, R.P., Haydon, P.G. (1998). Glutamate-dependent astrocyte modulation of synaptic transmission between cultured hippocampal neurons. *Eur. J. Neurosci.* 10: 2129-2142.
10. Parpura, V., Tong, W., Yeung, E.S., Haydon, P.G. (1998). Laser-Induced Native Fluorescence (LINF) imaging of serotonin depletion in depolarized neurons. *J. Neurosci. Meth.* 82: 151-158.
11. Araque, A., Sanzgiri, R.P., Parpura, V., Haydon, P.G. (1998). Calcium elevation in astrocytes causes an NMDA receptor-dependent increase in the frequency of miniature synaptic currents in cultured hippocampal neurons. *J. Neurosci.* 18: 6822-6829.
12. Parpura, V., Haydon, P.G. (1999). UV photolysis using a micromanipulated optical fiber to deliver UV energy directly to the sample. *J. Neurosci. Meth.* 87: 25-34.
13. Araque, A., Parpura, V., Sanzgiri, R.P., Haydon, P.G. (1999). Tripartite synapses: Glia, the unacknowledged partner. *Trends Neurosci.* 22: 208-215.
14. Trudeau, L-E., Parpura, V., Haydon, P.G. (1999). Activation of neurotransmitter release in hippocampal nerve terminals during recovery from intracellular acidification. *J. Neurophysiol.* 81: 2627-2635.
15. Parpura, V., Haydon, P.G. (1999). "Uncaging" using optical fibers to deliver UV-light directly to the sample. *Croatian Med. J.* 40: 340-345.
16. Araque, A., Sanzgiri, R.P., Parpura, V., Haydon, P.G. (1999). Astrocyte-induced modulation of synaptic transmission. *Can. J. Physiol. Pharmacol.* 77: 699-706.
17. Innocenti, B., Parpura, V., Haydon, P.G. (2000). Imaging extracellular waves of glutamate during calcium signaling in cultured astrocytes. *J. Neurosci.* 20: 1800-1808.
18. Parpura, V., Haydon, P.G. (2000). Physiological astrocytic calcium levels stimulate glutamate release to modulate adjacent neurons. *Proc. Natl. Acad. Sci. USA.* 97: 8629-8634.
19. Parvizi, J., Parpura, V., Greenleaf, J.F., Bolander, M.E. (2002). Calcium signaling is required for ultrasound-stimulated aggrecan synthesis by rat chondrocytes *J. Orthopaedic Res.* 20:51-57.
20. Grima G., Benz B., Parpura V., Cuenod M., Do K.Q. (2003). Dopamine-induced oxidative stress in neurons with glutathione deficit: implication for schizophrenia. *Schizophr Res.* 62:213-24.
21. Liu, W., Montana, V., Chapman, E.R., Mohideen U., Parpura, V. (2003). Botulinum Toxin type B Micromechanosensor, *Proc. Natl. Acad. Sci. USA.* 100: 13621-13625
22. Parpura, V., Scemes, E., Spray, D.C. (2004). Mechanisms of glutamate release from astrocytes: gap junction "hemichannels", purinergic receptors and exocytotic release. *Neurochem Int.* 45:259-264.
23. Hua, X., Malarkey E.B., Sunjara, V., Rosenwald, S.R., Li, W-H., Parpura, V. (2004) Ca^{2+} -dependent glutamate release involves two classes of endoplasmic reticulum Ca^{2+} stores in astrocytes. *J. Neurosci. Res.* 76: 86-97.
24. Montana, V., Ni, Y., Sunjara, V., Hua, X., Parpura, V. (2004) Vesicular glutamate transporter-dependent glutamate release from astrocytes, *J. Neurosci.* 24:2633-2642.
25. Hu, H., Ni, Y., Montana, V., Haddon, R.C., Parpura, V. (2004) Chemically functionalized carbon nanotubes as substrates for neuronal growth. *NanoLett.* 4: 507-511.
26. Parpura, V. (2005). Nanofabricated carbon-based detector. *Anal. Chem.* 77:681-686.

Principal Investigator/Program Director (Last, first, middle): Parpura, Vladimir

27. Bekyarova, E., Ni, Y., Malarkey, E.B., Montana, V., McWilliams, J.L., Haddon, R.C., Parpura, V. (2005). Applications of carbon nanotubes in biotechnology and biomedicine. *J. Biomed. Nanotech.* 1:3-17.
28. Li, Q.-J., Yao, M., Dueck, M., Fuegate, J.E., Parpura V., Martins-Green, M. (2005). cCXCR1 is a receptor for cIL8 (9E3/cCAF) and its N- and C-terminal peptides, and is also activated by hIL8 (CXCL8). *J. Leukoc. Biol.* 77: 421-431.
29. Hu, H., Ni, Y., Mandal, S.K., Montana, V., Zhao, B., Haddon, R.C., Parpura, V. (2005). Polyethyleneimine functionalized single-walled carbon nanotubes as a substrate for neuronal growth. *J. Phys. Chem. B* 109:4285-4289.
30. Ni, Y., Hu, H., Malarkey E.B., Zhao, B., Montana, V., Haddon, R.C., Parpura, V. (2005). Chemically functionalized water soluble single-walled carbon nanotubes modulate neurite outgrowth. *J. Nanosci. Nanotechnol.* 5: 1707-1712.
31. Parpura, V., Chapman, E.R. (2005) Detection of botulinum toxins: micromechanical and fluorescence- based sensors. *Croat. Med. J.* 46:491-497.
32. Ponzio, T.A., Ni, Y., Montana, V., Parpura, V., Hatton, G.I. (2006). Vesicular glutamate transporter expression in supraoptic neurons suggests a glutamatergic phenotype. *J. Neuroendocrinol.* 18:253-265.
33. Liu, W., Montana, V., Bai, J., Chapman, E.R., Mohideen U., Parpura, V. (2006). Single molecule mechanical probing of the SNARE protein interactions. *Biophys J.* 91:744-58.
34. Montana, V., Malarkey E.B., Verderio, C., Matteoli, M. Parpura, V. (2006) Vesicular transmitter release from astrocytes. *Glia* 54:700-715.
35. Ni, Y., Malarkey, E.B., Parpura, V. (2007) Vesicular release of glutamate mediates bidirectional signaling between astrocytes and neurons. *J. Neurochem.* 103: 1273-1284.
36. Malarkey, E.B., Parpura, V. (2008) Mechanisms of glutamate release from astrocytes. *Neurochem. Int.* 52:142-154.
37. Malarkey, E.B., Ni, Y., Parpura, V. (2008) Ca^{2+} entry through TRPC1 channels contributes to intracellular Ca^{2+} dynamics and consequent glutamate release from astrocytes. *Glia* 56: 821-835.
38. Liu, W., Montana, V., Parpura, V., Mohideen, U. (2008). Comparative energy measurements in single molecule interactions. *Biophys. J.* 95: 419-425.
39. Parpura, V., Mohideen, U. (2008). Molecular form follows function: (un)snaring the SNAREs. *Trends Neurosci.* 31: 435-443.
40. Reyes, C.R., Parpura, V. (2008) Mitochondria modulate Ca^{2+} -dependent glutamate release from rat cortical astrocytes. *J. Neurosci.* 28: 9682-9691.

C. Research Support.

Ongoing Research Support

"Calcium-dependent glutamate release from astrocytes"

Period: 06/01/04-05/31/09

Principal Investigator: Vladimir Parpura

Agency: National Institute of Health

Type: R01 MH 069791

The goal of this project is to investigate calcium-dependent glutamate release from astrocytes

Role: Principal Investigator

Completed Research Support

"A highly sensitive microcantilever-based immunosensor array"

Period: 10/01/06-9/30/09

Principal Investigator: Ashok Mulchandani

Agency: National Science Foundation

Type: BES-0617240

The major goal of this project is to build an immunosensor array

Role: co-Principal Investigator; completed as a co-PD on Sep 15, 2007 since it is linked to the UCR

"Polyamine signaling via glial connexin-43 hemichannels in retina

Period: 08/01/06-07/31/07

Principal Investigator: Yurii Kucheryavykh

Agency: The Puerto Rico Alliance for the Advancement of Biomedical Research Excellence

Type: RG

The major goal of this project is to study hemichannels in retina

Role: Collaborator

"Research Experiences for Undergraduates (REU) site:

Period: 04/01/06-3/31/09

Education and greater diversity through research in nanomaterials and nanodevices"

Principal Directors: Alexander Balandin and Vladimir Parpura

Agency: National Science Foundation

Type: EEC 0552562

The major goals of this project is to develop a program for undergraduate research in nanotechnology.

Role: co-Principal Director; completed a two-year term a co-PD on Aug 17, 2007 since it is linked to the UCR

"Center for Nanoscale Innovations in Defense"

Period: 7/26/02-9/30/07

Principal Investigator: Robert C. Haddon

Type: DOD/DMEA/DARPA ; DMEA90-02-2-216

The goal of this project is to establish a center.

Role: co-Investigator

"Modulation of calcium-dependent glutamate release from astrocytes"

Principal Investigator: Vladimir Parpura

Agency: Whitehall Foundation

Type: Research Grant #2000-05-17

Period: 5/1/00-5/31/04

The goal of this project is to investigate modulation of calcium-dependent glutamate release from astrocytes.

Role: Principal Investigator

"Nanofabricated Carbon Detector"

Principal Investigators: Julio M. Fernandez and Vladimir Parpura

Agency: National Nanofabrication Facility at Cornell/ NSF ECS-9319005

Type: Research project # 577-96

Period: 1/1/96-7/1/02

The goal of this project is to nanofabricate a carbon detector whose properties allow studies of individual synaptic vesicles.

Role: Principal Investigator

"Imaging secretion: UV-based Microscopy and Photolysis"

Principal Investigator: Philip G. Haydon

Agency: Iowa State University

Type: Biotechnology Competitive Grants Program

Period: 7/1/97-6/30/99

The goal of this interdisciplinary project was to develop a microscope that non-invasively detects the spatio-temporal release of chemical transmitter between individual neurons.

Role: co- Principal Investigator

"Astrocyte-neuron signaling"

Principal Investigator: Philip G. Haydon

Agency: NIH

Type: R01 (NS37585)

Period: 4/1/98-6/30/00

The goal of this project is to test the hypothesis that astrocytes modulate synaptic transmission.

Role: co- Principal Investigator

"Mechanism of calcium-dependent glutamate release from astrocytes"

Principal Investigator: Vladimir Parpura

Agency: Whitehall Foundation

Type: Grand-in-Aid #AA9838

Period: 6/1/98-6/30/00

The goal of this project is to elucidate the mechanism for calcium-dependent release from astrocytes.

Role: Principal Investigator

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 Lucas D. Pozzo-Miller		POSITION TITLE Associate Professor	
eRA COMMONS USER NAME pozzomiller			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Córdoba National University, Argentina	M.Sc.	1981-1986	Biology
Córdoba National University, Argentina	Ph.D.	1986-1989	Neurobiology
Case Western Reserve University, Cleveland, OH	Postdoc	1990-1992	Neurocytology
Roche Institute of Molecular Biology, Nutley, NJ	Postdoc	1992-1995	Neurophysiology / Imaging

A. POSITIONS AND HONORS

- 1995-1998 Senior Staff Fellow (Research-Track Assistant Professor equivalent). Laboratory of Neurobiology (Dr. Thomas S. Reese, Lab Chief), NINDS, National Institutes of Health (NIH), Bethesda, MD.
- 1998-2006 Assistant Professor. Department of Neurobiology, University of Alabama at Birmingham (UAB), Birmingham, AL.
- 2005-present Scientist, Vision Science Research Center, UAB.
- 2006-present Scientist, Civitan International Research Center, UAB.
- 2006-present Scientist, Center for Glial Biology in Medicine, UAB.
- 2006-present Member, Comprehensive Neuroscience Center, UAB.
- 2006-present Associate Professor (with tenure). Department of Neurobiology, UAB.

Awards and Other Professional Activities

- 1986 Predoctoral Fellowship of the National Council for Scientific Research (CONICET), Argentina.
- 1992 Postdoctoral Fellowship at the Roche Institute of Molecular Biology, Hoffman La Roche Inc., Nutley, NJ. Dr. John A. Connor, Mentor.
- 1994 The Grass Foundation Fellowship in Neurophysiology at the Marine Biological Laboratory, Woods Hole, MA. Dr. Rodolfo R. Llinás, Mentor.
- 1995 The Lakian Foundation Fellowship at the Marine Biological Laboratory, Woods Hole, MA.
- 1996 EMBO Fellowship.
- 1999 NIH Fellows Award for Research Excellence.
- 1999 Invited Speaker at the *Journal of Physiology* Symposium on "Neuronal Channels, Receptors and Compartmentalization: Signaling", Miami, FL.
- 2001-2006 Permanent Member of NIH MNPS Study Section (former MDCN-5).
- 2002 Ad-hoc Member of NIH NSD-C Study Section.

