

January 14, 2016

The McKnight Brain Research Foundation
c/o Ms. Melanie Cianciotto
Vice President for Foundations and Endowments
SunTrust Bank
200 South Orange Avenue
SOAB 10th Floor
Orlando, Florida 32801

Dear Ms. Cianciotto,

It is an honor to provide you with an update on the ongoing impact of The McKnight Brain Research Foundation's extraordinary philanthropy at UAB and within the Evelyn F. McKnight Brain Institute. Our commitment to excellence starts with the people that believe in our mission, and the Foundation's contributions are an incredible investment in the UAB professionals who devote themselves to aging-related memory disorders research every day.

We are fortunate to have the Foundation's outstanding support as we continue to bring scientific progress to the field. Philanthropic support is critical to accelerating the pace of discovery and ensuring that our work continues to shape the lives of patients around the world. The research efforts funded by the Foundation have great potential to improve the quality of life of so many people, and I want to personally thank you for believing in UAB and the important work we are doing. Please know how much we value your partnership with us.

I want to highlight that we have made tremendous progress in our recruitment efforts for translational medicine experts for both the *Geropsychiatry Research Chair* and the *F. Cleveland Kinney Endowed Chair in Geriatric Psychiatry*. We have two promising candidates who visited campus this past fall, and each are returning in the near future for a second site visit and discussions. We are excited about these individuals potentially joining our team of McKnight Brain Institute Investigators.

If you have any questions or need any additional information, please do not hesitate to contact me or Daphne B. Powell, Senior Director of Stewardship and Donor Relations, at (205) 934-1807, or by email to daphnep@uab.edu. Please share my gratitude with all of the trustees of the Evelyn F. McKnight Brain Research Foundation. We cannot thank you enough for your support.

Sincerely,



Tom Brannan
Interim Vice President for
Development and Alumni

Enclosure



Annual Report

2015

J. David Sweatt, Ph.D.

Professor

Evelyn F. McKnight Endowed Chair, Department of Neurobiology

Director, Evelyn F. McKnight Brain Research Institute

Director, Civitan International Research Center

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

Associate Professor

Virginia B. Spencer Endowed Professor, Department of Neurology

Co-Director, Evelyn F. McKnight Brain Research Institute

Co-Director, Center for Neurodegeneration and Experimental Therapeutics

Director, Alzheimer's Disease Center

The University of Alabama at Birmingham

Shelby Interdisciplinary Biomedical Research Building

1825 University Boulevard

Birmingham, Alabama 35294

OVERALL TABLE OF CONTENTS

Annual Report for the
McKnight Brain Research Foundation
Report Period: 2014/2015
Institution: The Evelyn F. McKnight Brain Institute at
The University of Alabama at Birmingham

1.	Overview	1.2
2.	Summary of Scientific Achievements Since Last Report	1.4
3.	Publication in Peer Reviewed Journals	1.5
4.	Publications (Other)	1.5
4.	Presentations at Scientific Meetings	1.5
5.	Presentations at Public (Non-Scientific) Meetings or Events	1.5
6.	Awards and Honors	1.5
7.	Faculty	1.5
8.	Trainees, Post-Doctoral, Pre-Doctoral, Other	1.6
9.	Clinical/Translational Programs	1.6
10.	Technology	1.6
11.	Budget Update	1.6
12.	Educational Programs Focusing on Age Related Memory Loss	1.6
13.	Collaborative Programs with other McKnight Institutes, Institutions and Research Programs	1.7
14.	Collaborative Programs with Non McKnight Institutes, Institutions and Research	1.7
15.	Prohibited Purpose Statement	1.7
16.	Modification to Purpose Statement	1.7
17.	Purpose Progress	1.7
18.	Progress Compared to Original Goals	1.7
19.	Negative Events Statement	1.8
20.	General Comments	1.8
21.	Submission Signature	1.8
22.	Finance	2.1
23.	Listing of Investigators and Individual Faculty Reports	3.1
24.	Appendices	4.1
25.	Articles and Other News Items	5.1

INSTITUTE DIRECTOR'S OVERALL REPORT

ANNUAL REPORT

McKnight Brain Research Foundation Report for Evelyn F. McKnight Brain Institute The University of Alabama at Birmingham October 2014 – September 2015

This report provides an overview and summary of the activities and accomplishments for 2015 of the UAB MBI as a whole. The first section is an executive summary prepared according to the suggested 17-point format provided by the MBRF. The second section is an overall list of the Investigators of the UAB MBI. In the third section, UAB MBI Investigators with an appointment at the faculty level have prepared his or her own individual annual report for 2015, which is in a shortened and abbreviated format and includes scientific achievements, publications, awards, and collaborations. Dr. Sweatt has prepared a separate scientific report as Evelyn F. McKnight Endowed Chair in the final section. The appendices include copies of documents referred to in the summary.

Overview

We are of course deeply grateful that the McKnight Brain Research Foundation has partnered with UAB to provide vital funding to the Institute, including the establishment of a permanent endowment to support the Institute. Highlights for the past year for the Evelyn F. McKnight Brain Institute at UAB include:

- UAB installed a new MRI system that will be the focus of human brain imaging research, replacing a magnet that is approaching its obsolescence. The new system, a Siemens Prisma 3T scanner, is considered the state-of-the-art scanner for this kind of research, and will position UAB neuroimaging research well for many years to come. The scanner is up and running, and scans have been conducted on initial subjects as part of calibrating the system and optimizing the scanning protocols. In accordance with the terms of the UAB-MBRF agreement, no MBRF funds were used for this project.
- There is a great deal of excitement about the upcoming McKnight Brain Aging Registry (MBAR) study, and much effort has been invested by many individuals to prepare for the first subject visits. Cognitive batteries and imaging protocols have been defined and submitted to our IRB for approval, and the arrival of the new Prisma MRI is a critical enabling development. Our target date for the first patient visit is February 1, 2016.
- The MBAR study will provide tremendous opportunities for learning more about cognitive aging, and UAB MBI investigators have already begun planning ways to leverage the study. Dr. Erik Roberson led the submission of a P30 proposal to the NIA Alzheimer's Disease Centers program that would allow for longitudinal follow-up of MBAR participants, as well as neuropathological examination of their brains at death. Dr. Kristina Visscher and Dr. Karlene Ball have submitted an R01 application that would support a Phase III study of cognitive enhancement protocols on activities of daily living in MBAR participants. Both of these applications are currently under review, and additional studies are in the planning stages.
- Dr. Erik Roberson was appointed Co-Director of the UAB MBI. Dr. Roberson is the Virginia B. Spencer Endowed Professor of Neuroscience and also leads the Center for Neurodegeneration and Experimental Therapeutics (with co-director Andy West) and the Alzheimer's Disease Center at UAB. As a physician-scientist working at the interface between basic science animal model studies and human clinical research, Dr. Roberson will help focus the translational research of the MBI.

- Dr. Roberson received the Derek Denny Brown Award from the American Neurological Association (ANA) this year, the ANA's most prestigious award.
- Co-Director Dr. Lori McMahon was appointed Dean of the Graduate School at UAB. UAB's graduate enrollment, up 43 percent in the past decade, is the highest among Alabama universities, at 5,937 in fall 2014. The diverse group, which is two-thirds female and nearly 30 percent minority, is pursuing degrees in 50 master's programs, 37 doctoral programs, and eight education specialist programs. Importantly, this position does not occupy Dr. McMahon's full effort, and she will continue to operate her laboratory, including training students and performing experiments.
- Dr. David Sweatt assumed leadership of the Civitan International Research Center at UAB. One of his major initiatives for this center, which is focused on cognitive impairments associated with intellectual disability disorders, is a precision medicine and epigenomics/bioinformatics initiative. The core facilities that will be established on the first floor of the Civitan building will also be available and will be utilized to support MBI studies on the epigenomics of cognitive aging.
- Candidates for two endowed faculty positions, the F. Cleveland Kinney Endowed Chair and the Geropsychiatry Research Chair, visited UAB for first visits in the fall. Second visits are planned in early 2016.
- The NIH awarded UAB funding for a Nathan Shock Center of Excellence in the Basic Biology of Aging. This is one of only five such centers in the U.S. and is led by MBI member Dr. Steve Austad, Chair of the Department of Biology at UAB. Each Nathan Shock Center has specialized areas of research emphasis. UAB is specializing in understanding how energetics affects aging. The Nathan Shock Centers' services are provided by specialized research cores, small startup grants, and the organization of meetings and symposia to highlight specific areas of research.
- The Roadmap Scholars Program, led by Dr. Farah Lubin and Dr. Lori McMahon, had a tremendous start in its first year. The first class of neuroscience graduate students enrolled in the program includes eight students from underrepresented backgrounds. The first NEURAL (National Enhancement of Underrepresented Academic Leaders) conference was held June 24-26 at UAB, with three keynote speakers representing some of the most prestigious leaders in neuroscience: Dr. Roger Nicoll, Dr. Erich Jarvis, and Dr. Kristen Harris. The conference was attended by approximately 75 students including 40 non-UAB students visiting from 20 different universities across the U.S.
- Dr. John Hablitz and Dr. David Sweatt collaborated to publish a paper in the high impact journal, *Science Signaling*, demonstrating a critical role for DNA methylation in homeostatic synaptic plasticity. Homeostatic plasticity is the process by which overall network activity is maintained at normal levels when some synapses undergo potentiation or depression. This form of synaptic plasticity is critical for normal neuronal functioning and studies in collaboration with Dr. Carol Barnes indicate that this type of plasticity is disrupted in aging.
- Dr. Jeremy Day received a prestigious Avenir Award from the NIH. The Avenir (meaning "future" in French) Award program supports early stage investigators proposing highly innovative studies that open new areas of research for the genetics or epigenetics of addiction. Dr. Day was one of only six recipients of these awards.
- Two UAB faculty received prestigious awards from UAB. Dr. David Sweatt received the Dean's Award for Excellence in Research, the highest research award given by UAB. Dr. Gwendalyn King received the Dean's Award for Excellence in Mentorship, recognizing her efforts in mentoring graduate students.
- Dr. Vladimir Parpura was elected President-Elect of the American Society for Neurochemistry.

1. Summary of Scientific Achievements Since Last Report

Individual McKnight Investigators' scientific accomplishments are noted in a separate section. The next few paragraphs highlight a few of the principal discoveries from the Institute this year.

Dr. John Hablitz and Dr. David Sweatt collaborated to publish a paper in the high impact journal, *Science Signaling*, demonstrating a critical role for DNA methylation in homeostatic synaptic plasticity. Homeostatic plasticity is the process by which overall network activity is maintained at normal levels when some synapses undergo potentiation or depression. This form of synaptic plasticity is critical for normal neuronal functioning and studies in collaboration with Dr. Carol Barnes indicate that this type of plasticity is disrupted in aging.

Dr. Erik Roberson and Dr. Harald Sontheimer collaborated to examine the effects of vascular amyloid deposition on vascular function. Vascular amyloid is the accumulation of amyloid material in the walls of cerebral blood vessels and is a common accompaniment of aging. There is a well-known risk of bleeding from affected vessels, but less was known about how it affected vascular function and the gliovascular unit, which is the ability of glial cells to regulate vascular tone. In a paper featured on the cover of *Brain*, these McKnight Institute investigators found that vascular amyloid impaired the ability of the gliovascular unit to regulate vessel tone. This would impair the ability of blood flow to be regulated in response to changing neuronal activity and could contribute to impaired neuronal function in affected brains.

McKnight Investigator Dr. Lucas Pozzo-Miller published his lab's discovery of an important new signaling mechanism for regulating synaptic function, a finding which has significant implications for synaptic plasticity and memory formation in the CNS with aging. The discovery, published in the journal *Hippocampus*, investigates the epigenetic regulator MeCP2. The gene Methyl-CpG-binding Protein-2 (MeCP2) is associated with intellectual disabilities, and loss-of-function mutations in the gene encoding this transcriptional regulator lead to profound learning and memory deficits in humans. Neuronal dysfunction and changes in cortical excitability occur in MeCP2-deficient patients, including hippocampal network hyperactivity and higher frequency of spontaneous multiunit spikes in the CA3 cell body layer. The Pozzo-Miller lab discovered impaired synaptic inhibition and an excitation/inhibition (E/I) imbalance in the hippocampus of acute slices from symptomatic Mecp2 knockout male mice. Moreover, they found that synaptic currents are smaller and less frequent in hippocampal fast-spiking basket cells of MeCP2-deficient mice, suggesting an impaired glutamatergic drive in this interneuron population. These results demonstrate that a loss-of-function mutation in the epigenetic regulator MeCP2 causes impaired excitation/inhibition balance onto hippocampal pyramidal neurons, leading to a hyperactive hippocampal network, likely contributing to memory dysfunction in individuals with a disruption of this signaling pathway. These findings suggest that this may be one locus whereby aging-associated changes in DNA methylation leads to age-related cognitive dysfunction.

The laboratory of Dr. Gwen King in the UAB MBI made an important technical breakthrough this past year in studies of the aging-related protein Klotho. Although antibodies are commercially available to allow investigation into the biology of the age-regulating protein Klotho, problems with commercial antibody specificity and application functionality have been significant barriers to progress. Chief among these limitations was the inability of current tools to allow in vivo validation of binding partners originally identified through transfection of tagged proteins. To overcome this barrier, the King lab generated a series of hybridoma cell lines by immunizing rats with a GST-KL1 fusion protein. Purified antibodies generated from these cell lines differentially detected human or mouse Klotho protein via Western blot,

immunocyto/histochemistry, and immunoprecipitation. Specificity of antibody binding to Klotho was confirmed by mass spectrometry following immunoprecipitation. With this confidence in antibody specificity, the lab is now positioned to use these tools to further investigate the CNS localization and function of Klotho, which is a potent regulator of organismal aging and of cognitive function in the CNS.

2. Publications in Peer Reviewed Journals

Investigators at the UAB MBI published a total of 68 research papers, reviews, and commentaries in peer-reviewed journals in 2015. The journals in which these papers were published included many of the leading scientific journals in the discipline of neuroscience.

3. Publications (Other)

- **Books**
One
- **Book Chapters**
One

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

Investigators at the UAB MBI presented a total of 76 scientific presentations in 2015. UAB MBI Investigators presented their work at numerous prestigious institutions and national meetings, including the American Neurological Association, the Society for Neuroscience, the American College of Neuropsychopharmacology, a Gordon Conference, the American Epilepsy Society, and a variety of other universities and biotech forums.

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 2015 is appended to this report.

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

Investigators at the UAB MBI presented 16 public-forum presentations in 2015.

6. Awards and Honors

Investigators at the UAB MBI received several national-level awards and honors in 2015. Dr. Erik Roberson won the Derek Denny-Brown Award, the most prestigious award of the American Neurological Association. Dr. Jeremy Day won one of only six Avenir Awards from the NIH. Dr. Gwendalyn King won the Dean's Award for Excellence in Mentoring, and Dr. David Sweatt won the Dean's Award for Excellence in Research.

7. Faculty

Two active searches are underway for MBI-affiliated positions in the Department of Psychiatry & Behavioral Neurobiology, the *Geropsychiatry Research Chair* and the *F. Cleveland Kinney Endowed Chair in Geriatric Psychiatry*. Candidates visited UAB for initial visits in the fall, and second visits are planned for early 2016.

8. Trainees, Post Doctoral, Pre-Doctoral, Other

The labs of MBI faculty currently involve the training of 37 graduate students and six post-doctoral fellows.

9. Clinical/Translational Programs

A. New Programs

The McKnight Brain Aging Registry, with both cognitive and imaging projects, will begin recruiting participants in early 2016. This project will utilize the new state-of-the-art Prisma MRI recently acquired at UAB, and the first participant visit is planned for February.

B. Update on Existing Clinical Studies

Not applicable

C. New Treatments

Not applicable

D. Drug Trials, Future Research and/or Clinical Initiatives

Not applicable

10. Technology

A. Patent Applications

Dr. Sweatt's laboratory (through UAB) filed an international patent application for histone H2A.Z as a novel target for memory enhancement.

B. Revenue Generated from Technology

Not applicable

11. Budget Update

A full financial report for 2014/2015 is included as Section 2.

12. Educational Programs Focusing on Age-Related Memory Loss

A. Scientific

The MBI was instrumental in establishing the new undergraduate honors Neuroscience major at UAB. It is a unique program—a joint offering between the undergraduate College of Arts and Sciences and the School of Medicine. This will be a recruiting platform for future medical and graduate students interested in memory research. For example, several of our 2014/2015 graduates from this program are currently in (or applying to) medical school or MD/PhD programs at UAB.

B. Public

Not applicable

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

UAB MBI Investigators have identified a total of 20 inter- and intra-MBI collaborations, representing all three other MBIs. More details on these collaborations are noted in the section with the individual investigators' data.

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

UAB MBI Investigators have identified a total of 47 inter- and intra-institutional collaborations locally, nationally, and internationally.