- 2002 Co-Organizer and Speaker at "Neurotrophin Regulation of Synaptic Transmission" Symposium, 3rd Forum of the Federation of European Neuroscience Societies, Paris, France.
- 2003 Session Chair at the Society for Neuroscience Annual Meeting, New Orleans, LA.
- 2004 Invited Speaker at the Gordon Conference on "Synaptic Transmission", Meriden, NH.
- 2005 Elected Member of the UAB Faculty Senate.
- 2005 McNulty Civitan Scientist Award, Civitan International Foundation.

B. Selected Peer-Reviewed Publications (out of a total of 40)

- Pozzo Miller LD, JJ Petrozzino & JA Connor (1995). G protein-coupled receptors mediate a fast excitatory postsynaptic current in CA3 pyramidal neurons in hippocampal slices. *J Neurosci* 15: 8320-8330.
- Petrozzino JJ, LD Pozzo Miller & JA Connor (1995). Micromolar Ca^{2+} transients in dendritic spines of hippocampal pyramidal neurons in brain slice. *Neuron* 14: 1223-1231.
- Pozzo Miller LD, JJ Petrozzino, G Golarai & JA Connor (1996). Ca^{2+} release from intracellular stores induced by afferent stimulation of CA3 pyramidal neurons in hippocampal slices. *J Neurophysiol* 76: 554-562.
- Figurov A, LD Pozzo-Miller, P Olafsson, T Wang & B Lu (1996). Regulation of synaptic responses to high-frequency stimulation and LTP by neurotrophins in the hippocampus. *Nature* 381: 706-709.
- Pozzo-Miller LD, N Pivovarova, RD Leapman, RA Buchanan, TS Reese & SB Andrews (1997). Activity-dependent calcium sequestration in dendrites of hippocampal neurons in brain slices. *J Neurosci* 17: 8729-8738.
- Gottschalk W, LD Pozzo-Miller, A Figurov & B Lu (1998). Presynaptic modulation of synaptic transmission and plasticity by BDNF in developing hippocampus. *J Neurosci* 18: 6830-6839.
- Pozzo-Miller LD, JE Moreira & RR Llinás (1998). The first-order giant neurons of the giant fiber system in the squid: electrophysiological and ultrastructural observations. *J Neurocytol* 27: 419-429. (Cover).
- Pozzo-Miller LD, T Inoue & D DiEuliis Murphy (1999). Estradiol increases spine density and NMDA-dependent Ca^{2+} transients in spines of CA1 pyramidal neurons from hippocampal slices. *J Neurophysiol* 81: 1409-1411.
- Pozzo-Miller LD, W Gottschalk, L Zhang, K McDermott, J Du, R Gopalakrishnan, C Oho, ZH Sheng & B Lu (1999). Impairments in high-frequency transmission, synaptic vesicle docking, and synaptic protein distribution in the hippocampus of BDNF knockout mice. *J Neurosci* 19: 4972-4983.
- Pozzo-Miller LD, JA Connor & SB Andrews (2000). Microheterogeneity of calcium signaling in dendrites. *J Physiol (Lond)* 525: 53-61.
- Tyler WJ & LD Pozzo-Miller (2001). BDNF enhances quantal neurotransmitter release and increases the number of docked vesicles at the active zones of hippocampal excitatory synapses. *J Neurosci* 21: 4249-4258.
- Dosemeci A, J-H Tao-Cheng, L Vinade, LD Pozzo-Miller & TS Reese (2001). Glutamate-induced transient modification of the postsynaptic density. *Proc Natl Acad Sci USA* 98: 10428-10432.
- Tartaglia N, J Du, WJ Tyler, E Neale, LD Pozzo-Miller & B Lu (2001). Protein synthesis dependent and independent regulation of hippocampal synapses by brain-derived neurotrophic factor. *J Biol Chem* 276: 37585-37593.

- McCutchen ME, C Bramham & **LD Pozzo-Miller** (2002). Modulation of neuronal Ca^{2+} signaling by neurotrophic factors. *Int J Dev Neurosci* 20: 199-207.
- Tyler WJ, S Perrett & **LD Pozzo-Miller** (2002). The role of neurotrophins in neurotransmitter release. *Neuroscientist* 8: 524-531.
- Tao-Cheng J-H, L Vinade, **LD Pozzo-Miller**, TS Reese & A Dosemeci (2002). Calcium/calmodulin-dependent protein kinase II clusters in adult rat hippocampal slices. *Neuroscience* 115: 435-440.
- Tyler WJ, MA Alonso, CR Bramham & **LD Pozzo-Miller** (2002). From acquisition to consolidation: On the role of brain-derived neurotrophic factor signaling in hippocampal-dependent learning. *Learn Mem* 9: 224-237. (Cover).
- Pivovarov NB, **LD Pozzo-Miller**, J Hongpaisan & SB Andrews (2002). Correlated calcium uptake and release by mitochondria and endoplasmic reticulum of CA3 hippocampal dendrites after afferent synaptic stimulation. *J Neurosci* 22: 10653-10661.
- Tyler WJ & **L Pozzo-Miller** (2003). BDNF and miniature synaptic transmission modulate dendritic spine growth and form in hippocampal CA1 pyramidal neurons. *J Physiol (Lond)* 553: 497-509.
- Alonso M, J Medina & **L Pozzo-Miller** (2004). ERK1/2 activation is necessary for BDNF to increase dendritic spine density in hippocampal CA1 pyramidal neurons. *Learn Mem* 11: 172-178. (Cover).
- Amaral MD & **L Pozzo-Miller** (2005). On the role of neurotrophins in dendritic calcium signaling: implications for hippocampal transsynaptic plasticity. In: *Synaptic Plasticity and Transsynaptic Signaling*, Stanton PK, Bramham CR, and Scharfman HE (Eds.), pp 185-200. New York: Springer Science and Business Media.
- Kushner SA, Y Elgersma, GC Murphy, D Jaarsma, GM van Woerden, MR Hojjati, Y Cui, JC LeBoutillier, DF Marrone, ES Choi, CI De Zeeuw, TL Petit, **L Pozzo-Miller** & AJ Silva (2005). Modulation of presynaptic plasticity and learning by the H-ras/ERK/synapsin I signaling pathway. *J Neurosci* 25: 9721-9734.
- Pozzo-Miller L** (2006). BDNF enhances dendritic Ca^{2+} signals evoked by coincident EPSPs and back-propagating action potentials in CA1 pyramidal neurons. *Brain Res* 1104: 45-54.
- Tyler WJ, X-L Zhang, K Hartman, J Winterer, W Müller, PK Stanton & **L Pozzo-Miller** (2006). BDNF increases release probability and the size of a rapidly recycling vesicle pool within hippocampal excitatory synapses. *J Physiol (Lond)* 574: 787-803.
- Amaral MD, CA Chapleau & **L Pozzo-Miller** (2007). Transient receptor potential channels as novel effectors of brain-derived neurotrophic factor signaling: Potential implications for Rett syndrome. *Pharmacol Ther* 113: 394-409.
- Chapleau CA & **L Pozzo-Miller** (2007). Activity-dependent structural plasticity of dendritic spines. In: *Learning and Memory: a Comprehensive Reference*, Byrne J (Ed.). Oxford, Elsevier.
- Amaral MD & **L Pozzo-Miller** (2007). TRPC3 channels are necessary for BDNF to activate a non-selective cationic current and to induce dendritic spine formation. *J Neurosci* (in press).

C. Research Support

Active

2 RO1 NS40593-06 (PI: Pozzo-Miller)

Actions of BDNF on Ca^{2+} Signals in Hippocampal Neurons

NIH, NINDS

Dates: 07/01/06 – 06/30/11

BDNF has recently emerged as a potent modulator of activity-dependent synaptic development and plasticity in the CNS. Dysfunctions in BDNF trafficking and release, as well as in intracellular signaling through its receptor TrkB, have been implicated in the etiology of numerous developmental and neurodegenerative brain disorders. The specific hypothesis to be tested is that BDNF triggers TrkB-dependent PLC γ activation followed by Ca²⁺ mobilization from IP3-sensitive stores in CA1 pyramidal neurons, leading to the activation of capacitative Ca²⁺ entry and a sustained inward current mediated by TRPC channels. We expect the proposed studies to provide the most comprehensive understating to date of the immediate actions of BDNF on neuronal membrane currents and Ca²⁺ homeostasis, leading to enduring changes in synaptic function, structure, and plasticity.

1 R21 NS057780-01 (PI: Pozzo-Miller)

Role of BDNF in Dendritic Pathologies Caused by Rett-Associated MeCP2 Mutations
NIH, NINDS

Expected Dates: 04/01/07 – 03/31/09

Considering that BDNF has recently emerged as a potent modulator of activity-dependent synaptic development and plasticity in the postnatal brain, including fundamental neuronal properties such as dendritic spine density and form and neuronal Ca²⁺ signaling, we hypothesize that a deregulation of BDNF signaling may underlie the dendritic pathologies observed in RTT. The specific hypothesis to be tested is twofold: 1) RTT-associated MECP2 mutations cause dendritic spine loss leading to impaired dendritic Ca²⁺ signaling in hippocampal pyramidal neurons through reduced BDNF signaling; 2) impaired dendritic structure in MECP2 mutant neurons can be reverted by BDNF treatment. The consequences of mutant MECP2 expression will be evaluated in neurons maintained in organotypic slice cultures and transfected by particle-mediated gene-transfer.

P30-HD38985 (PI: Percy)

UAB Mental Retardation Research Center (MRRC)
NIH, NICHD

Dates: 07/01/06 – 06/30/08

Project: Developmental Neurobiology Tissue Processing and Imaging Core C (Co-Directors: Pozzo-Miller and Sontheimer)

The objective of the Developmental Neurobiology Tissue Processing and Imaging Core is to provide state-of-the-art equipment and technical support for several experimental projects across the UAB campus related to mental retardation and the Mental Retardation Research Clinic Community mission statement. It provides state-of-the-art equipment unlikely to be acquired by any single investigator's research program, as well as highly trained staff for its maintenance. The shared use of the Core provides synergistic support to several projects within the MRRC community including: advances and improvements of common methodological and conceptual strategies, access to regular and reliable analytical methods for live cell imaging, quantitative image processing, and additional collaborations between the individual projects. The Core also provides simultaneous whole-cell recording and imaging of intracellular ion concentrations, presynaptic vesicle release and recycling, or morphological changes from single cells in culture or brain slices at sub-micrometer spatial and millisecond temporal resolution. Investigators can do high-resolution laser scanning and live imaging for long-term morphological studies of synapse formation, as well as time-lapse developmental studies of dendritic spines, dendritic arborizations, axonal projections, or astrocytic processes.

1 P30 NS057098 (PI: Roth)
Alabama Neuroscience Blueprint Core Center
 NIH

Dates: 10/01/07 – 09/30/12

Project: Neuroimaging Core D (Co-Directors: Keyser, Pozzo-Miller, Zinn)

This application proposes to establish the "Alabama Neuroscience Blueprint Core Center" at the University of Alabama at Birmingham, providing new interdisciplinary research core services to Neuroscience Blueprint Institute and Center funded investigators at UAB and participating institutions including Auburn University, University of South Alabama, Southern Research Institute, Tulane University, and Louisiana State University. The major mission of this Center is to provide neuroscientists access to the broad array of tools and expertise required to generate and characterize novel genetically modified small animal models of neurological and psychiatric function and dysfunction.

PENDING

COMPLETED

P01 HD38760 (PI: Friedlander)

Modulation of Glutamate Synapses in Neonatal Cortex

NIH, NICHD

Dates: 06/01/00 – 05/31/06

Project: Developmental Neurobiology Imaging Core B (Co-Directors: Pozzo-Miller and Friedlander)

The objective of the Developmental Neurobiology Imaging Core B was to provide state-of-the-art equipment and technical support to perform light and electron microscopical observations in experimental projects on the assembly and modulation of synaptic structure and function in the cerebral cortex. The Developmental Neurobiology Imaging Core will provide standardized processing of cells and tissues, using techniques that are common to each of the 5 projects in the Program Project. Thus, each PI and the Core Director will not have to duplicate in their respective laboratories the technicians and equipment necessary for these applications.

NMSS-PP0896 (PI: Barnum; co-PI: Pozzo-Miller)

Complement Anaphylatoxin Modulation of Ca^{2+} Signaling and Neuronal Excitability

National Multiple Sclerosis Society

Dates: 11/01/02 – 10/31/03

The aim of this pilot project was to examine the mechanisms underlying the ability of complement anaphylatoxins to modulate Ca^{2+} signaling and membrane depolarization in neurons.

NIH-NINDS Z01 (PI: Pozzo-Miller)

Calcium Signaling in Dendritic Spines of Hippocampal Neurons

Intramural Program, Laboratory of Neurobiology, NINDS (Thomas S. Reese, Lab Chief).