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

No

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

No

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

Yes

18. Briefly describe your progress compared to the original goals.

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 approved for renewed funding in 2009. We have focused on recruiting new faculty members as was originally proposed. The quality of the new investigators has been uniformly excellent. The current membership of the UAB MBI comprises 38 investigators, with a nicely diverse distribution of assistant, associate, and full professors including six current or former department chairs and one dean. The majority of the investigators are new appointees to the Institute since 2006, an exceptional expansion given the state of the economy over that time-frame.

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 full occupancy with Drs. Roberson, Lubin, Gamlin, Nakazawa, Ubogu, Goldberg, and Herskowitz occupying new labs there. Both the Neurology and Psychiatry departments are undertaking collaborative recruitments with the MBI to recruit additional new MBI-relevant professors into the MBI. Two important core laboratories, the *MBI Mouse Behavioral Assessment Core* and the *McKnight Rodent Physiological Assessment Core*, are in operation and provide an excellent platform for inter-Institute collaborations. These two cores 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 allow for collaborative opportunities with the other MBIs, which in general are not historically strong in the area of mouse genetic engineering. Finally, as already mentioned the new McKnight Inter-Institute Epigenetics and Bioinformatics Initiative provides a powerful platform for collaboration and cross-fertilization in the area of the epigenetics of cognitive aging.

19. 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

20. 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.

No additional comments.

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



J. David Sweatt, Ph.D.

Professor

Evelyn F. McKnight Endowed Chair

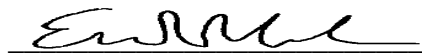
Director, Evelyn F. McKnight Brain Institute

Chairman, Department of Neurobiology

UAB School of Medicine

January 14, 2016

Date



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

Associate Professor

Virginia B. Spencer Endowed Professor

Co-Director, Evelyn F. McKnight Brain Institute

UAB School of Medicine

January 14, 2016

Date

FINANCE

McKnight Brain Research Foundation

Financial Summary Format:

(Institute) and/or (Endowed Chair)

Summary for 12 months ended 09/30/2015

Account Name: Evelyn F. McKnight Brain Institute Endowed Support Fund

A.	Beginning Balance on <u>10/01/2014</u>	\$ <u>5,481,153</u>
B.	Investment Growth	\$ <u>(721,442)</u>
C.	Distributions	\$ <u>250,968</u>
D.	Additional Contribution	\$ <u>0.00</u>
E.	Ending Balance on <u>09/30/2015</u>	\$ <u>5,010,679</u>

DEFINITIONS

DISTRIBUTION is the money transferred from the account to the spendable/operating account for the designated use.

BALANCE is the market value of the account as of the first or last day of the reporting year.

ADDITIONAL CONTRIBUTION is additional contribution by MBRF, the reporting institution, match etc.

INVESTMENT GROWTH (Loss) is the total undistributed interest, dividends, and realized and unrealized gains and losses.

BALANCE is the value of the account's corpus including all contributions, and applicable state match monies as of the date indicated.

McKnight Brain Research Foundation

Financial Summary Format:

(Institute) and/or (Endowed Chair)

Summary for 12 months ended 09/30/2015

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

A.	Beginning Balance on <u>10/01/2014</u>	\$ <u>1,557,271</u>
B.	Investment Growth	\$ <u>(204,972)</u>
C.	Distributions	\$ <u>71,304</u>
D.	Additional Contribution	\$ <u>0.00</u>
E.	Ending Balance on <u>09/30/2015</u>	\$ <u>1,423,603</u>

DEFINITIONS

DISTRIBUTION is the money transferred from the account to the spendable/operating account for the designated use.

BALANCE is the market value of the account as of the first or last day of the reporting year.

ADDITIONAL CONTRIBUTION is additional contribution by MBRF, the reporting institution, match etc.

INVESTMENT GROWTH (Loss) is the total undistributed interest, dividends, and realized and unrealized gains and losses.

BALANCE is the value of the account's corpus including all contributions, and applicable state match monies as of the date indicated.

**MCKNIGHT BRAIN INSTITUTE AT UAB
2015 ANNUAL REPORT
FINANCIAL SUPPLEMENT**

In compliance with Section 6.3 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 Institute (MBI) at UAB.

In compliance with Sections 9.2.1.2 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 7, and 9.1.5.3, 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	MBRF Chair, Gift and Endowment Distributions **	MBRF Funds Expended or Encumbered	Matching Fund Expended or Encumbered Endowment Distributions	Matching Funds Expended or Encumbered
Grand Totals	MBRF Prior Agreement	\$6,000,000	\$598,150	\$5,911,757	\$ -	\$ 12,357,436
2010	MBRF New Agreement	\$1,000,000		\$1,000,000		
		\$500,000				
	Sweatt Salary			\$81,617		
	Rumbaugh Salary			\$26,966		
	L. Wadiche Salary			\$72,485		
	J. Wadiche Salary			\$78,526		
	V. Parpura Salary			\$156,829		
	K. Visscher Salary			\$117,192		
	R. Lester Salary			\$12,594		
	F. Lubin Salary			\$11,677		
	J. Hablitz Salary			\$30,723		
	K. Speed Salary			\$24,455		
	V. Hixon Salary			\$6,734		
	I. Rivera Salary			\$4,851		
	M. Kilgore Salary			\$26,245		
	One Pilot Project			\$25,000		
	Evelyn F. McKnight Interdisciplinary Retreat			\$10,808		\$4,000

	V. Hixon and M. Kilgore Travel			\$2,833		
	M. Olsen Start Up Package					\$56,000
	G. King Start Up Package			\$35,000		\$65,000
	F. Cleveland Kinney Endowed Chair in Geriatric Psychiatry *				\$74,014	\$1,500,050
	Geropsychiatry Research Chair *				\$102,544	\$1,222,896
	Patsy W. and Charles A. Collat Scholar in Neuroscience - D. Geldmacher					\$500,000
	Dixon Scholar in Neurology - M. Gray					\$245,000
	Parpura Start Up Package			\$40,000		
	F. Lubin Start Up Package			\$8,750		
	J. Wadiche Start Up Package			\$55,000		
	L. Wadiche Start Up Package			\$10,000		
	MBRF Chair Spendable Earnings		\$83,499			
	MBRF Gift Earnings **		\$61,169			
	MBRF Institute Spendable Earnings		\$55,984			
	Previous MBRF Agreement Residual		\$409,277			
FY 10 Totals		\$1,500,000	\$609,929	\$1,838,285	\$176,558	\$4,892,946
2011	MBRF New Agreement	\$1,000,000		\$1,000,000		
		\$500,000				
	Sweatt Salary			\$74,605		
	L.Wadiche Salary			\$74,297		
	J. Wadiche Salary			\$80,489		
	V. Parpura Salary			\$156,829		
	K. Visscher Salary			\$103,503		
	F. Lubin Salary			\$55,208		

	J. Hablitz Salary			\$30,723		
	K. Speed Salary			\$12,505		
	V. Hixon Salary			\$6,532		
	S. Hyman Salary			\$4,924		
	G. Kass Salary			\$12,469		
	S. Ewell Salary			\$6,417		
	Evelyn F. McKnight Interdisciplinary Retreat			\$10,483		\$5,000
	F. Cleveland Kinney Endowed Chair in Geriatric Psychiatry *				\$67,724	
	Geropsychiatry Research Chair *				\$93,795	
	Warren Family Scholar					\$600,000
	Patsy W. and Charles A. Collat Scholar in Neuroscience - D. Geldmacher					\$300,000
	S. Phillips Development Grant					\$10,000
	SOM Additional Support					\$50,000
	Parpura Start Up Package			\$25,000		
	J. Wadiche Start Up Package			\$11,760		
	L. Wadiche Start Up Package			\$13,290		
	A. Theibert - Support			\$15,000		
	R. Lester - Support			\$20,000		
	MBRF Chair Spendable Earnings		\$79,969			
	MBRF Gift Earnings **		\$59,606			
	MBRF Institute Spendable Earnings		\$100,316			
	Previous MBRF Agreement Residual		\$317,881			
FY 11 Totals		\$1,500,000	\$557,772	\$1,714,034	\$161,519	\$965,000

2012	MBRF New Agreement	\$1,000,000		\$1,000,000		
	Sweatt Salary			\$74,432		
	L. Wadiche Salary			\$77,984		
	J. Wadiche Salary			\$81,004		
	V. Parpura Salary			\$153,611		
	K. Visscher Salary			\$89,463		
	F. Lubin Salary			\$93,245		
	J. Hablitz Salary			\$30,092		
	K. Speed Salary			\$13,601		
	V. Hixon Salary			\$6,528		
	G. King Salary			\$33,836		
	S. Ewell Salary			\$14,917		
	Evelyn F. McKnight Interdisciplinary Retreat			\$11,938		\$3,062
	F. Cleveland Kinney Endowed Chair in Geriatric Psychiatry *				\$65,269	
	Geropsychiatry Research Chair *				\$90,396	
	Warren Family Scholar *				\$39,775	\$1,000,000
	Jarman F. Lowder Endowed Professorship in Neuroscience - L. McMahon *				\$25,723	\$505,519
	Virginia B. Spencer Endowed Professorship in Neuroscience - E. Roberson *				\$24,041	\$500,000
	Patsy W. and Charles A. Collat Scholar in Neuroscience - D. Geldmacher *				\$14,125	
	L. Dobrunz - CCTS Pilot Project					\$15,000
	SOM Additional Support					\$50,000
	Evelyn F. McKnight Advertisement			\$4,463		

	L. Dobrunz - Pilot Project			\$52,000		
	A. Theibert - Support			\$10,000		
	R. Lester - Support			\$5,000		
	D. Sweatt - Travel			\$771		
	V. Hixon - Travel			\$1,214		
	MBRF Chair Spendable Earnings		\$73,369			
	MBRF Gift Earnings **		\$ 6,546			
	MBRF Institute Spendable Earnings		\$145,708			
	Previous MBRF Agreement Residual		\$174,079			
FY 12 Totals		\$1,000,000	\$399,702	\$1,754,099	\$259,329	\$2,073,581
2013	MBRF New Agreement	\$1,000,000		\$1,000,000		
	Sweatt Salary			\$75,262		
	L. Wadiche Salary			\$56,980		
	J. Wadiche Salary			\$81,979		
	V. Parpura Salary			\$88,679		
	K. Visscher Salary			\$79,244		
	J. Hablitz Salary			\$30,233		
	K. Speed Salary			\$11,311		
	V. Hixon Salary			\$6,531		
	Evelyn F. McKnight Interdisciplinary Retreat			\$11,043		\$4,500
	F. Cleveland Kinney Endowed Chair in Geriatric Psychiatry *				\$66,963	
	Geropsychiatry Research Chair *				\$92,742	
	Warren Family Scholar *				\$75,495	

	Jarman F. Lowder Endowed Professorship in Neuroscience - L. McMahon *				\$26,395	
	Virginia B. Spencer Endowed Professorship in Neuroscience - E. Roberson *				\$24,664	
	Patsy W. and Charles A. Collat Scholar in Neuroscience - D. Geldmacher *				\$19,400	
	SOM Additional Support					\$275,000
	SOM McKnight Recruitment					\$750,000
	L. Dobrunz - Pilot Project			\$7,000		
	A. Theibert - Support			\$35,000		
	V. Hixon - Travel			\$1,084		
	MBRF Chair Spendable Earnings		\$69,969			
	MBRF Gift Earnings **		\$3,741			
	MBRF Institute Spendable Earnings		\$188,781			
	Previous MBRF Agreement Residual		\$10,000			
FY 13 Totals		\$1,000,000	\$272,491	\$1,484,346	\$305,659	\$1,029,500
2014	MBRF New Agreement	\$1,000,000		\$1,000,000		
	Sweatt Salary			\$65,918		
	L.Wadiche Salary			\$53,000		
	J. Wadiche Salary			\$53,684		
	V. Parpura Salary			\$57,203		
	K. Visscher Salary			\$78,060		
	J. Hablitz Salary			\$7,506		
	V. Hixon Salary			\$6,970		

	Evelyn F. McKnight Interdisciplinary Retreat			\$ -		\$1,000
	F. Cleveland Kinney Endowed Chair in Geriatric Psychiatry *				\$68,424	
	Geropsychiatry Research Chair *				\$94,764	
	Warren Family Scholar *				\$77,142	
	Jarman F. Lowder Endowed Professorship in Neuroscience - L. McMahon *				\$26,972	
	Virginia B. Spencer Endowed Professorship in Neuroscience - E. Roberson *				\$25,202	
	Patsy W. and Charles A. Collat Scholar in Neuroscience - D. Geldmacher *				\$25,519	
	SOM Additional Support					\$375,000
	Jeremy Herskowitz Start Up Package					\$1,000,000
	Matthew Goldberg Start Up Package					\$1,000,000
	Kazu Nakasawa Start Up Package					\$925,000
	V. Hixon - Travel			\$1,416		
	MBRF Chair Spendable Earnings		\$71,896			
	MBRF Gift Earnings **		\$1,674			
	MBRF Institute Spendable Earnings		\$243,000			
	Previous MBRF Agreement Residual		\$5,000			
FY 14 Totals		\$1,000,000	\$321,570	\$1,323,757	\$318,023	\$3,301,000

2015	MBRF New Agreement					
	Sweatt Salary			\$63,735		
	L. Wadiche Salary			\$43,752		
	J. Wadiche Salary			\$36,587		
	V. Parpura Salary			\$48,465		
	K. Visscher Salary			\$98,068		
	V. Hixon Salary			\$10,202		
	Evelyn F. McKnight Interdisciplinary Retreat			\$ -		\$1,000
	F. Cleveland Kinney Endowed Chair in Geriatric Psychiatry *				\$70,077	
	Geropsychiatry Research Chair *				\$97,054	
	Warren Family Scholar *				\$79,006	
	Jarman F. Lowder Endowed Professorship in Neuroscience - L. McMahon *				\$27,623	
	Virginia B. Spencer Endowed Professorship in Neuroscience - E. Roberson *				\$25,811	
	Patsy W. and Charles A. Collat Scholar in Neuroscience - D. Geldmacher *				\$25,112	
	SOM Additional Support					\$1,000,000
	V. Hixon - Travel			\$1,501		
	MBRF Chair Spendable Earnings		\$71,304			
	MBRF Gift Earnings **		\$1,009			
	MBRF Institute Spendable Earnings		\$250,968			
	Previous MBRF Agreement Residual		\$2,500			

FY 15 Totals		\$ -	\$325,781	\$302,310	\$324,683	\$1,001,000
Grand Totals		\$6,000,000	\$2,487,245	\$8,416,831	\$1,545,771	\$13,263,027
	* denotes encumbered endowment match					
	** Original MBRF gift was set up as an interest bearing account. These items account for the interest over time (\$279,608 in the prior agreement and \$127,321 in the current agreement).					

Financial Schedule for the Evelyn F. McKnight Brain Institute at UAB					
	<i>MBRF CONTRIBUTION</i>		<i>UAB MATCH</i>		
Date	Endowment	Operations	Endowment	Operations	Endowment Distribution
10/1/2009	\$1,000,000	\$500,000	\$2,722,946	\$2,170,000	\$316,041
10/1/2010	\$1,000,000	\$500,000	\$ -	\$365,000	\$341,804
10/1/2011	\$1,000,000		\$500,000	\$100,000	\$480,918
10/1/2012	\$1,000,000		\$2,005,519	\$68,062	\$581,128
10/1/2013	\$1,000,000			\$1,029,500	\$646,699
10/1/2014				\$3,301,000	\$661,299
10/1/2015				\$1,000,000	
Total	\$5,000,000	\$1,000,000	\$5,228,465	\$8,033,562	\$3,027,889

Projected FY 15-16 Evelyn F. McKnight Brain Institute Budget

Category	McKnight Operations Amount	McKnight Endowment Spendable Earnings Amount	McKnight Endowed Chair Spendable Earnings Amount	UAB Encumbered Endowment Spendable Earnings Amount	Totals
Salary and Benefits	\$0	\$150,000	\$74,477		\$224,477
Pilot Projects for McKnight Investigators Utilizing the McKnight Behavioral Core		\$56,070			\$56,070
Pilot Projects for McKnight Investigators Utilizing the McKnight Physiology Core		\$56,069			\$56,069
F. Cleveland Kinney Endowed Chair in Geriatric Psychiatry				\$70,077	\$70,077
Geropsychiatry Research Chair				\$97,054	\$97,054
Warren Chair				\$79,006	\$79,006
Lowder Chair				\$27,623	\$27,623
Collat Chair				\$25,112	\$25,112
Spencer Chair				\$25,811	\$25,811
Total	\$0	\$262,139	\$74,477	\$324,683	\$661,299

MCKNIGHT BRAIN INSTITUTE AT UAB

Cumulative Endowment Total

Book Value at 9/30/2015: \$12,235,130
Market Value at 9/30/2015: \$12,640,456
Projected Spendable Earnings for FY 2015/16: \$661,299

Evelyn F. McKnight Brain Institute Endowed Support Fund

Date Approved: 2/4/2011

Book Value at 9/30/2015: \$5,000,000
Market Value at 9/30/2015: \$5,010,679
Projected Spendable Earnings for FY 2015/16: \$262,139

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

Date Approved: 10/1/2004

Current Occupant: J. David Sweatt, Ph.D.
Occupant Date: 2/3/2006

Book Value at 9/30/2015: \$1,500,000
Market Value at 9/30/2015: \$1,423,603
Projected Spendable Earnings for FY 2015/16: \$74,477

Geropsychiatry Research Chair

Date Approved: 6/28/1993

Current Occupant: Vacant

Book Value at 9/30/2015: \$1,222,895

Market Value at 9/30/2015: \$1,855,149

Projected Spendable Earnings for FY 2015/16: \$97,054

F. Cleveland Kinney Endowed Chair in Geriatric Psychiatry

Date Approved: 6/15/2007

Current Occupant: Vacant

Book Value at 9/30/2015: \$1,500,550

Market Value at 9/30/2015: \$1,339,488

Projected Spendable Earnings for FY 2015/16: \$70,077

Warren Family Endowed Chair in Neurology

Date Approved: 6/15/2012

Current Occupant: Vacant

Book Value at 9/30/2015: \$1,506,617

Market Value at 9/30/2015: \$1,510,156

Projected Spendable Earnings for FY 2015/16: \$79,006

Patsy W. and Charles A. Collat Endowed Professorship in Neuroscience

Date Approved: 4/4/2014

Current Occupant: David S. Geldmacher, M.D.

Occupant Date: 4/4/2014

Book Value at 9/30/2015: \$500,000

Market Value at 9/30/2015: \$480,004

Projected Spendable Earnings for FY 2015/16: \$25,112

Jarman F. Lowder Endowed Professorship in Neuroscience

Date Approved: 6/15/2012

Current Occupant: Lori L. McMahon, Ph.D.

Occupant Date: 6/15/2012

Book Value at 9/30/2015: \$505,618

Market Value at 9/30/2015: \$528,005

Projected Spendable Earnings for FY 2015/16: \$27,623

Virginia B. Spencer Endowed Professorship in Neuroscience

Date Approved: 9/14/2012

Current Occupant: Erik D. Roberson, M.D., Ph.D.

Occupant Date: 2/8/2013

Book Value at 9/30/2015: \$500,000

Market Value at 9/30/2015: \$493,372

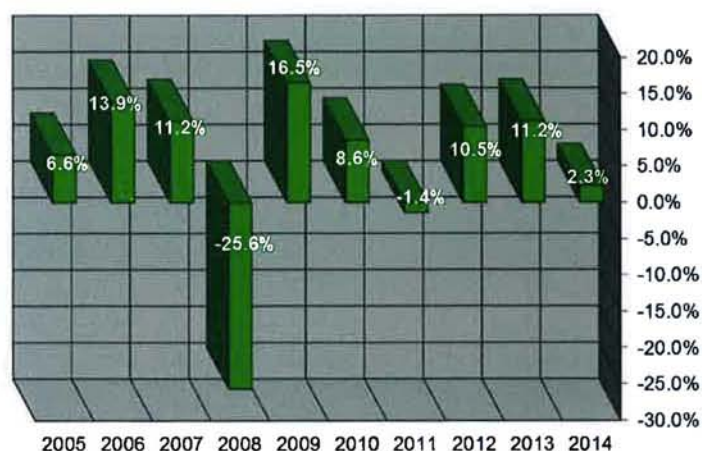
Projected Spendable Earnings for FY 2015/16: \$25,811

INVESTMENT REPORT

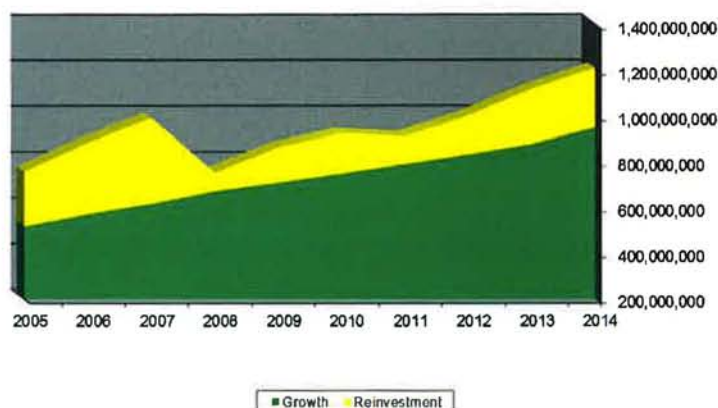
- Created in 1978, the University of Alabama Pooled Endowment Fund (UAPEF) is managed by the Chancellor's Office and is overseen by the Investment Committee of the Board of Trustees.
- As of December 31, 2014, the market value of the UAPEF was \$1.21 billion. Of this amount, 32.8%, or \$397.1 million, is attributable to UAB and the Hospital.
- The UAPEF had a ten-year annualized investment return of 4.6% for the period ending December 31, 2014, compared to a return of 4.4% for the custom index.*
- The Investment Committee oversees investment activities, monitors performance of professional money managers, and ensures the prudent control of the investment of funds.
- Participants include all three campuses of the University of Alabama System along with related foundations.
- The Board seeks superior investment returns through professional money management. Assets of the UAPEF are managed by 50 professional investment firms.
- The UAPEF also utilizes an investment consultant, Fund Evaluation Group, with expertise in investment policy development, spending policy analysis, manager evaluation and selection, and performance evaluation.

*The custom index is a blend of indices that closely represents the actual UAPEF portfolio and is used as a benchmark for comparison, both in terms of return and risk.

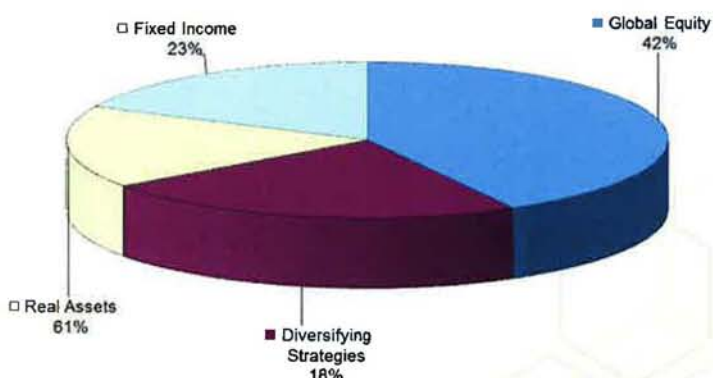
UAPEF Rates of Return
December 31, 2005 - December 31, 2014



UAPEF Growth in Endowment Funds
December 31, 2005 - December 31, 2014



Asset Allocation
as of December 31, 2014



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 \$5,531,727 in direct costs and \$7,569,695 in total costs broken down as follows:

NIH	\$4,681,320 Direct Costs
NSF	\$ 436,040 Direct Costs
Other Foundations	<u>\$ 414,367 Direct Costs</u>
Total	\$5,531,727 in Direct Costs

A detailed report of grant awards is attached.

Department of Neurobiology

Active Extramural Funding Fiscal Year 2015-2016

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
Day, Jeremy	PI	25%	R00 DA034681	NIH	07/01/14-06/30/17	Epigenetic Regulation of cocaine-Induced Neuroadaptations	169,388	79,612	249,000	508,164	238,836	749,000
Day, Jeremy	PI	25%	1DP1 DA039650-01	NIDA	07/01/15-06/30/20	Epigenetic Control of Brain Reward Systems	300,000	141,000	441,000	1,500,000	705,000	2,205,000
Day, Jeremy	Co-I	10%	R21 ES024850-01	NIH/Auburn	07/01/15-06/30/17	Behavioral Epigenetics of Developmental Methylmercury Exposure	60,772	28,563	89,335	91,614	43,059	134,673
Dobrunz	PI	25%	R01 MH098534-01	NIH	07/01/12 - 04/30/17	Interneuron Dysfunction Alters the Dynamics of the Inhibition Excitation Balance	250,000	116,250	366,250	1,250,000	581,250	1,831,250
Dobrunz	PI	30%	R01 MH108342-01	NIH-NIMH	09/01/15-05/31/20	Effects of NPY on Hippocampal Circuit Function	250,000	117,500	367,500	1,250,000	587,500	1,837,500
Hablitiz	PI	5%	P30 NS047466	NIH NINDS	02/1/10-11/31/16 - NCE	UAB Neuroscience Core Center	442,853	205,927	648,780	2,420,745	1,125,795	3,546,540
Hablitiz	PI	40%	R01 NS090041	NIH	09/15/14-07/31/18	Acquired HCN Channelopathies in Cortical Dysplasia	218,750	102,813	321,563	875,000	411,252	1,286,252
Lubin	PI	20%	1R25NS 089463-01	NIH	09/30/14-07/31/19	UAB Neuroscience Roadmap Scholars Program	241,809	19,345	261,154	1,159,045	92,724	1,251,769
Lubin	PI	34%	R01 MH097909-01	NIH	07/01/12-04/30/17	Chromatin Remodeling Mechanisms of Gene Transcription in Memory	262,224	121,934	384,158	1,402,908	676,762	2,079,670
Lubin	PI	15%	1R21NS 090250-01A1	NIH	07/01/15-06/30/17	Epigenetic Mechanisms in Epilepsy-Related Memory Formation	150,000	70,500	220,500	275,000	129,250	404,250
Lubin	PI		HSF-GEF Endowment	HSF-GEF	11/01/15-10/31/17	EEG System to Benefit the UAB Community	47,497	-	47,497	47,497	-	47,497

Parpura, Vladimir	PI	20%	R21 HD078678-01	NIH	12/01/13-11/30/16- NCE	The Role of Astroglia in the Enteric Nervous System and Gut Function	50,000	23,500	73,500	275,000	129,250	404,250
Pozzo-Miller	PI	20%	R01 NS065027	NIH	02/01/10-01/31/16-NCE	MECP2 Mutations and BDNF Signaling: Shared Mechanisms of Rett and Autism	120,000	55,800	175,800	1,093,750	508,595	1,602,345
Pozzo-Miller, Lucas	PI	0%	R01 NS065027 Administrative Supplement	NIH	06/01/13-01/31/16- NCE	MECP2 Mutations and BDNF Signaling: Shared Mechanisms of Rett and Autism	68,105	31,895	100,000	68,105	31,895	100,000
Pozzo-Miller, Lucas	PI	20%	1R21HD074418-01A1	NIH	06/10/13-05/31/16 -NCE	Reversing BDNF Impairments in Rett Mice with TRPC Channel Activators	97,200	45,198	142,398	272,200	126,573	398,773
Pozzo-Miller/ Xu	PI/Mentor		Mentored Grant	Rett Syndrome.org	01/01/15-12/31/16	Molecular Mechanisms of Homeostatic Synaptic Plasticity in Mecp2 Knockout Neurons	45,455	4,545	50,000	90,910	9,090	100,000
Pozzo-Miller	PI		HeART Grant	Rett Syndrome.org	01/01/15-12/31/16	Analogues of (1-3IGF-1 Glypromate) for the Improvement of Hippocampal Dysfunction in Female Mecp2 Heterozygous Mice: A Preclinical Trial for Rett Syndrome	68,182	6,818	75,000	68,182	6,818	75,000
Pozzo-Miller	PI		Basic Research Grant	Rett Syndrome.org	04/01/15-03/31/17	Inhibitory Interneuron Dysfunction in Network Activity in Female Mecp2 Mice	45,455	4,545	50,000	90,910	9,090	100,000
Pozzo-Miller	PI		RSRT 3124	Rett Syndrome Research Trust	01/01/15-12/31/15	Testing Whether the BDNF Loop Mimetic LM22A-4 Improves Hippocampal Function in Female Mecp2 Heterozygous Mice	100,000	10,000	110,000	100,000	10,000	110,000
Pozzo-Miller	PI		Rat Model Working Group Collaborative Agreement	Rett Syndrome.org	12/01/14-11/30/15	Investigating astrocytes and neurons in a Rat model of Rett syndrome	4,545	455	5,000	4,545	455	5,000
Sontheimer	PI		R01 NS036692 CR	NIH NINDS	04/01/14-03/31/19	The Role of Ion Transport in Glioma Cell Migration, Proliferation, and Apoptosis	275,537	129,502	405,039	1,377,685	647,510	2,025,195
Sweatt	PI	25%	R01MH057014 CR	NIH	07/01/15-06/30/20	Biochemical Mechanisms of Neuronal Plasticity	454,999	213,850	668,849	2,274,995	1,069,250	3,344,245

Sweatt	PI	15%	R01 MH0911 22	NIH- NIMH	06/03/11- 03/31/16	DNA Methylation in Memory Formation	250,000	116,250	366,250	1,250,000	561,250	1,831,250
Sweatt	PI	15%	R01 MH1041 50	NIH- NIMH	07/01/14- 06/30/19	Molecular and Behavioral Neurobiology of Transcription Factor TCF4	250,000	117,500	367,500	1,250,000	587,500	1,837,500
Sweatt	PI		T32NS0 61788 CR	NIH	07/01/13- 06/30/18	Training Program in the Neurobiology of Cognition and Cognitive Disorders	243,740	15,468	259,208	1,095,450	65,355	1,160,805
Sweatt/ Gamlin	Co- PI's	3%	MUSC Subcontr act	NSF	08/01/15- 07/31/19	R11 Track-2 FEC: Bridging Cognitive Science and Neuroscience Using Innovative Imaging Technologies	436,040	28,689	464,729	1,244,160	356,805	1,600,965
Visscher	PI		Patient- Oriented Research Award	HSF- GEF	11-01-14- 10/31/16	Visual Brain Core - Research Resources on Visual Dysfunction and Plasticity	103,233	-	103,233	164,300	-	164,300
Visscher	PI		419K60 2	NIH- Wiscons in	10/01/12- 07/31/16	Social Perception and Social Communication in Adults With Traumatic Brain Injury	3,401	1,599	5,000	21,880	10,175	35,055
Wadiche, Jacques/ Angie Nietz	PI/Me ntor		F31 NS 093960	NIH	08/01/15- 07/31/19	Extrasynaptic signaling to interneuron networks	35,076	-	35,076	140,304	-	140,304
Wadiche, Jaques	PI	35%	R01 NS0659 20	NIH- NINDS	06/01/14- 05/31/19	Timing of Neurotransmitter Release	218,750	102,813	321,563	1,093,750	506,770	1,600,520
Linda Wadiche	PI	40%	2R01NS 064025C R	NIH	04/01/15- 03/31/19	Newborn Neurons in the Adult Hippocampal Network	258,716	121,597	380,313	1,034,864	486,388	1,521,252
Wilson	PI	50%	R01 NS0475 33	NIH	02/1/10- 12/31/15 - NCE	The Role of Usp 14 in Regulating Neuronal Function	10,000	4,500	14,500	1,093,750	508,595	1,602,345
					Total Active Grants		5,531,727	2,037,968	7,569,695	24,884,713	10,222,792	35,132,505

**LISTING OF INVESTIGATORS
AND
INDIVIDUAL FACULTY REPORTS**

Investigators of the UAB McKnight Brain Institute

Professors

J. David Sweatt, Ph.D.

Evelyn F. McKnight Chair, Department of Neurobiology

Director, McKnight Brain Institute

Director, Civitan International Research Center

Area of Interest: Signal transduction and transcriptional control in memory and aging

Steve Austad, Ph.D.

Professor and Chair, Department of Biology

Area of Interest: Molecular and organismal biology of aging

Karlene Ball, Ph.D.

Professor and Chair, Department of Psychology

Area of Interest: Aging-related cognitive function

Michael Brenner, Ph.D.

Professor Emeritus, Department of Neurobiology

Area of Interest: Glial cell biology, Alexander Disease

Paul Gamlin, Ph.D.

Professor, Department of Ophthalmology

Area of Interest: Cell biology and systems neuroscience of vision and visual disorders

David Geldmacher, M.D.

Professor, Collat Scholar, Department of Neurology

Area of Interest: Aging-related memory disorders and visual cognition in AD.

John Hablitz, Ph.D.

Professor, Department of Neurobiology

Area of Interest: Modulation of excitability in neocortical circuits

Robin Lester, Ph.D.

Professor, Department of Neurobiology

Area of Interest: Nicotinic receptors in CNS function

Lori McMahon, Ph.D.

Professor and Dean, Graduate School

Professor, Department of Physiology/Biophysics

Director, UAB Comprehensive Neuroscience Center

Co-Director, McKnight Brain Institute

Area of Interest: Hormonal control of synaptic plasticity in aging

James H. Meador-Woodruff, M.D.

Professor and Chair, Department of Psychiatry and Behavioral Neurobiology

Area of Interest: Cellular and subcellular alterations of neural circuitry and molecular expression in psychiatric illnesses

Vlad Parpura, M.D., Ph.D.