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 Anne B. Theibert		POSITION TITLE	
eRA COMMONS USER NAME Anne Theibert		Associate Professor	
EDUCATION/TRAINING			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Goucher College, Baltimore, MD	BA	1979	Chemistry
Johns Hopkins University, Baltimore, MD	PhD	1985	Biochemistry
Johns Hopkins University, Baltimore, MD	Postdoc	1987	Biochemistry
Johns Hopkins University, Baltimore, MD	Postdoc	1991	Neuroscience

A. POSITIONS AND HONORS

1991-1996 Assistant Professor (Primary) of Cell Biology, University of Alabama at Birmingham
 1996-2000 Assistant Professor (Primary) of Neurobiology, University of Alabama at Birmingham
 2000-present Associate Professor (Primary) of Neurobiology, University of Alabama at Birmingham

Awards and Other Professional Activities

1976 Dean's Scholar Goucher College
 1984 Young Investigators Pre-doctoral Award: Johns Hopkins University School of Medicine
 1989-1990 NIDA Postdoctoral Fellowship Johns Hopkins University
 1998 Rolex Achievement Award
 2001-2006 NIH ZRG1 FO3B MDCN Study Section
 2005-2007 AHA National Center Basic Cell & Molecular Biology 3 Study Section Co-chair

B. Selected Publications (Out of a total of 45)

Theibert, A. and P. Devreotes. Guanine nucleotides are required for activation of adenylate cyclase in *Dictyostelium*. *J. Biol. Chem.*, 261:14121-14125, 1987.
 Devreotes, P., D. Fontana, P. Klein, J. Sherring, and A. **Theibert**. Transmembrane signaling in *Dictyostelium*. *Meth. Cell Biol.*, 1,28:299-331, 1987.
Theibert A., S. Supattapone, P. Worley, J. Baraban, J. Meek, and S. Snyder. Demonstration of Inositol 1,3,4,5 tetrakisphosphate receptor binding. *Biochem. and Biophys. Res. Comm.*, 148:1283-1289, 1987.
 Supattapone, S., S. Danoff, A. **Theibert**, S. Joseph, J. Steiner and S. Snyder. Cyclic AMP dependent phosphorylation of a brain inositol trisphosphate receptor decreases its release of calcium. *Proc. Natl. Acad. Sci.*, 85:8747-8750, 1988.
 Snyder, S., C. Ferris and A. **Theibert**. Second messenger receptors in the PI cycle. In: *Proceedings of the Biology of Cellular Transducing Signals*. Plenum Press, New York, ed. Jack Vanderhoek, 1989.
Theibert, A., S. Supattapone, C. Ferris, S. Danoff, R. Evans and S. Snyder. Solubilization and separation of inositol 1,3,4,5-tetrakisphosphate and inositol 1,4,5-trisphosphate binding proteins and metabolizing enzymes in rat brain. *Biochem. J.* 267:441-445, 1990.
Theibert, A., V. Estevez, C. Ferris, S. Danoff, R. Barrow, G. Prestwich and S. Snyder. Inositol 1,3,4,5-tetrakisphosphate and inositol hexakisphosphate receptor proteins: Isolation and characterization from rat brain. *Proc. Natl. Acad. Sci., USA*, 88:3165-3169, 1991.
Theibert, A. and S. Snyder. [³H]Inositol 1,3,4,5-tetrakisphosphate and hexakisphosphate employed to isolate and characterize IP₄ and IP₆ receptor proteins. *NEN/Dupont Biotech Update Newsletter*, 55-57, 1991.
Theibert, A.B., V.A. Estevez, R.J. Mourey, J.F. Marecek, R.K. Barrow, G.D. Prestwich, and S.H. Snyder. Photoaffinity labeling and characterization of isolated inositol 1,3,4,5-tetrakisphosphate and inositol hexakisphosphate-binding proteins, *J. Biol. Chem.*, 267:9071-9079, 1992.
 Voglmaier, S.M., J.H. Keen, J. Murphy, C.D. Ferris, G.D. Prestwich, S.H. Snyder, and A.B. **Theibert**. IP₆ receptor protein identified as the clathrin AP-2, *Biochem. Biophys. Res. Comm.*, 187:158-163, 1992.

Principal Investigator/Program Director (Last, First, Middle):

- Jackson, T.R., I.J. Blader, L.P. Hammonds-Odie, C.R. Burga, F. Cooke, P.T. Hawkins, A.G. Wolf, K.A. Heldman, and A.B. **Theibert**. Initiation and maintenance of NGF-stimulated neurite outgrowth requires activation of a phosphoinositide 3-kinase, *J. Cell Science*, 109:289-300, 1996.
- Hammonds-Odie, L.P., T.J. Jackson, I. Blader, A. Profit, C. Turk, G.D. Prestwich and A.B. **Theibert**. Identification and cloning of centaurin α : a novel PI(3,4,5)P₃ binding protein from rat brain. *J. Biol. Chem.* 271:18859-18868, 1996.
- Theibert**, A., Prestwich, G. and Hammonds-Odie, L. The purification and assay of inositol polyphosphate binding proteins. In: *Signaling by Inositol Lipids and Inositol Phosphates*. Ed. Steve Shears, Oxford University Press (UK) 1997.
- Oh, E.-S., A. Woods, S.-T. Lim, A.B. **Theibert**, and J. Couchman. Syndecan-4 proteoglycan cytoplasmic domain and PI(4,5)P₂ coordinately regulate protein kinase C. *J. Biol. Chem.* 273:10624-10629, 1998.
- Greenwood, J.A., M.A. Pallero, A.B. **Theibert**, and J.E. Murphy-Ullrich. Thrombospondin signaling of focal adhesion disassembly is mediated by phosphoinositide 3-Kinase. *J. Biol. Chem.* 273(3):1755-63, 1998.
- Kearns, M., D. Monks, M. Fang, M. Rivas, P. Courtney, G. Prestwich, A. **Theibert**, R. Dewey, and V. Bankaitis. Novel developmentally regulated PI binding proteins from soybean whose expression bypasses the requirement for an essential PI transfer protein in yeast. *EMBO Jour.* 17:4004-4017, 1998.
- Sims, B., R.E. Powers, R. Sabina, and A.B. **Theibert**. Elevated AMP deaminase activity in Alzheimer's disease brain. *Neurobiol. Aging* 19:385-391, 1998.
- Zachor, D.A., J.F. Moore, A.B. **Theibert** and A. Percy. Cocaine inhibited neuronal differentiation in NGF-induced PC12 cells and altered c-fos expression are reversed by c-fos antisense oligonucleotides. *Proc. New York Acad. Sci.*, 846:427-430, 1998.
- Blader, I.J., J.T.V. Cope, T. Jackson, A. Profit, A. Greenwood, D. Drubin, G. Prestwich, and A.B. **Theibert**. GCS1, an Arf GAP in *Saccharomyces cerevisiae*, is required for normal actin cytoskeletal organization *in vivo* and stimulates actin polymerization *in vitro*. *Mol. Biol. Cell*, 16:581-596, 1999.
- Sims, B., D. Mahnke-Zizelman, G. Prestwich, R. Sabina, and A.B. **Theibert**. Regulation of AMP deaminase by phosphoinositides. *J. Biol. Chem.* 274:25701-25707, 1999.
- Greenwood, J., A. **Theibert**, G. Prestwich, and J. Murphy-Ullrich. Restructuring of focal adhesion plaques by PI 3-kinase: regulation by PtdIns(3,4,5)P₃ binding to actinin. *J. Cell Biol.* 150: 627-642, 2000.
- Zachor, D.A., J.F. Moore, M.S. Brezaussek, A.B. **Theibert**, and A.K. Percy. Cocaine inhibits NGF-induced PC12 differentiation through D₁-type dopamine receptors. *Brain Res.* 869:1-2:85-97, 2000.
- Zachor, D., J. Moore, M. Brezaussek, A. **Theibert**, and A. Percy. Cocaine inhibition of neuronal differentiation in NGF-induced PC12 cells is independent of Ras signaling. *Int. J. Dev. Neurosci.*, 18:765-772, 2000.
- Jackson, T.R., B.G. Kearns, and A.B. **Theibert**. Centaurins and cytohesins: mediators of PI 3-kinase regulated Arf signaling. *Trends Biochem. Sci.* 25: 489-495, 2000.
- Randazzo P.A., K. Miura, Z. Nie, A. Orr, A.B. **Theibert**, and B.G. Kearns. Cytohesins and centaurins: mediators of PI 3-kinase regulated Arf signaling. *Trends Biochem. Sci.* 26:220-1, 2001.
- Dubois T. P. Kerai, E. Zemlickova, S. Howell, T. Jackson, K. Venkateswarlu, P. Cullen, A. **Theibert**, L. Larose, P. Roach, and A. Aitken. Casein kinase I associates with members of the centaurin-alpha family of phosphatidylinositol 3,4,5-trisphosphate-binding proteins. *J. Biol. Chem.* 276:18757-18764, 2001.
- Rodgers, E., and A. **Theibert**. Functions of PI 3-kinase in development of the nervous system. *Int. J. Dev. Neurosci.* 20:187-193, 2002.
- Couchman, J.R., S. Vogt, S.-T. Lim, E.-S. Oh, G. Prestwich, A. **Theibert**, W. Lee and A. Woods. Regulation of inositol phospholipid binding and signaling through syndecan-4. *J. Biol. Chem.* 277: 49296-303. 2002
- Thacker, E., B. Kearns, C. Chapman, J. Hammond, A. Howell, and A. **Theibert**. The Arf6 GAP centaurin a-1 is a neuronal actin binding protein which also functions via GAP independent activity to regulate the actin cytoskeleton. *Eur. J. Cell Biol.* 10:541-555, 2004.
- Moore, C., E. Rodgers, J. Larimore, D. Gaston, A. Underwood, B. Kearns, S. Patterson, T. Jackson, Chapleau, L. Pozzoz-Miller and A. **Theibert**. Centaurin a-1, a neuronal Arf GAP, modulates dendritic differentiation. *J. Cell Sci.*, 120:2683-93, 2007.
- Kahn, R.A., E. Bruford, H. Inoue, J. Logsdon Jr, S. Nie, R. Premont, P. Randazzo, M. Satake, A. **Theibert**, M. Zapp and D. Cassel. Consensus nomenclature for the human ArfGAP domain-containing proteins. *J. Cell Biol.* 182:1039-44, 2008.

C. Research Support

Current Research Support

Title: PI 3-Kinase Pathway in Dendritic Spine and Synapse Morphogenesis in Developing and Aging Rat Hippocampus

Principal Investigator: Anne Theibert, Ph.D.

Agency: Intramural Evelyn F. McKnight Brain Institute

Type: Pilot Research Grant Period 3/01/07-2/28/08

Goal: The research in this project will use viral vectors to manipulate expression of PI 3-kinase and its downstream targets in the developing and aging rat brain to investigate their function in regulation of dendritic and spine morphogenesis.

Title: UAB Mental Retardation Research Center

Co-Principal Investigators: Alan Percy, M.D. / Harald Sontheimer, Ph.D.

Core B Co-Director Anne B. Theibert, Ph.D.

Agency: NIH/NICHD

Type: P30 Period 9/1/08-8/30/13

Goals: The MRRC's mission is to increase scientific knowledge about developmental neurobiology and factors that affect CNS development; to develop preventive interventions for mental retardation and developmental disabilities (MR/DD) and to advance understanding about effective treatment strategies to ameliorate the personal, familial, and societal consequences of MR/DD. Core B provides technical expertise, support and resources in the construction of molecular probes and neuronal culture for studies by faculty and fellows.

Pending Research Support

Title: PI 3-Kinase Targets in Autism

Principal investigator: Anne Theibert, Ph.D.

Agency NIH

Type: R21 Period 6/01/07-5/30/09

Goals: The goal of this proposal is to investigate the role of the autism susceptibility gene centaurin gamma-2 in neuronal development using expression in hippocampal neurons and slices by transfection of mammalian expression vectors.

Completed Research Support

Title: Characterization of Inositol Polyphosphate Receptors

Principal Investigator: Anne Theibert, Ph.D.

Agency: NIH NIMH

Type: R01 MH 50102 Period: 7/1/93-4/30/06

Goals: This proposal is to identify and investigate the functional activity of inositol polyphosphate receptor binding proteins in the mammalian central nervous system.

Title: Function of the Autism Susceptibility Gene, Centaurin Gamma-2, in Neuronal Development

Agency: Civitan International – Chesapeake Foundation

Principal Investigator: Anne Theibert, Ph.D./ Trainee: Jennifer Larimore

Type: Emerging Scholars Award Period: 10/1/2005-9/30/2006

Goals: The overall goals of this project are to determine the developmental, regional, and subcellular expression of centaurin gamma-2 in mammalian brain and to investigate the role of centaurin

Theibert, Anne B.

Principal Investigator/Program Director (Last, First, Middle):

gamma-2 in developing neurons. Information generated by this project will be key to identify which neuronal populations express centaurin gamma-2 and thus may be affected in or contribute to autism.

Title: Centaurin Alpha Function in PI 3-Kinase Signaling in Brain

Agency: NIH NINDS

Principal Investigator: Anne Theibert, Ph.D./ Trainee: Brian G. Kearns, Ph.D.

Type: F32NS10678-02 Period: 3/1/1999-2/28/2001

Goals: The overall goals of this project are to further our understanding of the inositide signaling cascade in the brain. To accomplish these goals we have devised a strategy to investigate candidate receptors of the products of PI 3-kinase. This proposal is designed to examine the roles that centaurin plays in neuronal signaling and how these roles are related to the phosphoinositide and actin binding properties of this protein.