Professor, Department of Neurobiology

Area of Interest: Imaging approaches to investigating synaptic and glial cell function

Lucas Pozzo-Miller, Ph.D.

Professor, Department of Neurobiology

Area of Interest: Mechanisms controlling dendritic spine morphology

David Standaert, M.D., Ph.D.

Professor and Chair, Department of Neurology

Director, UAB Movement Disorders Center

Area of Interest: Striatal molecular and cellular biology, Parkinson's Disease

Anne Theibert, Ph.D.

Professor, Department of Neurobiology

Director, UAB Undergraduate Neuroscience B.S. Program

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

Erobo Ubogu, Ph.D.

Professor, Department of Neurology

Director of the Neuromuscular Division of Neurology

Area of Interest: Inflammatory neuropathies

Associate Professors

Virginia Wadley Bradley, Ph.D.

Associate Professor, Division of Gerontology, Geriatrics, and Palliative Care

Director, Dementia Care Research Program

Associate Director, Edward R. Roybal Center for Translational Research on Aging and Mobility

Area of Interest: Mild Cognitive Impairment, Alzheimer's disease, comorbid cerebrovascular disease

Lynn Dobrunz, Ph.D.

Associate Professor, Department of Neurobiology

Area of Interest: Regulation of short-term synaptic plasticity in the hippocampus

Matt Goldberg, Ph.D. (Recruited from UT Southwestern)

Associate Professor, Neurology

Area of Interest: Mechanisms of neurodegeneration

Alecia Gross, Ph.D.

Associate Professor, Department of Vision Sciences

Area of Interest: Signal transduction mechanisms in the CNS

David Knight, Ph.D.

Associate Professor, Department of Psychology

Area of Interest: Human imaging approached to investigating memory

Farah Lubin, Ph.D.

Associate Professor, Department of Neurobiology

Area of Interest: Signal transduction mechanisms in memory and memory disorders

Kazu Nakazawa, Ph.D.

Associate Professor, Department of Psychiatry

Area of Interest: Epigenetics and cognition

Linda Overstreet-Wadiche, Ph.D.

Associate Professor, Department of Neurobiology

Area of Interest: Adult neurogenesis in the dentate gyrus

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

Associate Professor, Department of Neurology

Co-Director, UAB Center for Neurodegeneration and Experimental Therapeutics

Co-Director, McKnight Brain Institute

Area of Interest: Aging-related memory disorders

Scott Wilson, Ph.D.

Associate Professor, Department of Neurobiology

Area of Interest: The ubiquitin/proteasome system in neuronal function

Jacques Wadiche, Ph.D.

Associate Professor, Department of Neurobiology

Area of Interest: Synaptic plasticity and function in the cerebellum

Assistant Professors

Mark Bolding, Ph.D.

Assistant Professor, Division of Advanced Medical Imaging Research

Area of Interest: Visual cognition, MRI, and neuroimaging

Jeremy Day, Ph.D.

Assistant Professor, Department of Neurobiology

Area of Interest: Epigenetic mechanisms in memory formation.

Tara DeSilva, Ph.D.

Assistant Professor, Physical Medicine and Rehabilitation

Area of Interest: Neural-glial signaling mechanisms in the CNS

Michelle Gray, Ph.D.

Assistant Professor, Dixon Scholar, Department of Neurology

Area of Interest: Neurogenetics, glial function, and Huntington's Disease

Jeremy Herskowitz, Ph.D. (Recruited from Emory SOM)

Assistant Professor, Department of Neurology

Area of Interest: Amyloid beta effects on neurons.

Gwen King, Ph.D.

Assistant Professor, Department of Neurobiology

Area of Interest: Memory and aging, Klotho proteins in aging and cognition

Michelle Olsen, Ph.D.

Assistant Professor, Department of Physiology and Biophysics

Area of Interest: Signal transduction mechanisms in the CNS, epigenetics

Scott Phillips, Ph.D.

Assistant Professor, Department of Neurobiology

Area of Interest: Neurogenetics, neurobiochemistry

Kristina Visscher, Ph.D.

Assistant Professor, Department of Neurobiology

Area of Interest: Human imaging approaches to investigating memory.

Research Scientists

Cristin Gavin, Ph.D

Scientific Director, UAB McKnight Synaptic Plasticity Core

Area of Interest: Epigenetic control of neuronal biophysical properties

Jing Wang, Ph.D.

Scientist, UAB McKnight Synaptic Plasticity Core

Area of Interest: Place cells in the hippocampus

Andrew Kennedy, Ph.D.

Director of the MBI Rodent Behavior Core

Area of Interest: Epigenetic mechanisms in memory formation

SWEATT McKNIGHT CHAIR REPORT

McKnight Brain Research Foundation

Annual Report 2015

J. David Sweatt, Evelyn F. McKnight Chair

The University of Alabama at Birmingham

This is an individual report for Dr. Sweatt as Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging at UAB.

1. Summary of Scientific Achievements for 2015

Aging-related memory decline is manifest prominently in declarative/episodic memory and working memory, memory modalities anatomically based largely in the hippocampus and prefrontal cortex, respectively. The neurobiological underpinnings of age-related memory deficits include aberrant changes in gene transcription that ultimately affect the ability of the aged brain to be “plastic.” This has led us to hypothesize that dysregulation of epigenetic control mechanisms and the accumulation of aberrant epigenetic marks are a driver for aging-related cognitive dysfunction. Specifically, given that the transcription of key memory-promoting genes are known to decline during aging, we propose that these changes are regulated by aberrant epigenetic marks and control mechanisms within brain regions particularly vulnerable to the aging process (i.e., hippocampus and prefrontal cortex), which together result in age-related cognitive deficits. In studies over the last year, we have made important discoveries concerning the role of epigenetic mechanisms in memory-associated areas of the CNS, which I will describe below.

One of our most important discoveries over the last year enabled identifying a specific type of neuronal plasticity that might be a target for epigenetic disruption in aging. In this study, which we performed collaboratively with MBI investigator John Hablitz, we found that DNA methylation controls cell-wide homeostatic synaptic plasticity. Enhanced receptiveness at all synapses on a neuron that receive glutamate input from other neurons is called synaptic upscaling. It is established that this type of synaptic plasticity is critical for long-term memory storage within cortical circuits. We hypothesized that this process also depends on epigenetic mechanisms, specifically covalent chemical modification of DNA. In our studies, we found that DNA cytosine demethylation mediates multiplicative synaptic upscaling of glutamatergic synaptic strength in cultured cortical neurons. Our data suggest that DNA methylation status controls transcription-dependent regulation of glutamatergic synaptic homeostasis. Furthermore, covalent DNA modifications may contribute to synaptic plasticity events that underlie the formation and stabilization of memories, a process which our earlier studies in collaboration with Carol Barnes indicates is disrupted in aging. These studies were published in the journal *Science Signaling*, a high-profile international journal. We also have received indications that this finding may also be profiled in the magazine *Discover* as one of the top discoveries in neuroscience in 2015.

In an additional series of collaborative translational studies the laboratory investigated structure-function relationships for an epigenetically targeted category of drugs with potential clinical applicability to age-related cognitive disruption. Histone deacetylases (HDACs) are promising therapeutic targets for neurological and psychiatric disorders that impact cognitive ability, but the relationship between various HDAC isoforms and cognitive improvement is poorly understood, particularly in mouse models of age-related memory impairment. A goal shared by many is to develop HDAC inhibitors with increased isoform selectivity in order to reduce unwanted side effects, while retaining procognitive effects. However, studies addressing this at the molecular, cellular, and behavioral level are limited. Therefore, we interrogated the

biological effects of class I HDAC inhibitors with varying selectivity and assessed a subset of these compounds for their ability to regulate transcriptional activity, synaptic function, and memory. We found that the HDAC-1, -2, and -3 inhibitors, RGFP963 and RGFP968, were most effective at stimulating synaptogenesis, while the selective HDAC3 inhibitor, RGFP966, with known memory enhancing abilities, had minimal impact. Furthermore, RGFP963 increased hippocampal spine density, while HDAC3 inhibition was ineffective. Genome-wide gene expression analysis by RNA sequencing indicated that RGFP963 and RGFP966 induce largely distinct transcriptional profiles in the dorsal hippocampus of mature mice. The results of bioinformatic analyses were consistent with RGFP963 inducing a transcriptional program that enhances synaptic efficacy. Finally, RGFP963, but not RGFP966, rescued memory in a mouse model of Alzheimer's disease. Together, these studies suggest that the specific memory promoting properties of class I HDAC inhibitors may depend on isoform selectivity and that certain pathological brain states may be more receptive to HDAC inhibitors that improve network function by enhancing synapse efficacy.

Significance - Over the course of the last fifteen years, we have generated evidence for an "epigenetic code" in the central nervous system that mediates synaptic plasticity, learning, and memory. Our findings indicate that specific epigenetic changes are regulated and may interact with each other during memory formation, and we are beginning to understand how these changes manifest functionally at the cellular and circuit levels. Aberrant epigenetic modifications may lead to cognitive disorders that affect learning and memory, and our results highlight the therapeutic potential of epigenetic treatments for the amelioration of these conditions. Thus, our findings demonstrate that epigenetic mechanisms play a role in synaptic plasticity and memory. As such, these findings greatly expand the known scope of the types of cellular mechanisms falling under the control of DNA methylation and histone modifications, and have allowed the development of new epigenetically targeted compounds with potential applicability to cognitive aging.

Plans - The project will continue to focus on the role of epigenetic mechanisms in hippocampus-dependent plasticity and memory and their identity as targets of synaptic activity in neurons. I believe that the novel targets of transcriptional regulation that we are investigating are the product of innovative thinking and that their pursuit will allow us to continue a leadership role in this area.

2. Publications in Peer Reviewed Journals

1. Roth ED, Roth TL, Money KM, SenGupta S, Eason DE, Sweatt JD. (2015) DNA methylation regulates neurophysiological spatial representation in memory formation. *Neuroepigenetics* 2:1-8.
2. Rumbaugh G, Sullivan SE, Ozkan ED, Rojas CS, Hubbs CR, Aceti M, Kilgore M, Kudugunti S, Puthanveetil SV, Sweatt JD, Rusche J, Miller CA. (2015) Pharmacological Selectivity Within Class I Histone Deacetylases Predicts Effects on Synaptic Function and Memory Rescue. *Neuropsychopharmacology*. 2015 Apr 3. doi: 10.1038/npp.2015.93. [Epub ahead of print]
3. Yokoi F, Chen HX, Dang MT, Cheetham CC, Campbell SL, Roper SN, Sweatt JD, Li Y. (2015) Behavioral and electrophysiological characterization of Dyt1 heterozygous knockout mice. *PLoS One*. Mar 23;10(3):e0120916. doi:10.1371/journal.pone.0120916.
4. Grubišić V, Kennedy AJ, Sweatt JD, Parpura V. (2015) Pitt-Hopkins Mouse Model has Altered Particular Gastrointestinal Transits In Vivo. *Autism Res*. 2015 Feb 26. doi: 10.1002/aur.1467.

5. Meadows JP, Guzman-Karlsson MC, Phillips S, Holleman C, Posey JL, Day JJ, Hablitz JJ, Sweatt JD. (2015) DNA methylation regulates neuronal glutamatergic synaptic scaling. *Science Signaling* 8(382):ra61.
6. Day JJ, Kennedy AJ, Sweatt JD. (2015) DNA Methylation and Its Implications and Accessibility for Neuropsychiatric Therapeutics. *Annu Rev Pharmacol Toxicol.* 55:591-611.
7. Heyward FD, Sweatt JD. (2015) DNA Methylation in Memory Formation: Emerging Insights. *Neuroscientist.* 2015 Apr 1. pii: 1073858415579635. [Epub ahead of print] Review.
8. Zovkic IB, Sweatt JD. (2015) Memory-Associated Dynamic Regulation of the "Stable" Core of the Chromatin Particle. *Neuron.* 87:1-4.

3. Publications (other)

Books

None

Book Chapters

None for 2015. Two invited book chapters are in preparation for 2016.

4. Recent (2015) Presentations at Scientific Meetings (also includes invited research seminars)

NIMH, Behavioral Neuroscience Seminar Series Speaker
 Behavioral Epigenetics Keystone Symposium, Invited Speaker
 Keynote Speaker UF/Northwest Florida Brain Week Symposium
 Arizona State University, BioDesign Institute Discovery Series speaker
 SouthEastern Clinical Club, Invited Speaker
 UT San Antonio, Neuroscience seminar series student invitee
 HHMI Janelia Farm Neuroepigenetics meeting, invited speaker and meeting organizer
 Pitt-Hopkins Research Foundation Research Symposium Speaker
 University of Michigan, Molecular, Cell and Developmental Biology Seminar Series
 University of Toronto, Neuroscience Distinguished Lecturer Series
 Vanderbilt University, Department of Pharmacology
 UT Southwestern, Department of Psychiatry

5. Presentations at Public (non-scientific) Meetings or Events

Presented at three public events:

Science Signaling Podcast

Presenter, Civitan International Annual Meeting

Chesapeake District Civitan International lay scientific overview

6. Awards and Honors

- Thomson Reuters Highly Cited Researchers 2015
- 2015 UAB School of Medicine Dean's Award for Research Excellence
- 2015 - Named Director, Civitan International Research Center, The University of Alabama at Birmingham

New or recently renewed Grant Awards:

- NIH Grant MH57014 - Biochemical Mechanisms for Long-term Potentiation D. Sweatt PI, 07/01/15 - 3/31/20, \$2,096,000 total direct costs
- NSF RII TRACK-2 FEC Award - Bridging Cognitive Science and Neuroscience Using Innovative Imaging Technologies, Peter Kalivas PI, D. Sweatt, UAB site PI 09/01/15 - 08/31/19, ~\$2,000,000 total UAB direct costs

7. Faculty

Three Research Assistant Professors work in my lab:

- Scott Phillips, Ph.D.
- Cristin Gavin, Ph.D.
- Garrett Kaas, Ph.D.

8. Trainees, Post-Doctoral, Pre-Doctoral, Other

I had a total of approximately 15 post-doc and grad student applications for my laboratory this year.

I currently have two graduate students, six post-doctoral fellows, one post-baccalaureate, and four undergraduate students working in my lab.

9. Clinical/Translational Programs

A. New Programs

As has been previously described, our DARPA project is translational, relating to the identification of novel constructs for cognitive enhancement. This program was renewed for funding this year, in collaboration with IBIS Pharmaceuticals.

B. Update on Existing Clinical Studies

Not applicable

C. New Treatments

Not applicable

D. Drug Trials, Future Research and/or Clinical Initiatives

Not applicable

10. Technology

A. Patent Applications

Dr. Sweatt's laboratory (through UAB) filed an international patent application for histone H2A.Z as a novel target for memory enhancement.

B. Revenue Generated from Technology

Not applicable

11. Budget Update

A full financial report for the MBI is included as Section 2.

12. Educational Programs Focusing on Age Related Memory Loss

A. Scientific

Not applicable, although see above for research presentations

B. Public

Not applicable, although see above for lay public presentations

13. External Collaborations

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

University of Arizona and UF – We are continuing a very fruitful collaboration with Carol Barnes and Tom Foster concerning the possible role of DNA methylation in controlling aging-related transcriptional alterations in the CNS.

UAB – We are collaborating with a number of MBI investigators here at UAB, including Farah Lubin, David Standaert, Scott Wilson, Gwen King, Erik Roberson, Alecia Gross, and John Hablitz.

B. Collaborative Programs with non-McKnight Institutes, Institutions and Research Programs

Temple University – We are collaborating with Dan Liebermann's laboratory to investigate the involvement of GADD45 in memory formation and LTP induction.

Johns Hopkins – We are collaborating with Honjun Song's laboratory to investigate the role of TET oxidases in active DNA demethylation in memory formation.

University of Maryland – We are collaborating with Susan Dorsey to investigate BDNF gene methylation in spinal cord plasticity.

University of Delaware – We are collaborating with Tania and Eric Roth to investigate the role of epigenetic mechanisms in stabilizing hippocampal place cell function.

Ibis Pharmaceuticals – This year, we obtained funding for an innovative collaborative project developing antisense oligonucleotide-based next-generation histone de-acetylase inhibitors as memory-enhancing agents. This project is funded by DARPA.

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

No

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

None

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

Yes

17. Briefly describe your progress compared to the original goals.

The laboratory is progressing nicely, in line with the original goals of our research program to investigate epigenetic mechanisms in memory and memory disorders. These two cores 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 allow for collaborative opportunities with the other MBIs, which in general are not historically strong in the area of mouse genetic engineering. Finally, as already mentioned the new McKnight Inter-Institute Epigenetics and Bioinformatics Initiative provides a powerful platform for collaboration and cross-fertilization in the area of the epigenetics of cognitive aging.

18. 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 for my lab.

19. 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.

No additional comments.