Title: Developmental Disabilities Prevention Research Center, Project IV: Excitotoxic Mechanisms in Developing Rat Neocortex

Principal Investigator: Sharon Ramey, Ph.D., PI, John J. Hablitz, Ph.D., Project IV Leader

Agency: NIH/NICHD

Type: P50 HD 32901 Period: 09/30/94-07/31/99

Goals: The major goal of this project is to investigate mechanisms of glutamate neurotoxicity in the developing rat neocortex and to better understand the developmental regulation of calcium transport mechanisms.

ASSISTANT PROFESSORS

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 David C. Knight	POSITION TITLE Assistant Professor		
eRA COMMONS USER NAME knightdav			
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
Truman State University, Kirksville MO	BS	5/94	Psychology
University of Wisconsin, Milwaukee WI	MS	5/99	Clinical Psychology
West Virginia University, Morgantown WV	Intern	7/01-7/02	Neuropsychology
University of Wisconsin, Milwaukee WI	PhD	8/02	Clinical & Neuroscience
National Institute of Mental Health, Bethesda MD		9/02-8/07	Cognitive Neuroscience

A. Positions and Honors.

Positions and Employment

1990-1994	Research Assistant, Psychophysiology Laboratory, Psychology Department, Truman State University.
1994-1995	Mental health support worker, Ozark Center, Joplin, Missouri.
1995-2001	Graduate Research, NMR Research Center, Medical College of Wisconsin & Psychology Department, University of Wisconsin-Milwaukee.
1995-1996	Teaching Assistant, Department of Psychology, University of Wisconsin-Milwaukee.
1998-2001	NRSA Predoctoral Fellow (NIMH), Department of Psychology, University of Wisconsin-Milwaukee.
2001-2002	Clinical Neuropsychology Intern, Department of Behavioral Sciences, West Virginia University Medical School, Morgantown, WV.
2002-2007	NIH Postdoctoral IRTA Fellow, Laboratory of Brain & Cognition, National Institute of Mental Health, Bethesda, MD.
2007-present	Assistant Professor, Departments of Psychology and Neurobiology, University of Alabama at Birmingham

Honors and Awards

1992	All American Scholar
1992, 93, 94	Edward D. Blanchard Award
1992, 1996	Association of Applied Psychophysiology and Biofeedback Outstanding Poster Award
1993	Psi Chi Honor Society
1997	Phi Kappa Phi Honor Society
1998	Sigma Xi Grant in Aid of Research
2000	Fazio Research Award
1998-2001	NIMH (MH11722), Predoctoral National Research Service Award
2004-2006	NIMH Seymour S. Kety Memorial Fellowship

Professional Societies

1990-1996	Association of Applied Psychophysiology and Biofeedback
1995-Present	Society for Neuroscience
1996-Present	Organization for Human Brain Mapping
2000-Present	American Psychological Association
2004-Present	Cognitive Neuroscience Society
2004-Present	Pavlovian Society

B. Peer-reviewed publications (in chronological order).

5.48

- Knight, D. C., Smith, C. N., Stein, E. A., & Helmstetter, F. J. (1999). Functional MRI of human Pavlovian fear conditioning: Patterns of activation as a function of learning. NeuroReport, 10 (17), 3665-3670.
- Cheng, D. T., Knight, D. C., Smith, C. N., Stein, E. A., & Helmstetter, F. J. (2003). Functional MRI of human amygdala activity during Pavlovian fear conditioning: Stimulus processing versus response expression. Behavioral Neuroscience, 117 (1), 3-10.
- Knight, D. C., Nguyen, H. T., & Bandettini, P. A. (2003). Expression of conditional fear with and without awareness. Proceedings of the National Academy of Sciences, 100 (25), 15280-15283.
- Knight, D. C., Cheng, D. T., Smith, C. N., Stein, E. A., & Helmstetter, F. J. (2004). Neural substrates mediating human delay and trace fear conditioning. Journal of Neuroscience, 24 (1), 218-228.
- Knight, D. C., Smith, C. N., Cheng, D. T., Stein, E. A., & Helmstetter, F. J. (2004). Amygdala and hippocampal activity during acquisition and extinction of human fear conditioning. Cognitive, Affective, and Behavioral Neuroscience, 4 (3), 317-325.
- Haut, M., Kuwabara, H., Leach, S., Moran, M., Arias, R., Knight, D. (2005). The effect of education on age-related functional activation during working memory. Aging, Neuropsychology, and Cognition, 12, 216-229.
- Knight, D. C., Nguyen, H. T., & Bandettini, P. A. (2005). The role of the human amygdala in the production of conditioned fear responses. NeuroImage, 26, 1193-1200.
- Knight, D. C., Nguyen, H. T., & Bandettini, P. A. (2006). The role of awareness in delay and trace fear conditioning in humans. Cognitive, Affective, and Behavioral Neuroscience, 5 (2), 157-162.
- Cheng, D. T., Knight, D. C., Smith, C. N., Stein, E. A., & Helmstetter, F. J. (2006). Human amygdala activity during the expression of fear responses. Behavioral Neuroscience, 120 (6), 1187-1195.
- Dunsmoor, J. E., Bandettini, P. A., & Knight, D. C. (2007). Impact of continuous versus intermittent CS-UCS pairing on human brain activation. Behavioral Neuroscience, 121 (4), 635-642.
- Dunsmoor, J. E., Bandettini, P. A., & Knight, D. C. (2008). Neural substrates of UCR diminution during Pavlovian conditioning. NeuroImage, 40, 811-817.
- Knight, D. C., Waters, N. S., & Bandettini, P. A. (In Press). Neural substrates of explicit and implicit fear memory. NeuroImage.

C. Research Support

Completed Research Support

F31 (MH11722)

1/1/98 - 12/31/00

Predocorial National Research Service Award
NIH/NIMH

Functional Neuroanatomy of Conditional Fear

The goal of this project was to investigate the neural substrates in the human brain that subserve aversive emotional states.

Role: Co-Investigator

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 Linda Overstreet-Wadiche		POSITION TITLE Assistant Professor	
eRA COMMONS USER NAME WadicheL			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
North Park University, Chicago, IL	B.S.	1992	Biology
Northwestern Univ Med School, Chicago, IL	Ph.D.	1997	Physiology
Vollum Institute, Oregon Health & Science Univ, Portland, OR	postdoc	1998-2004	Neuroscience

A. Positions and Honors.**Positions**

June 2006- Present Assistant Professor, Department of Neurobiology, University of Alabama at Birmingham
2004-2006 Research Assistant Professor, Vollum Institute, Oregon Health & Science University

Honors

2001 - 2002 Epilepsy Foundation Postdoctoral Fellowship
1999 - 2000 NRSA Postdoctoral Fellowship (5 F32 MH12400), Vollum Institute
1998 - 1999 NIH Training Grant Fellow (DA07262-07), Vollum Institute
1996 - 1997 NIH Training Grant Fellow (5T32 DC00015-15), Northwestern Univ
1990 - 1992 Wilson Science Scholarship, North Park College
1990 Discover Pharmacology fellow, Pharmacology Department, Loyola Univ

Invited speaker at international meetings

Nov 2008 Society for Neuroscience (DC) - Minisymposium: Adult neurogenesis, mental health and illness
April 2008 Experimental Biology 2008 (San Diego) - Symposium: Adult neurogenesis
May 2007 Neurogenesis 2007 (Tokyo) - International meeting on neurogenesis
Nov 2005 Society for Neuroscience (DC) - Minisymposium: New neurons in the adult brain
Feb 2003 Winter Conference on Neuroplasticity (Guadeloupe, French Antilles) - GABAergic mechanisms
Jan 2002 Winter Conference on Brain Research (Aspen, CO) - GABAergic synaptic transmission

B. Peer-reviewed publications (in chronological order).

Trommer BL, Kennelly JJ, Colley PA, **Overstreet LS**, Slater NT, Pasternak JF (1995) AP5 blocks LTP in developing rat dentate gyrus and unmasks LTD. *Experimental Neurology*, 131:83-92.

Pekhletski R, Gerlai R, **Overstreet LS**, Huang X, Agopyan N, Slater NT, Abramow-Newerly W, Roder JC, Hampson DR (1996) Impaired cerebellar synaptic plasticity and motor performance in mice lacking the mGluR4 subtype of metabotropic glutamate receptor. *Journal of Neuroscience*, 16:6364-6373.

Kessey K, Trommer BL, **Overstreet LS**, Ji T, Mogul D (1997) A role for adenosine A₂ receptors in the induction of long-term potentiation in the CA1 region of rat hippocampus. *Brain Research*, 756:184-190.

Kinney GA, **Overstreet LS**, Slater NT (1997) Prolonged physiological entrapment of glutamate in the synaptic cleft of cerebellar unipolar brush cells. *Journal of Neurophysiology*, 78:1320-1333.

Overstreet LS, Trommer BL, Colley PA, Slater NT, Pasternak JF (1997) Metabotropic glutamate receptor mediated long-term depression in developing hippocampus. *Neuropharmacology*, 36:831-844.

- Overstreet LS**, Kinney GA, Liu Y-B, Billups D, Slater NT (1999) Glutamate transporters contribute to the time course of synaptic transmission in cerebellar granule cells. *Journal of Neuroscience*, 19:9663-9673.
- Overstreet LS**, Jones MV, Westbrook GL (2000) Slow desensitization regulates the availability of synaptic GABA_A receptors. *Journal of Neuroscience*, 20:7914-7921.
- Overstreet LS**, Westbrook GL (2001) Paradoxical reduction of synaptic inhibition by vigabatrin. *Journal of Neurophysiology*, 86:596-603.
- Overstreet LS**, Westbrook GL (2003) Synapse density regulates independence at unitary inhibitory synapses. *Journal of Neuroscience*, 23:2618-26.
- Hentges ST, Nishiyama M, **Overstreet LS**, Stenzel-Poore M, Williams JT, Low MJ (2004) GABA release from proopiomelanocortin neurons. *Journal of Neuroscience*, 24:1578-83.
- Overstreet LS**, Hentges ST, Bumashny V, de Souza FJ, Smart JL, Santangelo AM, Low MJ, Westbrook GL, Rubinstein M (2004) A transgenic marker for newly born granule cells in dentate gyrus. *Journal of Neuroscience*, 24:3251-3259.
- Overstreet LS** (2005) Quantal transmission: not just for neurons. *Trends in Neurosciences*, 28:59-62.
- Overstreet Wadiche L**, Bromberg DA, Bensen AL, Westbrook GL (2005) GABAergic signaling to newborn neurons in dentate gyrus. *Journal of Neurophysiology* 94:4528-32.
- Song H, Kempermann G, **Overstreet Wadiche L**, Zhao C, Schinder AF, Bischofberger J (2005) New neurons in the adult mammalian brain: synaptogenesis and functional integration. *Journal of Neuroscience* 9:10366-8.
- Overstreet-Wadiche LS**, Bensen AL, Westbrook GL (2006) Delayed development of adult-generated granule cells in dentate gyrus. *Journal of Neuroscience*, 26:2326-34.
- Overstreet-Wadiche LS**, Bromberg DA, Bensen AL, Westbrook GL (2006) Seizures accelerate functional integration of adult-generated granule cells. *Journal of Neuroscience*, 26:4095-103.
- Overstreet-Wadiche LS**, Westbrook GL (2006) Functional maturation of adult-generated granule cells. *Hippocampus*, 16:208-15.
- Zhao C-S, **Overstreet-Wadiche LS** (2008) Integration of adult generated neurons during epileptogenesis. *Epilepsia*, 49 s5:3-12.
- Markwardt S, **Overstreet-Wadiche LS** (2008) GABAergic signaling to adult generated neurons. *Journal of Physiology*, 586:3745-9.
- Eisch AJ, Cameron HA, Encinas JM, Meltzer LA, Ming GL, **Overstreet-Wadiche LS** (2008) Adult Neurogenesis, Mental Health, and Mental Illness: Hope or Hype? *Journal of Neuroscience*, In press.

C. Research Support

Current Research Support

Epilepsy Foundation Research Grant

1/1/2007-12/31/2008

Functional integration of newborn neurons in epileptogenesis

The goal of this project is to study GABAergic synaptic input to seizure-induced adult generated neurons in the dentate gyrus.

Role: PI

Purdue-UAB Botanicals Research Center 10/1/2008 – 9/30/2009

Grape seed extract enhances adult neurogenesis

The goal of this project is to study the effects of grape seed extract on dentate neurogenesis.

Role: PI

NIH 1R01NS064025 (pending) 4/1/2009 – 3/30/2014

Newborn Neurons in the Adult Hippocampal Network

The goal of this project is to study the mechanisms underlying the survival of adult generated neurons.