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


J. David Sweatt, Ph.D.

Professor

Evelyn F. McKnight Endowed Chair

Director, Evelyn F. McKnight Brain Institute

Chairman, Department of Neurobiology

UAB School of Medicine

January 14, 2016

Date

INDIVIDUAL FACULTY REPORTS

1. Summary of Scientific Achievements for 2015

Brenner, Michael

- Learned how to use excel and to use it to analyze proteomic mass spec data in order to prepare data obtained by my former student, Michael Heaven, for publication. That manuscript has now been submitted.
- Learned how to do quantitative reverse-transcription PCR and used this technique to study the role of an AP-1 binding site, the TATA box sequence, and insulator sequences on the expression of GFAP transgenes. Completion of experiments and submission of two manuscripts are expected in September.

Day, Jeremy

- Identification and characterization of neuronal non-coding RNAs that interact with DNA methyltransferases to regulate the neuronal epigenome.
- Discovery that the epigenetic modifier Gadd45b is regulated by dopamine signaling and is critical for cocaine-related behavioral adaptations.
- Genome-wide characterization of transcriptional and epigenetic regulation following memory formation in rodent model systems.

Dobrunz, Lynn

- My lab has recently shown that short-term plasticity regulates the balance between excitation and inhibition (E/I) in hippocampus and that this regulates the output of hippocampus. In addition, we showed that short-term plasticity of E/I also modulates the temporal window over which CA1 pyramidal cells can integrate multiple inputs to cause spiking, dynamically regulating the extent to which they act as integrators or coincidence detectors.
- My lab has discovered that interneurons in the CA1 region of hippocampus that release the endogenous anti-anxiety peptide Neuropeptide Y (NPY) are differentially regulated by short-term plasticity. In addition, we found that a subset of NPY cells requires activation of both Schaffer collateral and temporammonic input pathways in order to drive NPY release.
- My lab has found that transcriptional dysregulation in hippocampal interneurons alters the way these interneurons respond to the antipsychotic haloperidol, which has potential implications for the use of this medication in treating schizophrenia patients.

Hablitiz, John

- Established optogenetic techniques for studying contribution of selective populations of GABAergic interneurons to synchronization of inhibitory networks.
- Demonstrated role of HCN channels in excitability of GABAergic interneurons and its' alteration in epilepsy.

King, Gwendalyn

- We have confirmed that we have the klotho conditional knockout that we've been attempting to develop for three years. The final straw was difficult with founders allowing litters to survive. With this tool in hand, several collaborations have opened up, and data for three grant applications between June 5 and July 21 have been enabled.
- We have discovered that klotho not only affects proliferation of neural stem cells, but also has an even bigger effect on maturation delaying expression of proteins required for immature neurons to mature.
- We have begun behavioral assays to measure cognitive function in our model systems. Testing is ongoing to determine whether FGF23 mediates klotho effects in the brain or we have two independent phenotypes.

Lester, Robin

- Patch-clamp recordings from kidney cells to study dysfunctional channels in polycystic kidney disease (PI: Cathy Fuller)

Lubin, Farah

- I had a very productive past year! Most exciting this year was the establishment of the annual NEURAL (National Enhancement of Under Represented Academic Leaders) at UAB. This conference has put UAB “on the map” for increasing diversity in the neurosciences in the southeastern region. I have attached the results from the post-conference survey.
- As Director of the UAB Roadmap Scholar Program, I have helped to enroll 13 scholars from the current pool of GBS graduate students and helped to recruit eight additional scholars for fall 2015.
- I continue to publish manuscripts (4 + 4 in Revision) and co-editing an Elsevier book entitled *Epigenetics and Neuroplasticity: Evidence and Debate*.
- I have been awarded three grants this past year and continue to pursue additional research funding through submission of grant applications (resubmission of NIH/NINDS R01 NS094743 and NIH/NINDS PPG P01). As such, I continue to make excellent progress, as detailed in my attached curriculum vitae.

Overstreet-Wadiche, Linda

- We are continuing to study how a specific extracellular matrix molecule controls the sequence and timing of GABA synaptic innervation of adult generated neurons, using cre/loxp systems to express channelrhodopsin in specific subtypes of hippocampal interneurons.
- We found that adult-born neurons compete with existing mature neurons for synaptic partners, leading to a redistribution of synaptic connectivity in the EC-DG circuit. We also found that expression of Bax is required for neurogenesis-induced loss of synapses on mature neurons (manuscript under review).
- We discovered that the low synaptic connectivity of immature adult-born neurons counteracts their high intrinsic excitability, potentially providing a mechanism by which highly excitable adult born neurons contribute to the computational function of pattern separation that relies on spare DG activity (manuscript under review).

Parpura, Vladimir

- We continue our interests in the area to opto-genetic approaches to evoke and visualize calcium dynamics in astrocytes in collaboration with Sergey Kasparov and Anja S. Teschemacher (Univ. of Bristol, Bristol, UK) (**JA 116**), as well as with Singhua Ding (University of Missouri, Columbia, MO) (**JA 120**). This work is related to the National Science Foundation (NSF) funded project with the goal to generate bio-mimetic robots (i.e., Cyberplasm) based on *C. elegans*-like locomotion (**JA 123**).
- We are making efforts related to brain pathologies/injuries by developing scaffolds and dispersible materials, most notably modified colloidal solutes and films of carbon nanotubes (CNTs) (**JA 124**). Chemically functionalized single-walled carbon nanotubes as solutes enhance the glutamate uptake characteristics of mouse cortical astrocytes.
- In collaboration with Dave Sweatt (UAB, Dept. of Neurobiology), we provided the first evidence that mice model of Pitt-Hopkins syndrome (PTHS), an autism spectrum disorder due to a loss of function of *Transcription factor 4 (TCF4)* gene, have specific gut malfunctions, namely reduced upper gastrointestinal and distal colonic transit velocities that resemble symptoms, i.e. gastroesophageal reflux and constipation, of the PTHS patients (**JA 125**). This work is related to the National Institutes of Health (NIH) funded project studying gut (patho) physiology.

Pozzo-Miller, Lucas

- The first demonstration that the hippocampus of *Mecp2* knockout mice is hyperactive due to an excitatory/inhibitory imbalance with reduced GABAergic inhibition in area CA3. Published in *Hippocampus*.
- The first demonstration that long-term potentiation is impaired in the hippocampus of *Mecp2* knockout mice due to the saturation of the plasticity range at already potentiated synapses that cannot recycle AMPARs. In preparation.
- The first demonstration that homeostatic synaptic plasticity is impaired in *Mecp2* knockout neurons due to already potentiated synapses that cannot recycle AMPARs. In preparation.

Roberson, Erik

- Examination of the effects of vascular amyloid deposition on vascular function. Vascular amyloid is the accumulation of amyloid material in the walls of cerebral blood vessels and is a common accompaniment of aging. There is a well-known risk of bleeding from affected vessels, but less was known about how it affected vascular function and the gliovascular unit, which is the ability of glial cells to regulate vascular tone.
- Showed that the hyperexcitability in hAPP mice originates in the dendrites, due to loss of the potassium channel Kv4.2. These changes are both dependent on tau, and tau reduction prevents the increase in dendritic hyperexcitability.
- Led three clinical trials directed at tau, including the first tau PET imaging study using the new UAB PET facility.

Theibert, Anne - none**Vischer, Kristina**

- Functional Connectivity between visual cortex and cognitive control regions differs between central vs peripheral visual representations. These patterns change with task. This slope tracks performance in visual but not auditory tasks. This implies that the contrast between functional connectivity in central to peripheral visual cortical regions is important for processing visual stimuli, constraining theories for visual information processing. (Griffis et al, 2015)
- Visual cortical areas representing peripheral vision are thicker in patients with macular degeneration than in controls. This result is consistent with the different usage of peripheral vision in MD participants vs. controls, and we suggest that this structural change may contribute to MD participants' relatively improved use of their spared vision. (Burge et al, submitted)
- Evidence for at least two distinct control processes acting on visual cortex. One has a transient temporal profile and is specific to portions of the visual field. The other is observed as a DC shift in ongoing activity and influences all of primary visual cortex as a whole (Elkhetali et al., 2015).

Wadiche, Jacques

- We are studying a previously unexplored property of AMPARs and their ion flux to test the hypothesis that AMPAR calcium permeability is dependent on ligand concentration or subunit heterogeneity. We are also studying how non-synaptic glutamatergic signaling at the input layer of the cerebellar cortex signals to Golgi cells.
- We have begun a close collaboration with D Bredt (Johnson and Johnson) and S Tomita (Yale Med School) to characterize novel AMPAR binding partner that regulate subunit localization and ion channel properties.
- We have begun to probe the signaling mechanisms that regulate vesicular release to test the idea that there's a dynamic balance of between univesicular and multivesicular release at individual synapses.

Wilson, Scott

- Determined that conditional inactivation of HRS in Schwann cells results in a juvenile onset demyelinating disease.
- Determined that HRS is regulating myelination in a novel manner that does not required its ESCRT-0 binding partner STAM1.
- USP14's ubiquitin hydrolase activity can be activated by binding to the E3 ligase TRAF6.

2. Publications in Peer Reviewed Journals**Brenner, Michael**

- Minkel, H.R., Anwer, T.Z, Arps, K.M., Brenner, M. and Olsen, M.L. (2015), Elevated GFAP induces astrocyte dysfunction in caudal brain regions: a potential mechanism for hind brain involved symptoms in type II Alexander disease. *Glia* (in press).

Day, Jeremy

- Day, J.J. (2014) New approaches to manipulating the epigenome. *Dialogues in Clinical Neuroscience* 16(3):345-57.
- Zovkic, I.B., Paulukaitis, B.S., Day, J.J., Etikala, D.M., & Sweatt, J.D. (2014). Histone H2A.Z subunit exchange controls transcription-dependent consolidation of recent and remote memory. *Nature* 515(7528): 582-586.
- Day, J.J., Kennedy, A., & Sweatt, J.D. (2015). DNA methylation and its implication and accessibility for pharmacological treatments in learning and memory. *Annual Reviews in Pharmacology and Toxicology* 6(55):591-611.
- Day, J.J., & Roberson, E.D. (2015). An epigenetic brake on genetic inheritance: DNA methylation slows effects of C9ORF72 mutations. *Neurology* 84(16):1616-1617. Manuscripts and chapters accepted, in press or published (give full reference and official status)
- Meadows, J., Guzman-Karllson, M.C., Holleman, C., Phillips, S., Day, J.J., Hablitz, J.J., & Sweatt, J.D. DNA methylation regulates cell-wide glutamatergic synaptic scaling. (In Press, *Science Signaling*).

Dobrunz, Lynn

- Bartley AF, Dobrunz LE (2015) Short-term plasticity regulates the excitation/inhibition ratio and the temporal window for spike integration in CA1 pyramidal cells. *Eur J Neurosci* 41:1402-1415.
- Lucas EK, Dougherty SE, McMeekin LJ, Reid CS, Dobrunz LE, West AB, Hablitz JJ, Cowell RM (2014) PGC-1 α provides a transcriptional framework for synchronous neurotransmitter release from parvalbumin-positive interneurons. *J Neurosci* 34:14375-14387.

Hablitz, John

- Dougherty, S.E., Hollimon, J.J., McMeekin LJ, Bohannon AS, West AB, Lesort M, Hablitz JJ, Cowell RM. Hyperactivity and cortical disinhibition in mice with restricted expression of mutant huntingtin to parvalbumin-positive cells. *Neurobiol. Dis.* 2014;62:160-171. PubMed PMID: 24121117
- Lucas EK, Dougherty SE, McMeekin LJ, Reid CS, Dobrunz LE, West AB, Hablitz JJ, Cowell RM. PGC-1 α provides a transcriptional framework for synchronous neurotransmitter release from parvalbumin-positive interneurons. *J. Neurosci.* 2015, 34: 14375-14387. PMID: 25339750.
- Williams SB, Hablitz JJ. Differential modulation of repetitive firing and Synchronous network activity in neocortical interneurons by inhibition of A-type K⁺ channels and I_h. *Fron Cell Neurosci.* 2015 Mar 18;9:89. PMID: 25852481.
- Meadows JP, Guzman-Karllsson MC, Phillips S, Holleman C, Posey JL, Day J, Hablitz JJ, Sweatt JD. DNA methylation regulates neuronal glutamatergic synaptic scaling. *Sci Signal.* 2015, 8:382.

- Albertson, A. and Hablitz, J.J. M Synaptic integration in layer 5 basket cells in malformed rat neocortex. *Front Cell Neurosci.* (In revision). Dobrunz, L, Bartley, A., Brady, L, Lucas, E, Li, Q, Hablitz, J and Cowell, R. Interneuron transcriptional dysregulation causes frequency-dependent alterations in the balance of inhibition and excitation in hippocampus. *J. Neurosci.* (In revision).

King, Gwendalyn

- Vaden JH, Bhattacharyya BJ, Chen PC, Watson JA, Marshall AG, Phillips SE, Wilson JA, King GD, Miller RJ, Wilson SM. Ubiquitin-specific protease 14 regulates c-Jun N-terminal kinase signaling at the neuromuscular junction. *Mol. Neurodegeneration* (2015)10(1):3. PMID:PMC4417291
- Maltare A, Nietz AK. Laszczyk AM, Dunn TS, Ballestas ME, Accavitti-Loper MA, King GD. Development and characterization of monoclonal antibodies to detect klotho. *Monoclon Antib Immunodiagn Immunother.* (2014) 33(6): 420-7. PMID:PMC4278077

Lester, Robin - none

Lubin, Farah

Current h-index =19, i10-index=24, 2601, based on Scopus and Google scholar database (07/11/2015).

- R.R. Parrish, S. Buckingham, K.L. Mascia, J.J. Johnson, M.M. Matyjasik, R.M. Lockhart, and F.D. Lubin. Methionine increases BDNF DNA methylation and improves memory in epilepsy. 2015. *Annals of Clinical and Translational Neurology.* 2015 Apr;2(4):401-16.
- S. Morse*, A. Butler*, R.L. Davis, W.D. Haselden, I. Solter and F.D Lubin. Environmental enrichment reverses age-related hippocampal histone methylation changes. 2015, *Biology.* Apr 1;4(2):298-313. * Equal Authorship
- S. Gupta-Agarwal, T.J. Jarome, J. Fernandez, and F.D. Lubin. NMDA receptor- and ERK-dependent changes in histone methylation in the lateral amygdala bidirectionally regulate fear memory formation. 2014, *Learning and Memory.* Jun 17;21(7):351-62.
- T.J. Jarome, J. S. Thomas, and F.D. Lubin. Epigenetics of memory consolidation, retrieval, and reconsolidation. 2014. *Neurobiology of Learning and Memory* Nov;115:116-27.

Overstreet-Wadiche, Linda

- Dieni CV, Wieckert, AJ, Overstreet-Wadiche L (2015) Development of glutamatergic innervation during maturation of adult-born neurons. *Frontiers in Biology*, in press.
- Overstreet-Wadiche L and McBain, C (2015) Neurogliaform Cells in Cortical Circuits. *Nature Reviews Neuroscience.* 16, 458–468.
- Wadiche JI and Overstreet-Wadiche L (2015) New Neurons Don't Talk Back. *Neuron* 85(1):3-5

Parpura, Vladimir

Published:

- Figueiredo, M., Lane, S., Stout, R.F. Jr., Liu, B.H., Parpura, V., Teschemacher, A.G., Kasparov, S. (2014) Comparative analysis of optogenetic actuators in cultured astrocytes. *Cell Calcium* 56: 208–214.
- Li, H., Wang, X., Zhang, N., Gottipati, M.K., Parpura, V., Ding, S. (2014). Imaging of mitochondrial Ca^{2+} dynamics in astrocytes using cell-specific mitochondria-targeted GCaMP5G/6s: Mitochondrial Ca^{2+} uptake and cytosolic Ca^{2+} availability via the endoplasmic reticulum store. *Cell Calcium.* 56: 457–466
- Wang, Y., Montana, V., Grubišić, V., Stout, R.F.Jr., Parpura, V, Gu, L-Q. (2015) Nanopore sensing of botulinum toxin type B by discriminating an enzymatically cleaved peptide from a synaptic protein synaptobrevin 2 derivative. *ACS Appl Mat Int* 7:184–192. Cavender, C.E., Gottipati, M.K., Parpura, V. (2015) Trafficking of excitatory amino acid transporter 2- laden vesicles in cultured astrocytes: a comparison between approximate and exact determination of trajectory angles. *Amino acids* 47:357-367.
- Grubišić, V., Parpura, V. (2015) Diversity in the utilization of glucose and lactate in synthetic mammalian myotubes generated by engineered configurations of MyoD and E12 in otherwise non-differentiation growth conditions. *Biomaterials* 43: 50-60.
- Gottipati, M.K., Bekyarova, E., Haddon, R.C., Parpura, V. (2015) Chemically-functionalized single-walled

carbon nanotubes enhance the glutamate uptake characteristics of mouse cortical astrocytes. *Amino Acids* 47:1379-1388

In press:

- Rodríguez-Arellano, J.J., Parpura, V., Zorec, R., Verkhratsky, A. (2015) Astrocytes in physiological aging and Alzheimer's disease. *Neuroscience*
- Grubišić, V. Kennedy, A.J., Sweatt, J.D., Parpura, V. (2015) Pitt-Hopkins mouse model has altered particular gastrointestinal transits *in vivo*. *Autism Res*
- Zorec, R., Verkhratsky, A., Rodríguez, J.J., Parpura, V. (2015) Astrocytic vesicles and gliotransmitters: Slowness of vesicular release and synaptobrevin2-laden vesicle nanoarchitecture. *Neuroscience*
- Verkhratsky, A., Zorec, R., Rodríguez, J.J., Parpura, V. (2015) Astroglipathology in neurodegeneration. *Eur J Neurodegen Disease*
- Verkhratsky, A, Parpura, V. (2015) Astroglipathology in neurological, neurodevelopmental and psychiatric disorders. *Neurobiol Dis*
- Lim, D., Rodriguez, J.J., Parpura, V., Zorec, R., Zeidan-Chulia, F., Genazzani, A.A., Verkhratsky, A. (2015) Calcium signalling toolkits in astrocytes and spatio-temporal progression of Alzheimer's disease. *Curr Alzheimer Res*

Pozzo-Miller, Lucas

Full research papers

- Calfa G, W Li, JM Rutherford & L Pozzo-Miller (2015). Excitation/inhibition imbalance and impaired synaptic inhibition in hippocampal area CA3 of *Mecp2* knockout mice. *Hippocampus* 25: 159-168.
- Xu X, A Kozikowski & L Pozzo-Miller (2014). A selective histone deacetylase-6 inhibitor improves BDNF trafficking in hippocampal neurons from *Mecp2* knockout mice: implications for Rett syndrome. *Frontiers in Cellular Neuroscience* 8: 68 (doi: 10.3389/fncel.2014.00068).