Role: PI

Principal Investigator/Program Director (Last, First, Middle):

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 Gavin Rumbaugh, Ph.D.		POSITION TITLE Assistant Professor	
eRA COMMONS USER NAME grumbau1			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as</i>			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Westminster College, New Wilmington, PA	BS	1992-1996	Biology
Georgetown University School of Medicine, Washington, DC	PhD	1996-2000	Biophysics/ Neuroscience
Johns Hopkins School of Medicine, Baltimore, MD		2000-2006	Advisor: Stefano Vicini Neuroscience/ Synaptic physiology

A. Positions and Honors.**Positions and Employment**

- 2000-present Postdoctoral Fellow, Laboratory of Richard L. Huganir, HHMI, Johns Hopkins University School of Medicine
- 2006-present Assistant Professor, Evelyn F. McKnight Brain Research Institute, Department of Neurobiology, The University of Alabama at Birmingham (UAB) School of Medicine

Professional Memberships

- 1997-present Member, The Society for Neuroscience

Honors

- 1996 NCAA/NAIA Academic All-America (Westminster College)
- 2002 National Research Scholar Award (NRSA: F32 NS043071-03; NINDS)
- 2006 Alabama Health Sciences Foundation Scholar

B. Selected peer-reviewed publications (in chronological order).

1. Rumbaugh G, Vicini S. (1999) Distinct synaptic and extrasynaptic NMDA receptors in developing cerebellar granule neurons. *J Neurosci* 19(24):10603-10.
2. Rumbaugh G, Prybylowski K, Wang JF, Vicini S. (2000) Exon 5 and spermine regulate deactivation of NMDA receptor subtypes. *J Neurophysiol* 83(3):1300-6
3. Prybylowski K, Rumbaugh G, Wolfe BB, Vicini S. (2000) Increased exon 5 expression alters extrasynaptic NMDA receptors in cerebellar neurons. *J Neurochem* 75(3):1140-6.
4. Ceccon M, Rumbaugh G, Vicini S. (2001) Distinct effect of pregnenolone sulfate on NMDA receptor subtypes. *Neuropharmacology* 40(4):491-500.

Principal Investigator/Program Director (Last, First, Middle):

5. Lee HK, Takamiya K, Han JS, Man H, Kim CH, Rumbaugh G, Yu S, Ding L, He C, Petralia RS, Wenthold RJ, Gallagher M, Huganir RL. (2003) Phosphorylation of the AMPA receptor GluR1 subunit is required for synaptic plasticity and retention of spatial memory. *Cell* 112(5):631-43.
6. Rumbaugh G, Sia GM, Garner CC, Huganir RL. (2003) Synapse-associated protein-97 isoform-specific regulation of surface AMPA receptors and synaptic function in cultured neurons. *J Neurosci* 23(11):4567-76
7. Rumbaugh G*, Tao YX*, Wang GD*, Petralia RS, Zhao C, Kauer FW, Tao F, Zhuo M, Wenthold RJ, Raja SN, Huganir RL, Brecht DS, Johns RA. (2003) Impaired NMDA receptor-mediated postsynaptic function and blunted NMDA receptor-dependent persistent pain in mice lacking postsynaptic density-93 protein. *J Neurosci* 23(17):6703-12.
*Equal contribution
8. Landree LE, Hanlon AL, Strong DW, Rumbaugh G, Miller IM, Thupari JN, Connolly EC, Huganir RL, Richardson C, Witters LA, Kuhajda FP, Ronnett GV. (2004) C75, a fatty acid synthase inhibitor, modulates AMP-activated protein kinase to alter neuronal energy metabolism. *J Biol Chem* 279(5):3817-27.
9. Hayashi T, Rumbaugh G, Huganir RL. (2005) Differential regulation of AMPA receptor subunit trafficking by palmitoylation of two distinct sites. *Neuron* 47(5): 709-723.
10. Rumbaugh G. (2005) Synapses fight for Glutamate Receptor 1. *J Neurosci* 25(38): 8347-8348.
11. Thomas GM, Rumbaugh G, Harrar DB, Huganir RL. (2005) RSK2 interacts with and phosphorylates PDZ domain-containing proteins and regulates AMPA-R transmission. *PNAS* 102(42):15006-11.
12. Rumbaugh G, Adams JP, Kim JH, Huganir RL. (2006) *Inaugural Article*: SynGAP regulates synaptic strength and mitogen-activated protein kinases in cultured neurons. *PNAS* 103(12):4344-51
13. Shepherd JS*, Rumbaugh G*, Chowdhury A, Huganir RL, Worley P. (2006) Arc regulates homeostatic synaptic scaling of AMPA receptors in cultured neurons. *Neuron*. 52(3):475-484.
*Equal contribution

C. Research Support.

Ongoing Research Support

UAB Department of Neurobiology Start-up Funds

12/01/2006-12/01/2009

Alabama Health Sciences Foundation Grant

12/01/2006-11/30/2007

Title: Construction of a hybrid confocal/two-photon laser scanning microscope

Role: PI

Completed Research Support

F32 NS043071 Rumbaugh (PI)

05/01/2002-04/30/2005

NINDS

Molecular Mechanisms of GluR1 Trafficking

Role: PI

Principal Investigator/Program Director (Last, First, Middle):

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 Jacques Wadiche		POSITION TITLE Assistant Professor	
eRA COMMONS USER NAME jwadiche		Department of Neurobiology	
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
Northwestern University; Evanston, IL	B.A.	1984-1988	Neurobio. and Physiology
Oregon Health Sciences Univ.- Vollum Inst.	Ph.D.	1992-1998	Neuroscience/Biophysics
Oregon Health Sciences Univ.- Vollum Inst	postdoctoral	1998-2006	Synaptic transmission

A. Positions and Honors.**Positions and Employment**

1987-88 Research Assistantship, Northwestern University
Advisor: Fred W. Turek, Ph.D,
1998-2006 Postdoctoral fellow, OHSU, Vollum Institute,
Advisor: Craig Jahr, Ph.D.
2004 Cold Spring Harbor Laboratories Imaging Course - Teaching assistant

Other Experience and Professional Memberships**Honors**

1992-94 Dean's Fellowship, Oregon Health Sciences University
1994 Biophysical Society Student Award
1994-96 NIDA Training Fellowship
1996 Medical Research Foundation Tartar Award
1998 Outstanding Doctoral Thesis, Oregon Health Sciences University
1999 NIMH Training Fellowship
2000-02 NIMH National Research Fellowship Award
2003 Cold Spring Harbor Laboratories Imaging Course

B. Peer-reviewed publications (in chronological order).

1. Wadiche, J.I. and von Gersdorff, H. (2006). Long-distance signaling via presynaptic glutamate transporters. *Nat Neurosci.* 9, 1352-3.
2. Wadiche, J.I., Tzingounis, A.V., and Jahr, C.E. (2006). Intrinsic kinetics determines the time course of neuronal synaptic transporter currents. *PNAS.* 103,1083-7.
3. Wadiche, J.I. and Jahr, C.E. (2005). Patterned expression of Purkinje cell glutamate transporters controls synaptic plasticity. *Nat. Neurosci.*, 8, 1329-34.

Principal Investigator/Program Director (Last, First, Middle):

4. Kushmerick, C., Price, G., Tashenberger, H., Puente, N., Renden, R., **Wadiche, J.I.**, Duvosin, R.M., Grandes, P., von Gersdorff, H. (2004). Retroinhibition of presynaptic Ca^{2+} currents by endocannabinoids released via postsynaptic mGluR activation at a calyx synapse. *J. Neurosci.*, *24*, 5955-65.
5. **Wadiche, J.I.** and Jahr, C.E. (2001). Multivesicular release at climbing fiber-Purkinje cell synapses. *Neuron*, *32*, 301-13.
6. **Wadiche, J.I.** and Kavanaugh, M.P. (1998). Macroscopic and microscopic properties of a cloned glutamate transporter/chloride channel. *J. Neurosci.*, *18*, 7650-7661.
7. **Wadiche, J.I.**, Amara, S.G., and Kavanaugh, M.P. (1995). Ion fluxes associated with excitatory amino acid transport. *Neuron*, *15*, 721-728.
8. **Wadiche, J.I.**, Arriza, J.L., Amara, S.G., and Kavanaugh, M.P. (1995). Kinetics of a human glutamate transporter. *Neuron*, *14*, 1019-1027.
9. Arriza, J.L., Fairman, W.P., **Wadiche J.I.**, Murdoch, G.H., Kavanaugh, M.P., and Amara S.G. (1994). Functional comparisons of three glutamate transporter subtypes cloned from human motor cortex. *J. Neurosci.*, *14*, 5559-5569.
10. Seguela, P., **Wadiche, J.**, Dinelly-Miller, K., Dani, J., and Patrick, J. (1993). Molecular cloning, functional expression and distribution of a rat neuronal nicotinic channel highly permeant to calcium. *J. Neurosci.*, *13*, 596-604.

C. Research Support

No current research support.

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Scott M. Wilson	Assistant Professor

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of South Florida	B.S.	1982-86	Biology
University of South Florida	M.S.	1987-89	Microbiology
University of Florida	Ph.D.	1992-96	Molecular Genetics and Microbiology
National Cancer Institute	Postdoc	1997-2002	Genetics

A. Positions and Honors:
Professional Positions:

1990-1991	Instructor, Introductory Biology, Hillsboro Community College, Tampa, Florida
1992-1996	Graduate student in Assistant Professor Maurice Swanson's Laboratory, Department of Molecular Genetics and Microbiology, University of Florida College of Medicine, Gainesville, Florida
1997-2002	Postdoctoral Fellow in the laboratory of Drs. Neal Copeland and Nancy Jenkins, National Cancer Institute, Frederick, MD.
8-02 to present	Department of Neurobiology, Birmingham, AL, Assistant Professor
11-03 to present	Secondary Appointment in the Department of Biochemistry and Molecular Genetics
11-04 to present	Secondary Appointment in the Department of Genetics
6-06 to present	Director SPIN
10-06 to present	Director of Molecular Recombineering Core. NIH Blueprint Core facility.

Awards and Other Professional Activities (Representative):

2006	McNulty Civitan Scientist Award
2003	NIH Travel award
2002	Alabama Parkinson's Association Research Award (\$15,000)
2001	Postdoctoral Research Competition Award, Frederick, MD
1996	First Place, Medical Guild Research Competition Award, Gainesville, FL
1994	Graduate Student Council Research Award, Gainesville, FL

B. Selected peer-reviewed publications:

- Klein, T.W., Yamamoto, Y., **Wilson, S.**, Newton, C., and Friedman, H. 1992. *Legionella pneumophila* infection and cytokine production. *Adv. Exp. Med. Biol.* 319:97-104.
- Anderson, J.T., **Wilson, S.M.**, Datar, K.V., and Swanson, M.S. 1993. NAB2: A yeast nuclear polyadenylated RNA-binding protein essential for cell viability. *Mol. Cell. Biol.* 13: 2730-2741.
- Wilson, S.M.**, Datar, K.V., Paddy, M.R., Swedlow, J.R., and Swanson, M.S. 1994. Characterization of nuclear polyadenylated RNA-binding proteins in *Saccharomyces cerevisiae*. *J. Cell Biol.* 127:1173-1184.
- Conrad N.K., **Wilson S.M.**, Steinmetz E.J., Patturajan M., Brow D.A., Swanson M.S., Corden J.L. 2000. A yeast heterogeneous nuclear ribonucleoprotein complex associated with RNA polymerase II. *Genetics* 154:557-71
- Wilson, S.M.**, Yip, R., Swing, D.A., O'Sullivan, T.N., Zhang, Y., Novak, E.K., Swank, R.T., Russell, L.B., Copeland, N.G., and Jenkins, N.A. 2000. A mutation in *Rab27a* causes the vesicle transport defects observed in *ashen* mice. *Proc. Natl. Acad. Sci. USA* 97:7933-7938.
- Wilson, S.M.**, Toth, P.T., Oh, S.B., Gillard, S.E., Volsen, S., Ren, D., Philipson, L.H., Lee, E.C., Fletcher, C.F., Tessarollo, L., Copeland, N.G., Jenkins, N.A., and Miller, R.J. 2000. The status of voltage-dependent calcium channels in α_{1E} knock-out mice. *J. Neurosci.* 20:8566-8571.
- Fletcher, C.F., Tottene, A., Lennon, V.A., **Wilson, S.M.**, Dubel, S.J., Paylor, R., Hosford, D.A., Tessarollo, L., McEnery, M.W., Pietrobon, D., Copeland, N.G., and Jenkins, N.A. 2001. Dystonia and cerebellar atrophy in *Cacna1a* null mice lacking P/Q calcium channel activity. *FASEB J.* 15:1288-1290.
- Wilson, S.M.**, Householder, D.B., Coppola, V., Tessarollo, L., Fritzsche, B., Lee, E.C., Goss, D., Carlson, G.A., Copeland, N.G., and Jenkins, N.A. 2001. Mutations in *Cdh23* cause nonsyndromic hearing loss in *waltzer* mice. *Genomics* 74:228-233.
- Hector R.E., Nykamp KR, Dheur S, Anderson J.T., Non P.J., Urbinati C.R., **Wilson S.M.**, Minvielle-Sebastia L, Swanson MS. 2002. Dual requirement for yeast hnRNP Nab2p in mRNA poly(A) tail length control and nuclear export. *EMBO J* 21:1800-10.
- Wilson, S.M.**, Bhattacharyya, B., Rachel, R.A., Coppola, V., Tessarollo, L., Householder, D.B., Fletcher, C.F., Miller, R.J., Copeland, N.G., and Jenkins, N.A. Synaptic defects in *ataxia* mice result from a mutation in *Usp14*, a ubiquitin-specific protease. *Nature Genetics* 32:420-5 2002
- Miller R.J., **Wilson S.M.** Neurological disease: UPS stops delivering! *Trends Pharmacol Sci* 24:18-23 2003.
- Anderson, C, Crimmins, S., Wilson, JA, Knobel, GA, Ploegh and **Wilson, SM.** 2005. Loss of *Usp14* results in reduced levels of ubiquitin in *ataxia* mice. *J Neurochem* 95(3):724-31.
- Crimmins, S., Youngam Jin, Crystal Wheeler, Alexis K. Huffman, Carlene Chapman, Lynn E. Dobrunz, Alan Levey, Kevin A. Roth, Julie A. Wilson and **Wilson, S.M.** Transgenic rescue of *ataxia* mice with neuronal-specific expression of *Usp14*. *J Neuroscience* 26(44) Nov 1 2006.
- Wilson, S.M.**, and Rumbaugh, G. 2008. Regulated protein degradation facilitates memory reconsolidation. *CellScience Reviews* 4: 31-35.
- Crimmins, S., Chen, P.C., Huffman, A.K., , Roth, K.A., Sutovsky, M., Sutovsky, P., Wilson, J.A., and **Wilson, S.M.** Transgenic rescue of ataxia mice reveals a male-specific sterility defect. **Accepted** *Developmental Biology*

Walters, B.¹, Campbell, S.L.¹, Chen, P.C.¹, Dobrunz, L.E.¹, Wilson, J.A.¹, Artavanis-Tsakonas, K.², Ploegh, H.L.², Taylor, A.P.³, Schroeder, D.G.³, Cox, G.A.³ and **Wilson, S.M.** Differential effects of *Usp14* and *Uch-*

Chen, P.C., Qin, L.C., Walters, B., Dobrunz, L., Wilson, J.A., Mei, L., and **Wilson, S.M.** Motor endplate disease in the ubiquitin-specific protease 14 deficient *ataxia* mice. **Submitted** to Journal of Neuroscience.

Bhattacharyya, B., **Wilson S.M.**, and Miller R.J. Altered neurotransmitter release machinery in *ataxic* mice associated with mutations in the de-ubiquitinating enzyme, *usp14*. **Under revision**.

Liyan Qiao, Shusei Hamamichi, Kim A. Caldwell, Guy A. Caldwell, Talene Yacoubian, **Scott Wilson**, Zuo-Lei Xie, Lisa Speake, Rachael Parks, Donna Crabtree, Qiuli Liang, Stephen Crimmins, Lonnie Schneider, Yasuo Uchiyama, Genta Ito, Yi Zhou, Lisheng Peng, YouMing Lu, David Standaert, Ken Walls, John Shacka, Kevin Roth, and Jianhua Zhang. Lysosomal enzyme cathepsin D protects against neuronal α 3B1;-synuclein aggregation and toxicity. **Submitted** to Journal of Neuroscience.

Corinna Lappe-Siefke, Sven Löbrich, Wulf Hevers, Michaela Schweizer, Jean-Marc Fritschy, Jens Eilers, **Scott M. Wilson** and Matthias Kneussel. Ax¹ mutation of the ubiquitin-specific protease 14 gene alters *in vivo* GABA_A receptor α 1 subunit surface expression and Purkinje cell function. **Submitted** to Genes and Development.

Anna E. Cartier, Stephen N. Djakovic, **Scott M. Wilson** and Gentry Patrick. Regulation of synaptic structure by the Ubiquitin C-terminal hydrolase UCH-L1. **Under revision**.

C. Research Support.

Wilson, S.M.

Ongoing Research Projects:

RO1 NS047533-01 Wilson (PI) -
NIH/NINDS

01/01/04-12/31/08

The role of Usp14 in neuronal function.

The major goals of this proposal are to determine the role of Usp14 in the ubiquitin-proteasome pathway, potential substrates for Usp14 and neuropathology of the *ataxia* mice.

NIH Neuroscience Blueprint Core Grant NS57098

10/01/06-9/31/11

Molecular Engineering Core Director. The Molecular Engineering Core will function to generate targeting cassettes for the production of both transgenic and knockout animals.

Completed Projects

March of Dimes Basil O'Connor Award Wilson (PI)

02/01/04-01/31/06

Role of Usp14 in the development of the nervous system

The major goals of this proposal are to construct a conditional allele of Usp14 and to determine the isoforms of Usp14 required for normal development.

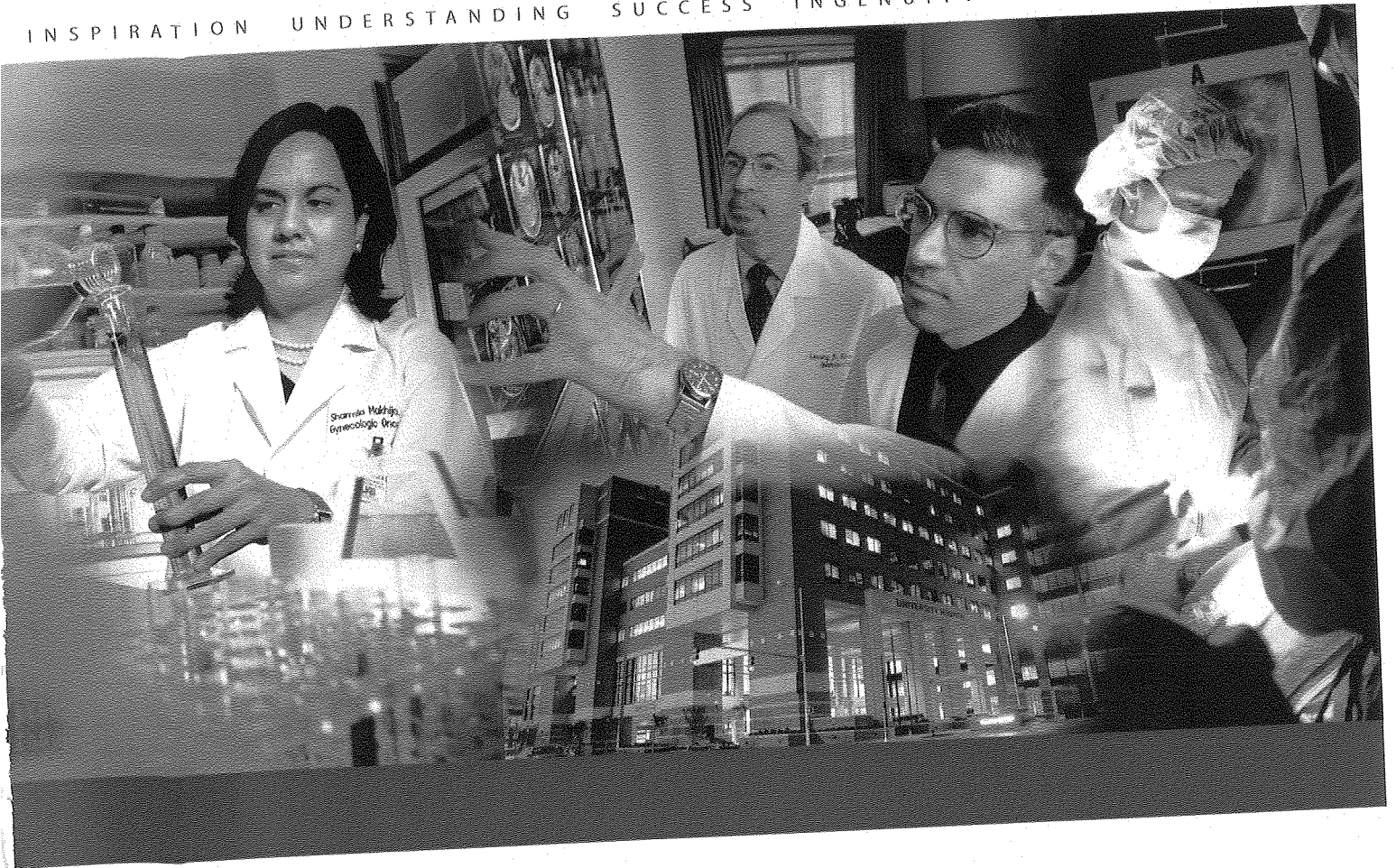
APPENDICES

Department of Neurobiology
&
The Evelyn F. McKnight Brain Institute
Seminar Series
2008

1/10/2008	Craig E. Jahr, Ph.D. Senior Scientist	Vollum Institute Oregon Health & Science University	<i>"Neural-Glia Interactions"</i>
1/24/2008	Peter Penzes, Ph.D. Assistant Professor Department of Physiology	Northwestern University	<i>"Molecular Mechanisms of Synaptic Structural Plasticity and Pathology"</i>
2/12/2008	Michelle Grey Postdoctoral Fellow	David Geffen School of Medicine at UCLA	<i>"BACHD Mice Recapitulate Huntington's Disease Pathology and Demonstrate Pathological Cell-Cell Interactions"</i>
2/21/2008	Stephen F. Traynelis, Ph.D. Associate Professor	Emory University Dept. of Pharmacology Atlanta, GA	<i>"Zn²⁺ Control of NMDA Receptor Gating"</i>
2/26/2008	T. Chris Gamblin, Ph.D. Assistant Professor Department of Molecular Biosciences	The University of Kansas	<i>"Modeling Tau Polymerization in Alzheimer's Disease"</i>
3/6/2008	Hengbin Wang, Ph.D. Department of Biochemistry & Molecular Genetics	University of Alabama at Birmingham	<i>"Epigenetic Regulation of Transcription "</i>
3/20/2008	Manzoor Bhat, M.S., Ph.D. Associate Professor Department of Cell & Molecular Physiology, UNC Neuroscience Center	University of North Carolina at Chapel Hill SOM	<i>"Organizing Principles of Axo-Glial Junctions Across Species"</i>
3/27/2008	David Gadsby, Ph.D. Patrick A. Gerschel Family Professor Laboratory of Cardiac/Membrane Physiology	Rockefeller University	<i>"Mapping the Ion Pathway through the Living Na,K-ATPase Pump in Situ"</i>
3/28/2008	Anastassios Tzingounis, Ph.D. Postdoctoral Fellow Roger Nicoll lab	University of California, San Francisco, CA	<i>"Seizing the Brake: How Global Calcium Limits Neuronal Excitability"</i>
4/1/2008	Danielle Simmons, Ph.D. Postdoctoral Researcher Department of Psychiatry	University of California, Irvine	<i>"Up-Regulating BDNF as a Therapeutic Strategy for Huntington Disease"</i>
4/3/2008	Kristina Visscher, Ph.D. Postdoctoral Researcher	Brandeis University	<i>"Background Activity Alters the Way We Perceive and Remember"</i>
4/8/2008	Chad Antony Dickey, Ph.D. Assistant Professor Department of Molecular Pharmacology and Physiology	University of South Florida College of Medicine	<i>"Chaperones and Kinases Converge to Regulate Tau Proteotoxicity"</i>
4/24/2008	R. Douglas Fields, Ph.D. Chief, Nervous System Development & Plasticity Section	National Institutes of Health, NICHD	<i>"Activity-Dependent Myelination: Plasticity Beyond the Synapse"</i>