Peer-reviewed Reviews

- Pozzo-Miller L, S Pati & AK Percy (2015). Rett syndrome: reaching for clinical trials. *Neurotherapeutics* in press.
- Wang H, S Pati, L Pozzo-Miller & LC Doering (2015). Targeted pharmacological treatment of autism spectrum disorders: fragile X and Rett syndromes. *Frontiers in Cellular Neuroscience* 9: 55 (doi: 10.3389/fncel.2015.00055).
- Phillips M & L Pozzo-Miller (2015). Dendritic spine dysgenesis in Autism Related Disorders. *Neuroscience Letters* in press (doi: 10.1016/j.neulet.2015.01.011).
- Xu X, EC Miller & L Pozzo-Miller (2014). Dendritic spine dysgenesis in Rett syndrome. *Frontiers in Neuroanatomy* 8: 97 (doi: 10.3389/fnana.2014.00097).
- Li W & L Pozzo-Miller (2014). BDNF deregulation in Rett syndrome. *Neuropharmacology* 76: 737-746.

Peer-reviewed Book Chapters

- Percy AK, C Chapleau, JB Lane & L Pozzo-Miller (2014). Defining and Diagnosing Rett Syndrome: Correlating Symptoms and Pathogenesis with Autism. In: "*The Comprehensive Guide to Autism*", V Patel, V Preedy, C Martin (Eds.), pp. 2581-2601. Berlin: Springer Reference, Springer-Verlag.

Published Abstracts

- Li W & L Pozzo-Miller (2014). Excitatory CA3->CA1 synapses are stronger in *Mecp2* knockout mice and saturate long-term potentiation. *Society for Neuroscience Abstracts* 11.08 Xu X, J Garcia, R Ewalt & L Pozzo-Miller (2014). The *BDNF* val-66-met polymorphism impairs dendritic complexity and dendritic spine density and form in hippocampal neurons of *Mecp2* knockout mice. *Society for Neuroscience Abstracts* 515.20

Roberson, Erik

- Day, J.J., and **E.D. Roberson**. (2015). An epigenetic brake on genetic inheritance: DNA methylation slows effects of *C9ORF72* mutations. *Neurology* 84:1616–1617.
- Hall, A.M., B.T. Throesch, S.C. Buckingham, S.J. Markwardt, Y. Peng, Q. Wang, D.A. Hoffman, and **E.D. Roberson**.[†] (2015). Tau-dependent Kv4.2 depletion and dendritic hyperexcitability in a mouse model of Alzheimer's disease. *J. Neurosci.* 35:6221–6230.
- Gannon, M., P. Che, Y. Chen, K. Jiao, **E.D. Roberson** and Q. Wang. (2015). Noradrenergic dysfunction in Alzheimer's disease. *Front. Neurosci.*, 9:220.
- Arrant, A.E., A. Patel, and **E.D. Roberson**. (2015). Effects of exercise on progranulin levels and gliosis in progranulin-insufficient mice. *eNeuro*, DOI: 10.1523/ENEURO.0061-14.2015.
- Cochran, J.N., T. Rush, S. Buckingham, and E.D. Roberson. A role for the Alzheimer's disease risk factor CD2AP in mediating blood-brain barrier integrity. *Hum Mol Genet* 24:6667–6674.
- Kimbrough, I.F., S. Robel, **E.D. Roberson**, and H. Sontheimer. (2015). Vascular amyloidosis impairs the gliovascular unit in a mouse model of Alzheimer disease. *Brain* 138:3716–3733.

Theibert, Anne - none**Visscher, Kristina**

- Elkhatali, A.S., Griffis, J.C., Vaden, R.J., Pool, S.M., Visscher, K.M. (2015) Distinct Effects of Trial Driven and Task Set-Related Control in Primary Visual Cortex. *NeuroImage*. (in press).
- Griffis JC, Elkhatali AS, Burge WK, Chen RH, Visscher KM. (2015) Retinotopic patterns of background connectivity between V1 and fronto-parietal cortex are modulated by task demands. [Front Hum Neurosci](#). 2015 Jun 8;9:338 PMID: 26106320
- Elkhatali, A.S., Vaden, R.J., Pool, S.M., Visscher, K.M. (2015) Early visual cortex reflects initiation and maintenance of task set. *NeuroImage*, (107, 277-278). PMID 25485712
- Vaphiades, M., Visscher, K.M., Rucker, J., Vattoth, S., Roberson, G. (2015) Functional MRI and MRI tractography in progressive supranuclear palsy-like syndrome. *Neuro-Ophthalmology*.

Wadiche, Jacques

- Rudolph S, Tsai MC, VonGersdorff H & Wadiche JI (2015). The ubiquitous nature of multivesicular release. *Trends in Neurosciences* 38:428-38.
- Wadiche JI & Overstreet-Wadiche L (2015). New neurons don't talk back. *Neuron* 85:3-5.
- Chancey JH, Poulsen DJ, Wadiche JI & Overstreet-Wadiche L (2014). Hilar mossy cells provide the first glutamatergic synapses to adult-born dentate granule cells. *J. Neurosci.*, 34: 2349-54.

Wilson, Scott

- Watson JA, Bhattacharyya BJ, Vaden JH, Wilson JA, Icyuz M, Howard AD, Phillips E, DeSilva TM, Siegal GP, Bean AJ, King GD, Phillips SE, Miller RJ, Wilson SM. 2015. Motor and Sensory Deficits in the teetering Mice Result from Mutation of the ESCRT Component HGS. *PLoS Genet*. 2015 Jun 26;11(6):e1005290.
- Vaden JH, Watson JA, Howard AD, Chen PC, Wilson JA, Wilson SM. 2015. Distinct effects of ubiquitin overexpression on NMJ structure and motor performance in mice expressing catalytically inactive USP14. *Front Mol Neurosci*. 2015 Apr 23;8:11.
- Vaden JH, Bhattacharyya BJ, Chen PC, Watson JA, Marshall AG, Phillips SE, Wilson JA, King GD, Miller RJ, Wilson SM. 2015. Ubiquitin-specific protease 14 regulates c-Jun N-terminal kinase signaling at the neuromuscular junction. *Mol Neurodegeneration* 10(1):3

3. Publications – Other

Brenner, Michael - none
Day, Jeremy - none
Dobrunz, Lynn <ul style="list-style-type: none"> Dobrunz, L.E. (2015) Short-term synaptic changes. <i>International Innovation</i> 177: 54-56.
Hablitz, John - none
King, Gwendalyn - none
Lester, Robin - none
Lubin, Farah <ul style="list-style-type: none"> 2015. Epigenetics and Neuroplasticity: Evidence and Debate. Farah D. Lubin and Schahram Akbarian (Co-editors) (Publishing editor, Elsevier).
Overstreet-Wadiche, Linda <ul style="list-style-type: none"> Ge S, Overstreet-Wadiche L and Enikolopov G (2015) Viral and Transgenic Reporters and Genetic Analysis of Adult Neurogenesis (ed. F. Gage, H. Song). Cold Spring Harbor Laboratory Monograph Series. Cold Spring Harbor Press, New York. In press.
Parpura, Vladimir Publications (other) Books: (1) <ul style="list-style-type: none"> Verkhratsky, A., Parpura, V. Physiology of Astroglia: Channels, Receptors, Transporters, Ion Signaling and Gliotransmission. In: Colloquium Series on Neuroglia in biology and medicine: From physiology to disease (Verkhratsky, A., Parpura, V., Eds). Morgan & Claypool Publishers, Colloquium Digital Library of Life Sciences; DOI: 10.4199/C00123ED1V01Y201501NGL004 (March 2015; 174 pp) Edited volumes/series: (2) <ul style="list-style-type: none"> Verkhratsky, A., Parpura, V. (Guest Eds.) Special Issue on Calcium Channels. <i>European Journal of Pharmacology</i>, Volume 739: 1-106 (2014) (Journal-Special Issue) Peng, L., Parpura, V., Verkhratsky, P. (Guest Eds.) Thematic Issue: Neuroglia as a Central Element of Neurological Diseases: An Underappreciated Target for Therapeutic Intervention. <i>Current Neuropharmacology</i>, Volume 12 (4): 303-386 (2014) (Journal-Special Issue) Commentaries: (3) <ul style="list-style-type: none"> Parpura V. (Ed.) American Society for Neurochemistry (ASN) Newsletters. July, 2014 issue. Peng, L., Parpura, V., Verkhratsky, A. (2014) Neuroglia as a central element of neurological diseases: An underappreciated target for therapeutic intervention. <i>Curr Neuropharmacol</i> 12 : 303-309. [Editorial] Grubišić, V., Parpura, V. (2015) The second brain in autism spectrum disorder: Could connexin 43 expressed in enteric glial cells play a role? <i>Front. Cell. Neurosci.</i> 9:242. doi: 10.3389/fncel.2015.00242 [opinion]-peer reviewed
Pozzo-Miller, Lucas - none
Roberson, Erik <ul style="list-style-type: none"> Wang, L., A.C. Naj, R.R. Graham, P.K. Crane, B.W. Kunkle, C. Cruchaga, J.D. Murcia, L. Cannon-Albright, C.T. Baldwin, H. Zetterberg, K. Blennow, W.A. Kukull, K.M. Faber, N. Schupf, M.C. Norton, J.T. Tschanz, R.G. Munger, C.D. Corcoran, E. Rogaeva, C. Lin, B.A. Dombroski, L.B. Cantwell, A. Partch, O. Valladares, H. Hakonarson, P. St George-Hyslop, R.C. Green, A.M. Goate, T.M. Foroud, R.M. Carney, E.B. Larson, T.W. Behrens, J.S. Kauwe, J.L. Haines, L.A. Farrer, M.A. Pericak-Vance, R. Mayeux, G.D. Schellenberg, National Institute on Aging-Late-Onset Alzheimer's Disease Family Study, Alzheimer's Disease Genetics Consortium [including E.D. Roberson]. (2015). Rarity of the Alzheimer disease-protective <i>APP</i> A673T variant in the United States. <i>JAMA Neurol.</i> 72:209–216.

- Jun, G., C.A. Ibrahim-Verbaas, M. Vronskaya, J.C. Lambert, J. Chung, A.C. Naj, B.W. Kunkle, L.S. Wang, J.C. Bis, C. Bellenguez, D. Harold, K.L. Lunetta, A.L. Destefano, B. Grenier-Boley, R. Sims, G.W. Beecham, A.V. Smith, V. Chouraki, K.L. Hamilton-Nelson, M.A. Ikram, N. Fievet, N. Denning, E.R. Martin, H. Schmidt, Y. Kamatani, M.L. Dunstan, O. Valladares, A.R. Laza, D. Zelenika, A. Ramirez, T.M. Foroud, S.H. Choi, A. Boland, T. Becker, W.A. Kukull, S.J. van der Lee, F. Pasquier, C. Cruchaga, D. Beekly, A.L. Fitzpatrick, O. Hanon, M. Gill, R. Barber, V. Gudnason, D. Campion, S. Love, D.A. Bennett, N. Amin, C. Berr, M. Tsolaki, J.D. Buxbaum, O.L. Lopez, V. Deramecourt, N.C. Fox, L.B. Cantwell, L. Tarraga, C. Dufouil, J. Hardy, P.K. Crane, G. Eiriksdottir, D. Hannequin, R. Clarke, D. Evans, T.H. Mosley, Jr., L. Letenneur, C. Brayne, W. Maier, P. De Jager, V. Emilsson, J.F. Dartigues, H. Hampel, M.I. Kamboh, R.F. de Bruijn, C. Tzourio, P. Pastor, E.B. Larson, J.I. Rotter, M.C. O'Donovan, T.J. Montine, M.A. Nalls, S. Mead, E.M. Reiman, P.V. Jonsson, C. Holmes, P.H. St George-Hyslop, M. Boada, P. Passmore, J.R. Wendland, R. Schmidt, K. Morgan, A.R. Winslow, J.F. Powell, M. Carasquillo, S.G. Younkin, J. Jakobsdottir, J.S. Kauwe, K.C. Wilhelmsen, D. Rujescu, M.M. Nothen, A. Hofman, L. Jones, IGAP Consortium [including **E.D. Roberson**], J.L. Haines, B.M. Psaty, C. Van Broeckhoven, P. Holmans, L.J. Launer, R. Mayeux, M. Lathrop, A.M. Goate, V. Escott-Price, S. Seshadri, M.A. Pericak-Vance, P. Amouyel, J. Williams, C.M. van Duijn, G.D. Schellenberg, and L.A. Farrer. (2015). A novel Alzheimer disease locus located near the gene encoding tau protein. *Mol Psychiatry*. DOI:10.1038/mp.2015.23.
- Østergaard, S.D., S. Mukherjee, S.J. Sharp, P. Proitsi, L.A. Lotta, F. Day, J.R. Perry, K.L. Boehme, S. Walter, J.S. Kauwe, L.E. Gibbons, Alzheimer Disease Genetics Consortium [including **E.D. Roberson**], GERAD1 Consortium, EPIC-InterAct Consortium, E.B. Larson, J.F. Powell, C. Langenberg, P.K. Crane, N.J. Wareham, and R.A. Scott. (2015). Associations between Potentially Modifiable Risk Factors and Alzheimer Disease: A Mendelian Randomization Study. *PLoS Med* 12:e1001841.
- Ghani, M., C. Reitz, R. Cheng, B.N. Vardarajan, G. Jun, C. Sato, A. Naj, R. Rajbhandary, L.S. Wang, O. Valladares, C.F. Lin, E.B. Larson, N.R. Graff-Radford, D. Evans, P.L. De Jager, P.K. Crane, J.D. Buxbaum, J.R. Murrell, T. Raj, N. Ertekin-Taner, M. Logue, C.T. Baldwin, R.C. Green, L.L. Barnes, L.B. Cantwell, M.D. Fallin, R.C. Go, P.A. Griffith, T.O. Obisesan, J.J. Manly, K.L. Lunetta, M.I. Kamboh, O.L. Lopez, D.A. Bennett, H. Hendrie, K.S. Hall, A.M. Goate, G.S. Byrd, W.A. Kukull, T.M. Foroud, J.L. Haines, L.A. Farrer, M.A. Pericak-Vance, J.H. Lee, G.D. Schellenberg, P. St George-Hyslop, R. Mayeux, E. Rogaeva, and Alzheimer's Disease Genetics Consortium [including **E.D. Roberson**]. (2015). Association of Long Runs of Homozygosity With Alzheimer Disease Among African American Individuals. *JAMA Neurol*. doi: 10.1001/jamaneurol.2015.1700

Theibert, Anne – none

Vischer, Kristina – none

Wadiche, Jacques - none

Wilson, Scott - none

4. Presentations at Scientific Meetings

Brenner, Michael - none

Day, Jeremy

- Invited Speaker, “Epigenetics: Bridging Development and Disease” Conference in Boston, MA (05/20/2015)
- Invited Speaker, McKnight Brain Research Foundation Inter-Institutional Meeting in Miami, FL (5/1/2015)
- Invited Speaker, UAB Comprehensive Neuroscience Center (4/10/2015)
- UAB Center for Neurodegeneration and Experimental Therapeutics retreat (3/27/2015)
- Seminar Speaker, University of Utah, Department of Neurobiology and Anatomy (12/2/2014)
- Invited Speaker, 5th Annual EpiCongress Conference in Boston, MA (07/23/2014)

Dobrunz, Lynn

- UAB CNC Retreat, 4-10-2015

Hablitz, John - none

King, Gwendalyn

- Age, Los Angeles CA June 2015. National meeting, poster presentation
- CNC- UAB annual retreat – April 2015
- Aging Symposium UAB – October 2014
- Oakwood Bio-medical Student Association – October 2014 – joint scientific and SPIN advertising visit to Oakwood University – HBCU partner on the SPIN REU grant.