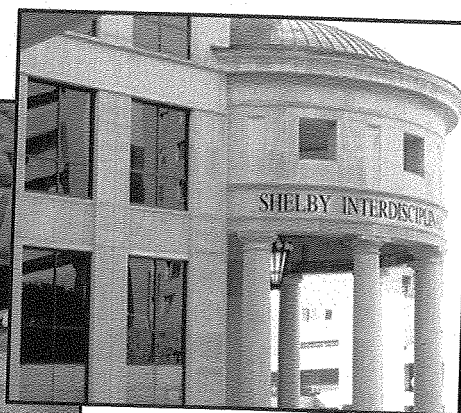
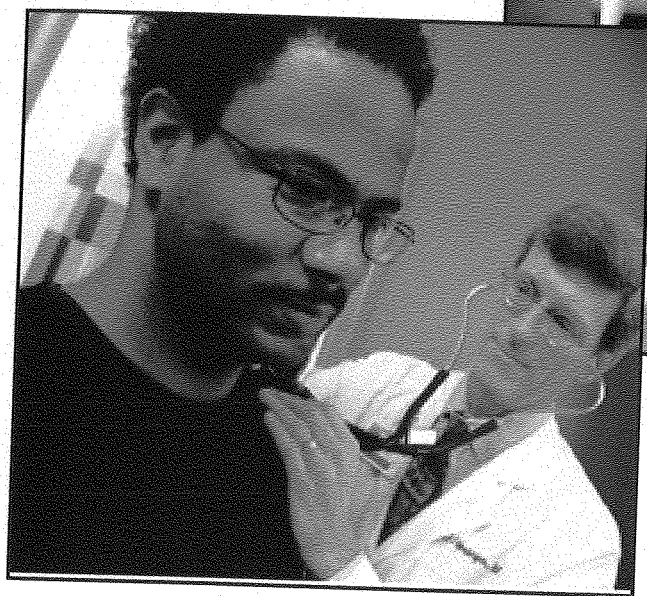
5/1/2008	Richard Robitaille, Ph.D. Associate Professor Department of Physiology	Université de Montréal	<i>"Glial Cells Govern Synaptic Plasticity"</i>
5/15/2008	Randy Blakely, Ph.D. Professor Pharmacology & Psychiatry	Vanderbilt University	<i>"Suck It Up, Pay Attention and Get Moving: Dopamine, Dopamine Transporters and ADHD"</i>
5/22/2008	Wen-Biao Gan, Ph.D. Associate Professor Department of Physiology & Neuroscience	Skirball Institute Program New York University	<i>"Structural Dynamics of Synapses and Microglia in Vivo"</i>
5/29/2008	Farah Lubin, Ph.D. Postdoctoral Fellow Dept. of Neurobiology Faculty Candidate	University of Alabama at Birmingham	<i>"Epigenetic Gene Regulation in the Adult Hippocampus: Implications in Memory Formation and Epilepsy"</i>
6/3/2008	Ghazaleh Sadri-Vakili, Ph.D. Instructor Department of Neurology	Mass General Hospital Mass General Institute for Neurodegenerative Disease	<i>"Transcriptional Dysregulation in Huntington's"</i>
9/18/2008	Chenjian Li, PhD Assistant Professor Department of Neurology & Neuroscience	Cornell University Medical College	<i>"Tales of Two Kinases: PINK1 and LRRK2 for Parkinson's Disease"</i>
10/16/2008	Huaxi Xu, PhD Professor, Acting Director, Degenerative Disease Research	Burnham Institute for Medical Research	<i>"Proteolytic Processing and Patho/Physiological Functions of Alzheimer's Beta-Amyloid Precursor Protein "</i>
10/22/2008	Vladimir Parpura, M.D., Ph.D. Erik Roberson, M.D., Ph.D. Gavin Rumbuagh, Ph.D. Linda Overstreet Wadiche, Ph.D. Kristina Visscher, Ph.D. David Knight, Ph.D. J. David Sweatt, Ph.D. Jacques Wadiche, Ph.D. Lori McMahon, Ph.D.	University of Alabama at Birmingham	<i>Symposium on Memory and Aging</i>
11/6/2008	Linda Wadiche, Ph.D. Assistant Professor Department of Neurobiology	University of Alabama at Birmingham	<i>"Activity Dependent Control of Neurogenesis in the Dentate Gyrus "</i>
12/9/2008	Roger Colbran, Ph.D. Professor & Interim Vice Chair Department of Molecular Physiology & Biophysics	Vanderbilt University	<i>"Coordination of Signaling by CaMKII and PP1 in Dendritic Spines "</i>

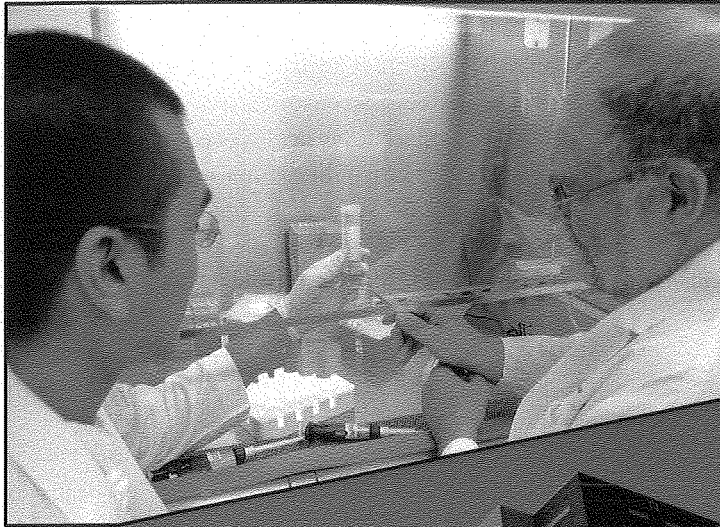
INSPIRATION UNDERSTANDING SUCCESS INGENUITY INNOVATION



UAB Highlights

UAB Development Office





UAB Development Office

School of Medicine Highlights

THE SCHOOL OF MEDICINE has five medical specialties that ranked in the top 20 nationally by *U.S. News & World Report*. These specialties include AIDS, women's health, internal medicine,

geriatrics, and pediatrics. The School is also ranked 34th in the primary care category, ahead of Mayo Medical School and Emory University.

BEST DOCTORS IN AMERICA lists 277 UAB physicians in its latest edition. UAB faculty and physicians comprise 60 percent of the 460 Birmingham metropolitan area medical specialists in the latest list.

UAB HOSPITAL was listed among the nation's 223 top hos-

pitals in the 2006/07 Consumer Choice Awards by The National Research Corporation. The award is given in terms of consumer perceptions of quality and image.

UAB HOSPITAL WAS SELECTED AS ONE OF AMERICA'S most customer-friendly hospitals by the American Alliance of Health-care Providers. UAB has earned the Hospital of Choice Award for the first quarter of 2008 from the alliance for its unparalleled commitment to good citizenship and community service.

TO ADDRESS THE HIGH VOLUME OF ANNUAL PATIENT ENCOUNTERS (approximately one million last year) additional facilities are being constructed.

THE UNIVERSITY has received the largest gift ever from a living individual to help construct a new radiation oncology facility to provide improved care to cancer patients. Thanks in large part to a gift of \$5 million from W. Cobb "Chip" Hazelrig, the Hazelrig-Salter Radiation Oncology Facility will soon become a reality.

THE WOMEN AND INFANTS CENTER AT UAB is being made possible by a generous lead gift from The Daniel Foundation of Alabama. The Center will provide comprehensive services in the areas of obstetrics and gynecology and neonatal intensive care.

A NEW FACILITY, UAB HIGHLANDS, was acquired in 2007, allowing the expansion of existing clinical services in orthopedic and plastic surgery. The Work Place, an occupational and rehabilitation medicine facility, is also housed at UAB Highlands.

IN 2007, UNIVERSITY HOSPITAL AND UAB HIGHLANDS performed 27,829 surgical procedures and served approximately 65,421 emergency room patients—an average of 180 patients per day.

THE UAB HEALTH SYSTEM CONTINUES TO GROW. In addition to The Kirklin Clinic, UAB Hospital, and surrounding facilities, the System also encompasses UAB Highlands, UAB Medical West, and multiple health centers in Greater Birmingham, Tuscaloosa, Huntsville, Selma, and Montgomery.

UAB'S NEW RHEUMATOID ARTHRITIS CLINIC at The Kirklin Clinic provides state-of-the-art care to adult rheumatoid arthritis patients. In light of the sometimes irreversible radiographic damage that results from delayed treatment, physicians can see patients with new-onset synovitis within two weeks of referral.

EQUAL ACCESS BIRMINGHAM and free clinic is run by an all-volunteer group of UAB medical students, undergraduates and physicians who believe that high quality healthcare is the right of all individuals, families and communities and that such care must be provided regardless of socioeconomic or health status. The free clinic is made possible through a partnership between the School of Medicine at UAB and M-POWER Ministries.

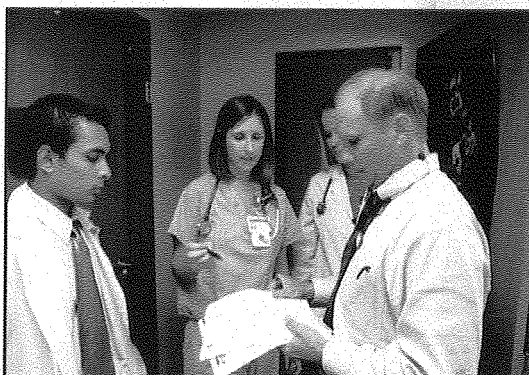
THE NATIONAL INSTITUTES OF HEALTH HAS DESIGNATED UAB one of only six Diabetes Research and Training Centers (DRTC) in the country. This designation puts UAB at the forefront in the development of new methods to treat, prevent, and ultimately cure diabetes and its complications. The NIH award provides UAB with a \$6.3 million grant over five years to grow its diabetes initiatives. The DRTC is part of the UAB Comprehensive Diabetes Center.

THE COMPREHENSIVE CANCER CENTER HAS IMPLEMENTED an Integrated Multidisciplinary Clinical Cancer Program (IMCCP) to distinguish the basic, clinical, translational, prevention, and control characteristics unavailable at cancer centers that are not designated comprehensive. Five components of the IMCCP are in various stages of development: patient care coordinators, Cancer Center ambassadors, off-hours emergency access, the patient navigator program and the research referral unit.



Education

IN 2006, THE SCHOOL OF MEDICINE was reaccredited for eight years by the Liaison Committee for Medical Education. Notable strengths pointed out by site visitors include the collegiality of the faculty and campuses and the School's robust research enterprise.



THE SCHOOL OF MEDICINE'S

STUDENT GRADING system was changed in 2006 to a simple pass-fail system to reduce intra-class and group competitiveness and to promote the focus on life-long learning.

THE CLASS OF 2011 BECAME THE FIRST CLASS TO study under a new curriculum based on interdisciplinary approaches to learning and scholarly activity. The new curriculum is organized into four essential elements:

- Pre-clerkship phase (20 months)
- Clerkship phase (12 months)
- Scholarly activity phase (3 months)
- Pre-residency phase (10 months)

THE 160 MEMBERS OF THE CLASS OF 2008 will undergo their residency training at hospitals from New England to California, with more than 80 percent remaining in the Southeast. Forty-three percent will remain in Alabama, and nearly 37 percent will conduct their residency training in one of the primary care fields.

THE EARLY MEDICAL SCHOOL

ACCEPTANCE PROGRAM (EMSAP) is an program for 10 mature graduating seniors. UAB's program increasingly attracts applicants not just from Alabama but from across the Southeast and nation. The minimal test scores recommended to apply for the program are 30 ACT and/or 1320 SAT. Those admitted to the program have an average SAT score of 1450 and ACT score of 32. The majority of the students completed math and science advanced placement courses in high school. An entering class typically consists of National Merit Finalists and students with perfect SAT scores.

SCHOOL OF MEDICINE STUDENTS CONSISTENTLY perform at or above the national mean on the United States Medical Licensing Exam Step 2 examination. The Step 2 examination is the examination that students take during their fourth year of study and provides insight into how well prepared students are upon entering residency programs.

TO ADDRESS PHYSICIAN SHORTAGE CONCERNS, the School of Medicine has increased the class size by ten percent and has increased the number of students assigned to the Tuscaloosa and Huntsville campuses to attract additional physicians to rural communities.

THE HOWARD HUGHES MEDICAL INSTITUTE awarded 13 schools a portion of \$10 million to modify the education of graduate students and improve the translation of basic science discoveries into new medical treatments. Thomas Clemens, M.D., (Pathology) received an award of \$650,000 from this initiative to establish the Hughes Med-Grad Fellowship Program at UAB to develop synergies between the graduate and medical curricula.

IN CONJUNCTION WITH THE UAB GRADUATE SCHOOL, the School of Medicine established the Office of Graduate Biomedical Sciences, a new administrative structure for graduate programs in the biomedical sciences designed to streamline administrative processes and provide a support structure for NIH-funded training programs.

NEW INTERDISCIPLINARY TRAINING PROGRAMS in Genetics and Neurosciences were established in 2007, and a new undergraduate Neuroscience major was created in conjunction with the UAB School of Social and Behavioral Sciences. This new major will create a potential pipeline to the School of Medicine graduate programs.

MEDICAL SCHOOL NOW A TEAM SPORT AT UAB.

UAB wants the physicians it trains to approach medicine as a team sport, so incoming first-year medical students will spend a day in team-building and leadership exercises. The medical students will work in small groups in accomplish a variety of tasks and challenges. "Teamwork is the primary goal," said Lawrence Tyson, Ph.D., associate professor of Counselor Education. "The quiet follower needs to learn leadership skills while the aggressive leader must understand that all members of a group bring valuable skills to a project. The teamwork of this core group should let them learn from the skill sets of each other."

Faculty and Research

IN 2006, THE SCHOOL OF MEDICINE IMPLEMENTED its Research Strategic Plan designed to build on the School's current strengths, to develop major areas of funding opportunities, and to identify areas for programmatic development. Over 200 faculty members across seven of UAB's 12 schools convened and recommended 30 specific areas in which opportunities are available. Six disease-based concentration areas in which UAB is considered a leader or has the potential for excellence were also identified. These include:

- Cancer
- Cardiovascular Biology
- Diabetes, Obesity and Metabolic Disease
- Immunology, Autoimmunity, and Transplantation
- Infectious Diseases and Vaccines
- Neurosciences

THE *CHRONICLE OF HIGHER EDUCATION* RANKED UAB tenth out of 375 research universities in terms of the scholarly activity of their PhD faculty.

THE *SCIENTIST* NEWSPAPER RANKED UAB for the last four years as one of the 10 best places in the U.S. for postdocs to work.

DAVID RANDOLPH, M.D., (PEDIATRICS) BECAME ONE of UAB's first awardees of the brand new Transition to Independence Awards from the NIH. This distinction allows Randolph to be awarded a K99-Career Transition Award which will later be transferred to an R00-Research Transition Award when he becomes an independent faculty member.