Lester, Robin

- Emory University, Department of Pharmacology Seminar, September 16, 2014 “The Medial Habenula: Reindeer don’t smoke”

Lubin, Farah

- 2015 F.D. Lubin. Department of Molecular and Integrative Physiology at the University of Illinois at Urbana-Champaign. Invited by Dr. Catherine Christian.
- 2015 F.D. Lubin. Behavioral Epigenetics: Conserved Mechanisms in Diverse Model Systems in at the HHMI/Janelia Research Campus. Invited by Drs. Ulrike Heberlein (HHMI/Janelia), Michael Meaney (McGill University), Eric Nestler (Mount Sinai School of Medicine).
- 2015 F.D. Lubin. Neuroepigenetics, at the Neuroscience School for Advanced Studies in Cortona in Tuscany/Italy. Invited by the NSAS director, Dr. Pulvirenti and Dr. Schahram Akbarian.
- 2015. F.D. Lubin. Summer Health Enrichment Program (SHEP) at the UAB School of Medicine. Invited by Dr. Marquita Hicks.
- 2015 F.D. Lubin. Exploring chromatin for the reversal of memory deficits associated with epilepsy. University of North Dakota seminar series. Grand Forks, ND. Invited by Dr. Jonathan Geiger.
- 2015 F.D. Lubin. Neuroscience Café at Hoover Library. Invited by the CNC director, Dr. Lori McMahon.
- 2015 F.D. Lubin. Comprehensive Neuroscience Center (CNC) Neuroscience Café at Homewood Library. Invited by the CNC director, Dr. Lori McMahon.
- 2014 F.D. Lubin. Epigenetics, Memory, and Memory Deficits. The Robert S. Dow Neurobiology Laboratories seminar series. Portland, Oregon. Invited by Dr. Detlev Boison.
- 2014 F.D. Lubin. Methyl supplementation rescues memory deficits associated with TLE. UCI (University of California, Irvine) EpiCenter (Epilepsy Research Center) seminar series. Invited by Drs. Tallie Baram, Chris Gall, Al Goldin, Ivan Soltesz & John Weiss.

Overstreet-Wadiche, Linda

- Invited speaker at 2014 Mechanisms of Epilepsy and Neural Synchronization Gordon Research Conference, Aug 17-22, Mount Snow, VT
- Sept 17 2014, Department of Neurobiology, Penn State University
- June 25 2015 Institut des Neurosciences Cellulaires et Integratives, Strasbourg, France

Parpura, Vladimir

Parpura-Invited talks (11)

- 7/4/2014 “Ca²⁺ sources for the exocytotic glutamate release from astrocytes: health and disease”, Conference on “Calcium Signaling: from basic to bedside”, Stockholm, Sweden.
- 7/7/14 “Calcium dynamics in (patho)physiology of astrocytes: Exocytotic release of glutamate”, Symposium on “Basic and translational neurochemistry: Glia and neurons in health and disease”, Rijeka, Croatia
- 7/11/14 “Probing neurons and astrocytes with carbon nanotubes: Implications for translational medicine”, Workshop on “Astroglia 2014”, Ljubljana, Slovenia

- 7/13/14 “Tripartite synapse: New glial roles”; two talks “Part 1: Mechanisms of glutamate release from astrocytes” and “Part 2: Astroglial cells release glutamate by regulated exocytosis in health and disease”, “Gliotransmission in Physiology and Pathology” Neuroscience School of Advanced Studies, Bressanone-Abbazia di Novacella, Italy
- 7/25/14 “Tripartite synapse-astrocytic regulation of glutamate in health and disease”, Collaborative Program in Neuroscience, University of Toronto, Toronto, Canada
- 8/29/14 “Exocytotic glutamate release from astrocytes: Intracellular Ca²⁺ and Na⁺ dynamics” in Symposium “Sodium Signalling in Astroglia” (organizer and chair: Alexei Verkhratsky, The Manchester University, Manchester, UK; co-chair: Csaba Fekete, Hungarian Academy of Sciences, Budapest, Hungary). Joint Meeting of the Federation of European Physiological Societies and the Hungarian Physiological Society, Budapest, Hungary
- 9/29/14 “Tripartite synapse: New glial roles”; two talks “Part 1: Mechanisms of glutamate release from astrocytes” and “Part 2: Vesicular release of glutamate mediates bidirectional signaling between astrocytes and neurons”, Argentine Society for Neuroscience and International Society for Neurochemistry small conference and course: “New mechanisms of neuro-glial interaction: Their contribution to nervous system development and repair”, Huerta Grande, Córdoba, Argentina
- 10/03/14 The role of mitochondria in exocytotic glutamate release from astrocytes. 1st International Bordeaux Neurocampus/Brain Conference, Bordeaux, France
- 10/13/14 “Calcium dynamics of glial cells and genetic influences on behavior of the nematode *Caenorhabditis elegans*”, Bevil Conference on Glial Biology in Medicine, Birmingham, AL
- •3/16/15 “On vesicular fusions in astrocytes: Single vesicle/molecule approaches” in Symposium “Astrocytes as Obligatory Partners in Purinergic and Glutamatergic Neurotransmission” (Organizer and Chair: Arne Schousboe, University of Copenhagen, Denmark; co-Organizer and co-Chair: Vladimir Parpura), 46st Annual Meeting of the American Society for Neurochemistry, Atlanta, GA
- •3/29/15 “Exocytotic glutamate release from astroglia: Emphasis on mitochondria and immunophilins” in Symposium “Gliotransmission and Behavior” (Organizer and Chair: Vladimir Parpura) Experimental Biology 2015, Boston, MA
- Laboratory: (8)
- 10/12-14/14 Cavender, C.E.¹, Gottipati, M.K.², Parpura, V. (2014) On trajectory angles of secretory vesicles in cultured astrocytes: a comparison between approximate and exact determination. Conference on Glial Biology in Medicine, Birmingham, AL; poster presentation
- 10/12-14/14 Gottipati, M.K. ², Bekyarova, E., Brenner, M. Haddon, R.C., Parpura, V. (2014) Probing Astrocytes with Carbon Nanotubes and Assessing Their Effects on Astrocytic Structural and Functional Properties. Conference on Glial Biology in Medicine, Birmingham, AL; poster presentation
- 10/12-14/14 Montana, V. ³, Gottipati, M.K.², Sontheimer, H. Parpura, V. (2014) Vesicular glutamate release from glioblastoma multiforme” Conference on Glial Biology in Medicine, Birmingham, AL; poster presentation
- 10/24/14 Gottipati, M.K. ², Bekyarova, E., Brenner, M., Haddon, R., Parpura, V. (2014) Probing astrocytes with carbon nanotubes and assessing the role of glial fibrillary acidic protein in their effects on astrocytic morphology and proliferation. Biomedical engineering Society 2014 Annual Meeting, Platform session “Nanobiointerfaces”, Talk
- 3/2, 3/15 Ding, S. Wang, X., Zhang, N., Gottipati, M.K. ², Parpura, V. (2015) Imaging of mitochondrial Ca²⁺ dynamics in astrocytes using cell-specific mitochondria-targeted GCaMP5G/6s. Gordon Research Conference on “Glial biology: functional interactions among glia and neurons”, Ventura, CA. Poster presentation

- 3/15/15 Montana, V. ³, Flint, D. Wilson, L., Waagepetersen, H.S., Schousboe, S., Parpura, V. (2015) Metabolic regulation of vesicular glutamate release from cultured astrocytes. In Symposium “Glial Vesicular, Metabolic and Morphologic Function in Health and Disease” (Organizer and Chair: Robert Zorec, University of Ljubljana, Slovenia; (co-Organizer and co-Chair: Vladimir Parpura, UAB), 46st Annual Meeting of the American Society for Neurochemistry, Atlanta, GA; Talk
- 3/14,15/15 Ding, S. Wang, X., Zhang, N., Gottipati, M.K. ², Parpura, V. (2015) Imaging of mitochondrial Ca²⁺ dynamics in astrocytes using cell-specific mitochondria-targeted GCaMP5G/6s. In Poster Session I. 46st Annual Meeting of the American Society for Neurochemistry, Atlanta, GA; Poster
- ¹ Undergraduate Student, ² Graduate student, ³ Post-doctoral fellow in my laboratory

Pozzo-Miller, Lucas

- Department of Neurology, Department of Neurobiology & Behavior, and Institute of Neuroscience, Stony Brook University, Stony Brook NY.
 - Speaker at the 13th Annual Meeting of the International Rett Syndrome Foundation, Chantilly, VA.
 - Behavioral Neuroscience Program, Department of Psychology, College of Arts & Sciences, UAB.
- Speaker at “*Cortical dysfunction in Rett Syndrome: Opportunities for new treatment development*” panel, Winter Conference on Brain Research, Steamboat Springs, CO.

Roberson, Erik

- 2015 California State University, Fullerton HHMI Scholars Program Seminar
- 2015 American Neurological Association Meeting, Chicago, Derek Denny-Brown Symposium
- 2015 American Neurological Association Meeting, Chicago, Special Interest Group
- 2015 Genentech, South San Francisco
- 2015 Baylor College of Medicine Neuroscience Seminar (scheduled)
- 2015 Keynote speaker, UAB MSTP retreat
- 2015 Alzheimer’s of Central Alabama: “Alzheimer’s Family Conference and Research Symposium”
- 2015 McKnight Brain Institute symposium

Theibert, Anne

- Fall 2014: UAB Undergraduate Neuroscience Colloquium-Seminar

Vischer, Kristina

- Emory Eye Center and Center for Visual and Neural Rehabilitation (May, 2015, workshop and award lecture) Structure and function of visual cortex following central vision loss
- Vision Sciences Society meeting (May 2015, yearly meeting, I was session organizer and speaker). Central vs. peripheral primary visual cortex differ in cortical thickness and functional connectivity
- Evelyn F. and William L. McKnight Brain Institute Annual Inter-Institutional Meeting (April, 2015, yearly meeting) Brain networks defined by functional connectivity: relating cortical thickness to executive function performance in older adults
- Comprehensive Neuroscience Center Retreat, UAB (April, 2015, yearly meeting) The role of Attention in Cortical Plasticity
- UAB/Auburn Neuroimaging Retreat, (July, 2014, yearly meeting) Vision and Neuroimaging

Wadicke, Jacques

- Synaptic Physiology Special seminar, Université Paris Descartes, Paris, France, 2015 Jun
- Institut de Neurosciences Cellulaires et Intégratives, Université de Strasbourg, Strasbourg, France, 2015 Jun

Wilson, Scott

- 2014 Society for Neuroscience Meeting. Mini-symposium Invited Speaker.
- 5th Ubiquitin Research and Drug Discovery Conference. Invited Speaker.

5. Presentations at public (non-scientific) meetings or events

Brenner, Michael - none
Day, Jeremy - none
Dobrunz, Lynn Research on changes in the brain in an animal model related to aspects of schizophrenia. Neuroscience Café, sponsored by the UAB Comprehensive Neurosciences Center. Hoover Library 8-18-14, Homewood Library 1-22-15
Hablitz, John - none
King, Gwendalyn - none
Lester, Robin - none
Lubin, Farah <ul style="list-style-type: none"> The research being conducted at the Civitan international research center. University of Alabama at Birmingham, Birmingham, Alabama. Invited by CIRC to talk to guests at local Civitan Clubs. Career options in research. University of Alabama at Birmingham, Birmingham, Alabama. Spoke to students in SPIN (Summer Program in Neuroscience). Grant writing workshop sponsored by the Postdoctoral Association. University of Alabama at Birmingham, Birmingham, Alabama. Spoke to postdocs and faculty about the NIH-K99 funding mechanism.
Overstreet-Wadiche, Linda - none
Parpura, Vladimir - none
Pozzo-Miller, Lucas <ul style="list-style-type: none"> <i>Neuroscience Café</i>, UAB Comprehensive Neuroscience Center, Homewood Public Library. People-Behind-the-Science Web Radio Interview.
Roberson, Erik <ul style="list-style-type: none"> 2015 Linden Baptist Church, Linden, AL 2015 Neuroscience Café, Hoover Public Library
Theibert, Anne <ul style="list-style-type: none"> Spring 2015 Panel Discussion on UAB Undergraduate Neuroscience Program at Birmingham Women's Network
Visscher, Kristina <ul style="list-style-type: none"> Osher Lifelong Learning Institute, Tuscaloosa, AL October 7, 2014, "Attention: Changing the way your brain processes information." University of Alabama, Tuscaloosa Psychology interest group October 14, 2015, "Attention: Changing the way your brain processes information." McWane Science Center Science Café, John's City Diner, Birmingham AL. October 21, "Attention: Changing the way your brain processes information." Civitan District Meeting, Tupelo MS, Feb 20, 2015. "Understanding attention, and Hello from the Research Civitan Club." Featured speaker at the meeting.
Wadiche, Jacques - none
Wilson, Scott - none

6. Awards

Brenner, Michael - none
Day, Jeremy <ul style="list-style-type: none"> Avenir Award from National Institute on Drug Abuse (2015) Early-career award supporting investigators proposing highly innovative studies that open new areas of research for the genetics or epigenetics of addiction

<ul style="list-style-type: none"> Travel Award from American College of Neuropsychopharmacology (2015) Early-career travel award supporting attendance at the annual meeting for the American College of Neuropsychopharmacology
Dobrunz, Lynn - none
Hablitz, John - none
King, Gwendalyn <ul style="list-style-type: none"> Graduate School Dean's award for excellence in mentorship
Lester, Robin - none
Lubin, Farah <ul style="list-style-type: none"> 2013-2016, American Epilepsy Society Basic Sciences Committee 2014-Present, Director of UAB Neuroscience Roadmap Scholar Program
Overstreet-Wadiche, Linda - none
Parpura, Vladimir <ul style="list-style-type: none"> 1/1/14-Member (3-year term), Physiology and Medicine Section Committee, Academia Europaea 3/17/15-President-Elect (2-year term), American Society for Neurochemistry
Pozzo-Miller, Lucas - none
Roberson, Erik <ul style="list-style-type: none"> Derek Denny-Brown Neurological Scholar Award, American Neurological Association, 2015
Theibert, Anne - none
Vischer, Kristina <ul style="list-style-type: none"> Research Civitan Club award for exemplary science outreach
Wadiche, Jacques - none
Wilson, Scott - none

7. External collaborations with other McKnight Institutes, institutions and research programs

Brenner, Michael - none
Day, Jeremy – none
Dobrunz, Lynn - none
Hablitz, John - none
King, Gwendalyn - none
Lester, Robin - none
Lubin, Farah <ul style="list-style-type: none"> Carol Barnes-University of Arizona Tom Foster-University of Florida Matt Huentelman- Tgen
Overstreet-Wadiche, Linda <ul style="list-style-type: none"> Jacques Wadiche, UAB Gwen King, UAB Jeremy Day, UAB
Parpura, Vladimir - none
Pozzo-Miller, Lucas - none
Roberson, Erik <ul style="list-style-type: none"> Dr. Erik Roberson and Dr. Harald Sontheimer collaborated to examine the effects of vascular amyloid deposition on vascular function.
Theibert, Anne - none

Vischer, Kristina

- Member of the McKnight MRI Standardization Workgroup. Worked with representatives at each of the centers to develop strategies for comparing data across sites. This developed into a funded research project: The McKnight Brain Aging Registry project, which is described in the Current Grant Funding section.
- Collaborating with Adam Woods from University of Florida, Gainesville on a project looking at augmenting useful field of view training by using transcranial direct current stimulation.