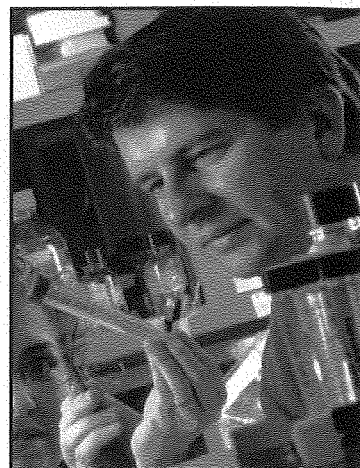
THE UAB MINORITY HEALTH RESEARCH CENTER (MHRC) was awarded a five-year, \$4.5 million grant to fund continued development of the MHRC as a comprehensive health disparities research center by The National Center on Minority Health and Health Disparities.

THE NATIONAL INSTITUTES OF HEALTH (NIH) has picked UAB as one of just five institutions nationwide—and the only university in the Southeast—to lead a massive, national research assault on congestive heart failure. UAB is receiving \$18 million to fund a Specialized Center of Clinically Oriented Research program focusing specifically on heart failure research.

IN 2008, UAB RECEIVED THE LARGEST SINGLE NIH GRANT in the institution's history. UAB was awarded \$26.9 million to establish the Center for Clinical and Translational Science at UAB. A Key focus of the grant is increasing interaction between UAB researchers and the community to share information about community needs and available resources.

THE EVELYN F. MCKNIGHT BRAIN INSTITUTE at

UAB has been made possible by a generous grant from the McKnight Brain Research Foundation and is located in the Richard C. and Annette N. Shelby Interdisciplinary Biomedical Research Building. The Institute promotes research and investigation of the brain in the fundamental mechanisms that underlie the neurobiology of memory, with a clinical relevance to the problems of age-related memory loss.



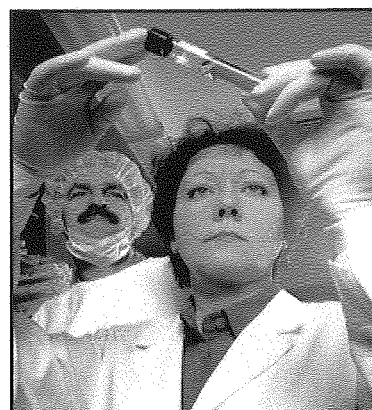
THE UAB COMPREHENSIVE DIABETES CENTER, which is also housed in the Shelby Building, provides diabetes research and treatment programs in an effort to treat and cure the serious and growing national health crisis of diabetes.

UAB HAS BEEN DESIGNATED BY THE NIH AS ONE OF ONLY SIX Diabetes Research and Training Centers in the country, putting UAB at the forefront in the development of new methods to treat, prevent, and ultimately cure diabetes and its complications. The \$6.3 million award over five years will help increase UAB's diabetes initiatives.

UAB WAS AWARDED A FIVE-YEAR, \$16.3 million grant to support clinical and laboratory research in the U.S., Europe, and Africa to study changes that occur in the immune system and in the HIV virus in people newly infected with HIV. The grant is part of the Grand Challenges in Global Health Initiative funded by the Bill & Melinda Gates Foundation.

UAB WAS NAMED AN AMERICAN PARKINSON DISEASE ASSOCIATION (APDA) Center for Advanced Research. One of nine APDA-supported centers in major research institutions across the United States.

JIRI MESTECKY, M.D., (MICROBIOLOGY) RECEIVED the 2007 Czech Mind Prize. This prize is the highest scientific honor in the Czech Republic. Recipients often include Czech nationals working in other countries.



TIM TOWNES, M.D., (BIOCHEMISTRY) ALONG WITH a team from the Whitehead Institute, reported successfully curing sickle cell anemia in mouse models using induced pluripotent stem (iPS) cells, a new stem cell technique that uses skin cells and does not require embryos.

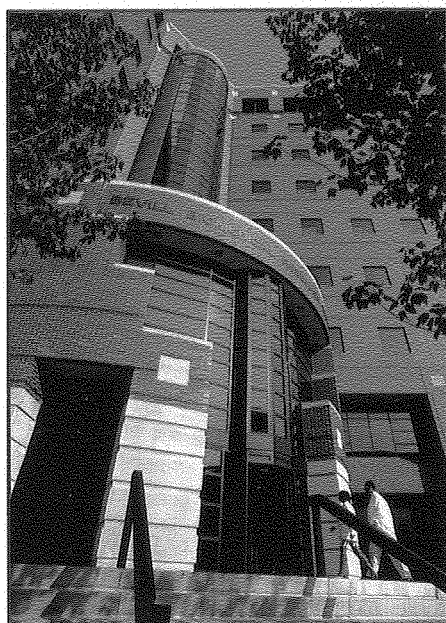
THE DEPARTMENT OF MICROBIOLOGY ESTABLISHED a new program in Mycobacterium Tuberculosis, which includes bacterial geneticists and immunologists who are identifying new drug targets to overcome this microbe's ability to resist antibiotics. Scientists are also identifying new therapeutic targets in anthrax that focus on the bacterial spore.

EARLY TESTS OF A CYSTIC FIBROSIS DRUG PROVE promising as the clinical trial data shows the drug diminishes basic signs of the disease. Dr. Steven M. Rowe is heading UAB's portion of the trial.

UAB'S COMPREHENSIVE CANCER CENTER was awarded an \$11.5 million renewal of its Specialized Program of Research Excellence grant for breast cancer research and treatment.

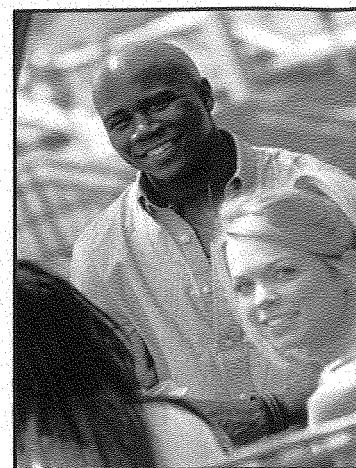
ROBERT J. STANLEY, M.D., PROFESSOR OF RADIOLOGY, will receive a 2008 American Roentgen Ray Society (ARRS) Gold Medal for Distinguished Service to Radiology. This award is the organization's highest honor and recognizes individuals who have made distinguished contributions to the profession of radiology and to the improvement of patient care.

THE DEEP SOUTH RESOURCE CENTER FOR MINORITY AGING RESEARCH has been established and will be housed within UAB's Center for Aging. The Center will be aimed at increasing research into the health problems of older adult minorities.



Campus-Wide

UAB IS AMONG 165 SCHOOLS in the Princeton Review's *America's Best Value Colleges*. Students comment that UAB is a "mecca of multiculturalism...our professors are very knowledgeable...opportunities for internships abound...this administration is really bending over backwards to improve every aspect of UAB."



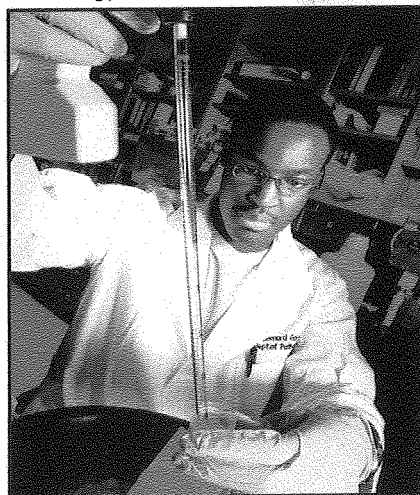
THE UNIVERSITY RECENTLY COMPLETED a re-accreditation process with the Southern Association of Colleges and Schools (SACS). SACS reviewed UAB's Quality Enhancement Place (QEP), which is focused on improving fundamental learning competencies at the undergraduate level. The QEP calls for improved student learning in writing, quantitative literacy, and ethics and civic responsibility. The review team said UAB's program was so well conceived that they recommend no changes. SACS is using UAB's program as a model for other schools.

SINCE 2002, UAB HAS PRODUCED seven Alpha Lambda Delta Scholars, five Barry M. Goldwater Scholars, four Phi Kappa Phi Fellows, and two Harry S. Truman Scholars. Just in the past year, there have been three Fulbright Scholars, bringing the total awards to six.

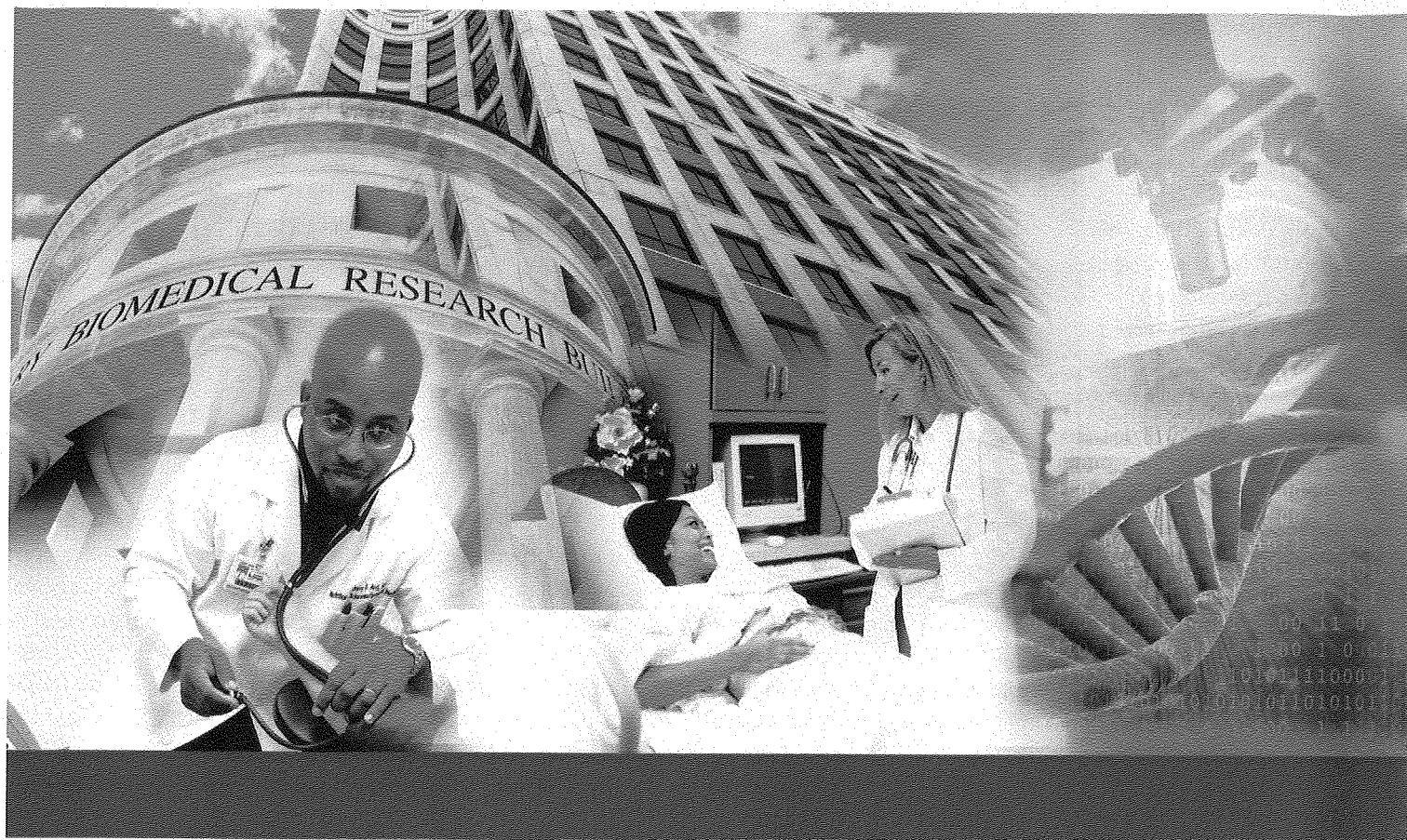
UAB'S OVERALL ECONOMIC IMPACT on the Birmingham-Metropolitan Area reaches more than \$3 billion, and UAB is responsible for creating some 53,000 full-time equivalent jobs throughout the state. For every dollar the state invests in UAB, the University returns \$12.

UAB MADE *SOUTHERN BUSINESS AND DEVELOPMENT* magazine's top 10 list of universities in the South that drive economic development.

THE UAB RESEARCH FOUNDATION'S commercialization of faculty discoveries has, since 1986, created more than \$31 million in royalty and license fees, generating 330 licensing agreements, and negotiated more than \$22 million in research agreements for the University. It has also generated 33 startup companies based on its technologies and distributed more than \$25 million back to the University, its inventors, and its various academic departments.



KNOWLEDGE SPIRIT ACHIEVEMENT DISCOVERY OPPORTUNITY VISION



UAB UNIVERSITY
DEVELOPMENT

Daphne B. Powell
Director of Stewardship
AB 1228
1530 3rd Avenue South
Birmingham, Alabama 35294-0112
205.934.1807
Daphnep@uab.edu

This publication was published in house.