Wadicke, Jacques

- Linda Wadicke, UAB
- Gwen King, UAB
- Jeremy Day, UAB

Wilson, Scott - none

8. Collaborative programs with non-McKnight institutes, institutions and research programs**Brenner, Michael****A. Within the UAB system**

- Dr. Anthony Nicholas, Associate Professor of Neurology: The role of GFAP deimidation in Alexander disease
- Dr. Stephen Barnes, Professor of Pharmacology: Proteomic analysis of Rosenthal fibers in Alexander disease
- Dr. Michelle Olsen, Assistant Professor of Cell, Developmental & Integrative Biology: Injury response of GFAP-driven transgenes
- Dr. Vlad Parpura, Associate Professor of Neurobiology: Role of GFAP in the response of astrocytes to nanoparticles

B. Outside the UAB system

- Dr. Albee Messing, University of Wisconsin, Madison: Studies of GFAP transcription; analyses of Alexander disease cases
- Dr. David C. Muddiman, North Carolina State University: Proteomic analysis of Rosenthal fibers in Alexander disease

Day, Jeremy**A. Within the UAB System**

- Sarah Clinton, UAB, Project using whole-genome sequencing approaches to identify epigenetic modifications in rat models of emotional behavior
- David Sweatt, UAB, Project to characterize extra-coding RNAs in neuronal systems

B. Outside the UAB System

- Brandon J. Aragona, University of Michigan, Project investigating epigenetic mechanisms in social attachment in prairie voles
- Charles Gersbach, Duke University, Project using CRISPR/Cas based systems for epigenetic editing
- Chris Newland, Auburn University, Project using whole genome sequencing to identify epigenetic signatures of developmental methylmercury exposure

Dobrunz, Lynn**A. Within the UAB system**

- Ongoing collaborations with Rita Cowell, John Hablitz, Lori McMahon, Mark Bevensee, Gwen King; New collaboration with Kazu Nakazawa

B. Outside the UAB system

- New collaboration with Stephen Foulger, Clemson; Jason Weick, University of New Mexico

Hablitz, John - none

King, Gwendalyn**A. Within the UAB System**

- Dr. Brian Simms to develop a neurosphere model for the study of klotho in neurogenesis
- Dr. Sarah Clinton to study the role of GRIK5 in depression.
- Dr. Linda Wadiche – neurogenesis and behavior
- Dr. Scott Wilson – ubiquitin signaling in neurons
- Yabing Wang – klotho function in the vascular system

B. Outside the UAB system

- Dr. Darryl Quarles, University of Tennessee to characterize the brain in FGF23 knockout mice and share resources relevant to our research programs. Dr Quarles is interested in klotho in kidney and we are interested in klotho in brain.

Lester, Robin - none**Lubin, Farah****A. Within the UAB system**

- Standaert Lab
- Chatham Lab
- Ver Hoef Lab
- Riley Lab
- Riddle Lab
- Roberts Lab

B. Outside the UAB system

- Nguyen- University of Toronto
- Huentelman- Tgen
- Nigel Jones-University of Melbourne, Australia
- Robert Lipsky, INOVA
- Molly Meffert, John Hopkins
- Laura Schrader, Tulane University

Overstreet-Wadiche, Linda**A. Within the UAB system**

- Gut malfunctions in a mice model of Pitt-Hopkins syndrome (J.D. Sweatt)
- The role of astrocytes in Huntington's disease (M. Gray)
- The role of GFAP in EAAT2 trafficking in astrocytes (M. Brenner)
- Trafficking of rhodopsin (A. Gross)
- The role of sodium-bicarbonate exchangers in astrocytes (M. Bevensee)

B. Outside the UAB system

- Cyberplasm (J. Ayers, Northeastern University, MA)
- CFTR/ENaC plasma membrane interactions (B. Berdiev, Nazarbayev University at Astana, Kazakhstan)
- Pools of glutamate for exocytotic glutamate release (H.S. Waagepetersen and A. Schousboe; Univ of Copenhagen, Denmark)
- The role of connexin 43 in astrocytic exocytosis (E. Scemes and D.C Spray, Albert Einstein College of Medicine, NY)
- Optogenetic approaches for stimulation of astrocyte in vivo (S. Kasparov, Univeristy of Bristol, UK and P.G. Haydon, Tufts Univ, Boston, MA)
- CNTs in modulation of neuronal growth, astrocytic maturation/stellation (R.C. Haddon, Univ of California Riverside, CA)

- SNARE complex proteins (R. Zorec, Univ of Ljubljana, Slovenia)
- BDNF- and VGLUT-laden vesicle trafficking in astrocytes (R. Zorec, Univ of Ljubljana, Slovenia)
- The role of presenilins in vesicular trafficking in astrocytes (R. Zorec, Univ of Ljubljana, Slovenia)
- Purinergic status in astrocytes (S. Stojilkovic, NIH)
- The role of Homer in calcium dynamics and exocytosis from astrocytes (P. Bezzi, University of Lausanne, Switzerland)
- Graphene in biological applications (V. Jekanović, Vinča Institute, Belgrade, Serbia)
- Mechanisms underlying GFAP modulation of hyposmotic regulation of hypothalamic vasopressin neuron activity (Y-F. Wang, Harbin Medical University, P.R. China)
- Exocytotic glutamate release from gliomas (H. Sontheimer, Virginia Tech University)

Overstreet-Wadiche, Linda

A. Within the UAB system

- Candace Floyd, UAB

B. Outside the UAB system

- Dave Poulson, University of Montana Missoula
- Karoly Mirnics, Vanderbilt
- Brad Aimone, Sandia Labs
- Roberto Panichi, University of Perugia, Italy
- Chay Kuo, Duke University

Pozzo-Miller, Lucas

A. Within the UAB System

- Sandipan Pati (Neurology)
- Michelle Olsen (Cell, Developmental & Integrative Biology)
- Alan Percy (Pediatrics)
- Manimaran Ramani (Pediatrics)
- Victor Mark (Physical Medicine and Rehabilitation)
- Ed Taub (Psychology)
- Gitendra Uswatte (Psychology)

B. Outside the UAB system

- Frank Longo, Stanford University, San Francisco, CA
- Tien-Le Xu, Jiao-Tong University, Shanghai, China.
- James Eubanks, Toronto Western Hospital, Canada.
- Alan Kozikowski, University of Illinois.
- Steve Gray, University of North Carolina at Chapel Hill
- Suzanne Oberholster, Samford University, Birmingham, AL.
- Takafumi Inoue, Waseda University, Tokyo, Japan.
- Arturo Romano, University of Buenos Aires, Argentina.

Roberson, Erik

- Dax Hoffman, NICHD on the effect of tau on dendritic excitability
- Harald Sontheimer, Virginia Tech on the effect of vascular amyloid on the gliovascular unit
- Adam Boxer, UCSF on new tau-directed treatment strategies

Theibert, Anne - none

Vischer, Kristina**A. Within the UAB system**

- Karlene Ball and Despina Stavrinos, Psychology Department. We wish to examine how ongoing brain activity as measured with fMRI may be altered after training on a visual processing speed task. This task has been shown to have great behavioral gains for older adults, thought to arise from changes in speed of processing of visual attention, which is likely to be mediated by attention. We have submitted four grant proposals (two funded) about this general topic. (One was a section of a PO1 proposal, the other was a funded CCTS pilot program proposal. A version of this project, in younger adult participants, is part of my recent RO1 proposal. Another version of the project, using older adult data, but exploring connectivity, was funded by a pilot grant in October of 2013 by the UAB Interdisciplinary Institute for Imaging). In conjunction with Sherry Willis, from the University of Washington, we are developing a randomized controlled trial to examine the neural and behavioral effects of two effective training paradigms for older adults.
- Cynthia Owsley and Dawn DeCarlo, Ophthalmology Department. Both Dr. Owsley and Dr. DeCarlo are involved in the macular degeneration and training project described above and in the 'grants' section. Dr. Owsley's expertise in training and vision loss, and Dr. DeCarlo's clinical expertise with low vision populations have been a great team for examining this question. My lab's project on cortical effects of macular degeneration, funded by the Dana Foundation, requires this collaboration.
- Daniel Marson, Neurology Department. Dr. Marson's NIH funded grant studies the relationship between financial abilities and brain structure and function in participants with Mild Cognitive Impairment. My role in the project is to assist with methods, interpretations and analyses of MRI and fMRI data. We are examining how the integrity of connections among brain networks may predict participants' behavioral scores indicating their financial capacity. I work closely with Dr. Marson's lab members to analyze and interpret their data.
- Adrienne Lahti, Psychiatry Department. Dr. Lahti studies patients with Schizophrenia. We are collaborating to implement and describe more robust methods for examining functional connectivity in these patients, removing some artifacts due to head movement.
- Jerzy Szaflarski, Neurology Department. Dr. Szaflarski's focus is on epilepsy. He has used simultaneous EEG/fMRI methods to localize the origin of seizure activity. With Dr. Szaflarski, we are collecting simultaneous EEG/fMRI data in a group of healthy participants as well as a group of patients with epilepsy. We will compare oscillatory EEG signals that change depending on a participant's task set with modulations in functional MRI activity.

B. Outside the UAB system

- Professor Aaron Seitz, UC Riverside. Dr. Seitz's lab focuses on implicit learning. Our collaborative project examines how ongoing fluctuations in EEG alpha power are influenced by learning. Data were presented at the Vision Sciences Society meeting in 2014, and our paper is currently under review.
- Associate Professor John Serences, UCSD. Dr. Serences's lab focuses on visual attention. He is sharing the MRI data from a recent study with our lab in order for us to perform supplementary analyses examining how training in visual attention influences brain anatomy and function.
- Professor Lyn Turkstra, University of Wisconsin, Madison. Dr. Turkstra studies how traumatic brain injury impacts social cognition. I am a collaborator on her NIH RO1 funded grant examining how eye movements interact with these effects. Data examining eye movements in traumatic brain injury were presented at the International Brain Injury Association World Congress in March 2014.

- Professor Sherry Willis, University of Washington. Dr. Willis has been a leader in examining training paradigms for older adults. Her work has focused on a training paradigm called Reasoning training. As described above, in association with Karlene Ball in Psychology, we are putting together a proposal for a randomized controlled trial to study behavioral and brain effects of this training paradigm.

Wadiche, Jacques

A. Within the UAB system

- Gwen King, UAB
- Tara DeSilva, UAB
- William Britt, UAB
- Laura Volpicelli-Daley, UAB
- Andrew West, UAB

B. Outside the UAB system

- Anastassios Tzingounis, University of Connecticut Storrs
- Loren Looger, JFRC
- David Bredt, Jessen Pharma; Johnson and Johnson
- Susumu Tomita, Yale Medical School

Wilson, Scott

A. Within the UAB system

- Elizabeth Stzul
- Erobohene E. Ubogu
- Gwen King
- Tara DeSilva

B. Outside the UAB system

- Steven Scherer- University of Pennsylvania
- Laura Feltri- University of Buffalo
- Andrew Bean, The University of Texas Graduate School of Biomedical Sciences at Houston
- Richard Miller, Northwestern University
- Matthew Harms, Washington University

APPENDICES

List of Seminar Speakers sponsored by the Evelyn F. McKnight Brain Institute at UAB

Evelyn F. McKnight Brain Institute Seminars 2015		
01-08-2015	David Krizaj, Ph.D. Professor University of Utah SOM	"The role of TRP channels in vertebrate vision"
01-29-2015	Amelia J. Eisch, Ph.D. Associate Professor University of Texas, Southwestern	"Adult hippocampus neurogenesis: What is it good for? And what is good for it?"
02-12-2015	Gentry Patrick, Ph.D. Associate Professor UC, San Diego	"Ubiquitin at the synapse"
02-19-2015	Elise F. Stanley, Ph.D. Professor University of Toronto	"The calcium channel and the gating of fast transmitter release "
02-26-2015	Daniel Forger, Ph.D. Professor University of Michigan	"From a network of 10,000 neurons to an iPhone app with 100,000 users: linking scales in biological rhythms"
03-19-2015	Stephen Traynelis, Ph.D. Professor Emory University	"NMDA Receptor Gating and Human Disease"
04-02-2015	Michael R. Bruchas, Ph.D. Assistant Professor Washington University School of Medicine	"Dissecting GPCR Signaling and Neural Circuits in Stress"
07-23-2015	Hongjun Song, Ph.D. Professor Johns Hopkins School of Medicine	"Plasticity in the adult mammalian brain: neurogenesis and neuroepigenetics"
09-10-2015	Todd Eliot Golde, MD, PhD Professor University of Florida	"Novel Insights into the Role of Innate Immunity in Neurodegenerative Disorders"
09-17-2015	Dena Dubal, MD, PhD Assistant Professor UC, San Francisco	"Longevity and the Aging Brain"
10-23-2015	Robert Zorec, Ph.D. Professor University of Ljubljana, Slovenia	"Why large and small exocytotic vesicles exhibit different fusion probability? Lessons from endocrine and gliocrine cells"

10-28-2015	Steve Austad, Ph.D. Karlene Ball, Ph.D. Jeremy Day, Ph.D. John Hablitz, Ph.D. Andrew Kennedy, Ph.D. Lori McMahon, Ph.D. Erik Roberson, M.D., Ph.D.	“Memory and Aging: Novel Mechanisms and Therapeutic Approaches”
10-29-2015	Aaron Haeusler, Ph.D. Post Doc Johns Hopkins University	"Disentangling the molecular mechanisms of C9ORF72-linked disease"
11-05-2015	Christopher Gregg, PhD Assistant Professor University of Utah	"Maternal and Paternal Gene Networks in the Brain"
11-09-2015	Prakash Kara, Ph.D. Associate Professor Medical University of SC	"Bridging macro-and micro scales of brain function with all optical physiology"
11-12-2015	Andrew Nguyen Research Associate Harvard University	“Progranulin: at the interface of neurodegenerative and metabolic diseases”
12-03-2015	Patricio O’Donnell, M.D., Ph.D. Sr. Research Fellow Pfizer	“Novel pharmacological tools to enhance cortical interneuron function”

ARTICLES AND OTHER NEWS ITEMS

UAB The Mix

Stories and Insights from UAB Research

<http://www.uab.edu/mix/>

Exploring the building blocks of memory

October 28, 2015

By J. David Sweatt

J. David Sweatt, Ph.D., an international expert in the field of learning and memory, is Evelyn F. McKnight Chair of the UAB Department of Neurobiology and director of the McKnight Brain Institute and Civitan International Research Center at UAB. In this story and its accompanying video, he explains how fundamental discoveries in his lab are pointing toward new treatments for learning and memory disorders.

When I was a graduate student, getting close to finishing up and getting my Ph.D., I realized I was probably going to spend the rest of my life working on one single thing. So I asked myself the question: What's the most interesting thing in the world? And to me, that is how memories are formed and stored. I've been fortunate to be able to spend the last 25 years of my career exploring that question.

One of the major breakthroughs in the learning and memory field in the past two decades or so was the discovery that active changes in gene readout in the brain are necessary for anyone to make a long-term memory. If you remember something tomorrow that you experienced today, it will be in part because you had a change in gene readout in parts of the brain that are critically important for memory formation. My lab wants to understand how that works.

A hidden layer between nature and nurture

It turns out there's a layer of mechanisms, known as epigenetic mechanisms, that sit above the level of the genes and all the cells in your body, including in your brain. These mechanisms were discovered only fairly recently, and they're really pretty amazing — a previously hidden layer that acts as an interface between environmental stimuli and the genes that make up the DNA coding system in your cells.

Epigenetic mechanisms were originally discovered as a basic information storage mechanism in all the cells in your body. We all basically started out as a ball of embryonic stem cells, and some of those cells got a signal to turn into nerve cells and liver cells and muscle cells and so on and so forth. And those nerve cells and liver cells have stayed nerve cells and liver cells for your entire lifespan.

That tells you right on its face that there has to be some lifelong information storage mechanism in cells that allows them to stay the kind of cell that they're supposed to be. So we got interested in the epigenetic mechanisms that underlie that information storage, and hypothesized that maybe some of those same mechanisms are used when we have experiences and store acquired information in our brain. And it turns out that is the case. My lab discovered — about 10 years

ago — that everyday experiences tap into these epigenetic mechanisms. The events we experience drive changes in epigenetic mechanisms, and that's critically important for long-term memory formation and the stable storage of long-term memory. It's quite exciting.

What that means in biochemical terms is that when you have an experience that causes a long-term memory to be formed, that experience actually changes the three-dimensional and chemical structure of the DNA in your brain.

Blocking, erasing and enhancing memories

We've discovered in the lab that these basic mechanisms might give us some really important tools that we can try to use to treat learning and memory disorders. In animal studies, very talented postdoctoral fellows and graduate students who work in my lab have discovered that, by manipulating the epigenome with targeted drugs, we can block memory formation. We can actually erase a pre-existing memory by manipulating the three-dimensional structure and chemical structure of DNA in the brain, and most importantly — really in terms of thinking about drug development — we can enhance memory formation by boosting up some of these epigenetic mechanisms.

That is in normal animals, but really more important is what we have been able to do in animal models of things like Alzheimer's disease and learning disabilities. In laboratory experiments with genetically engineered mouse models, we can use these epigenetic regulating drugs to restore normal learning and memory capacity back to these animals.

You can't fix something that's broken, completely, until you understand how the process works normally. Basic research allows us to understand how things work normally so we can restore a disrupted process in diseases such as Alzheimer's or intellectual disabilities. We can restore that broken mind back to normal function by understanding what normal function really is.

<http://www.uab.edu/mix/stories/exploring-the-building-blocks-of-memory>