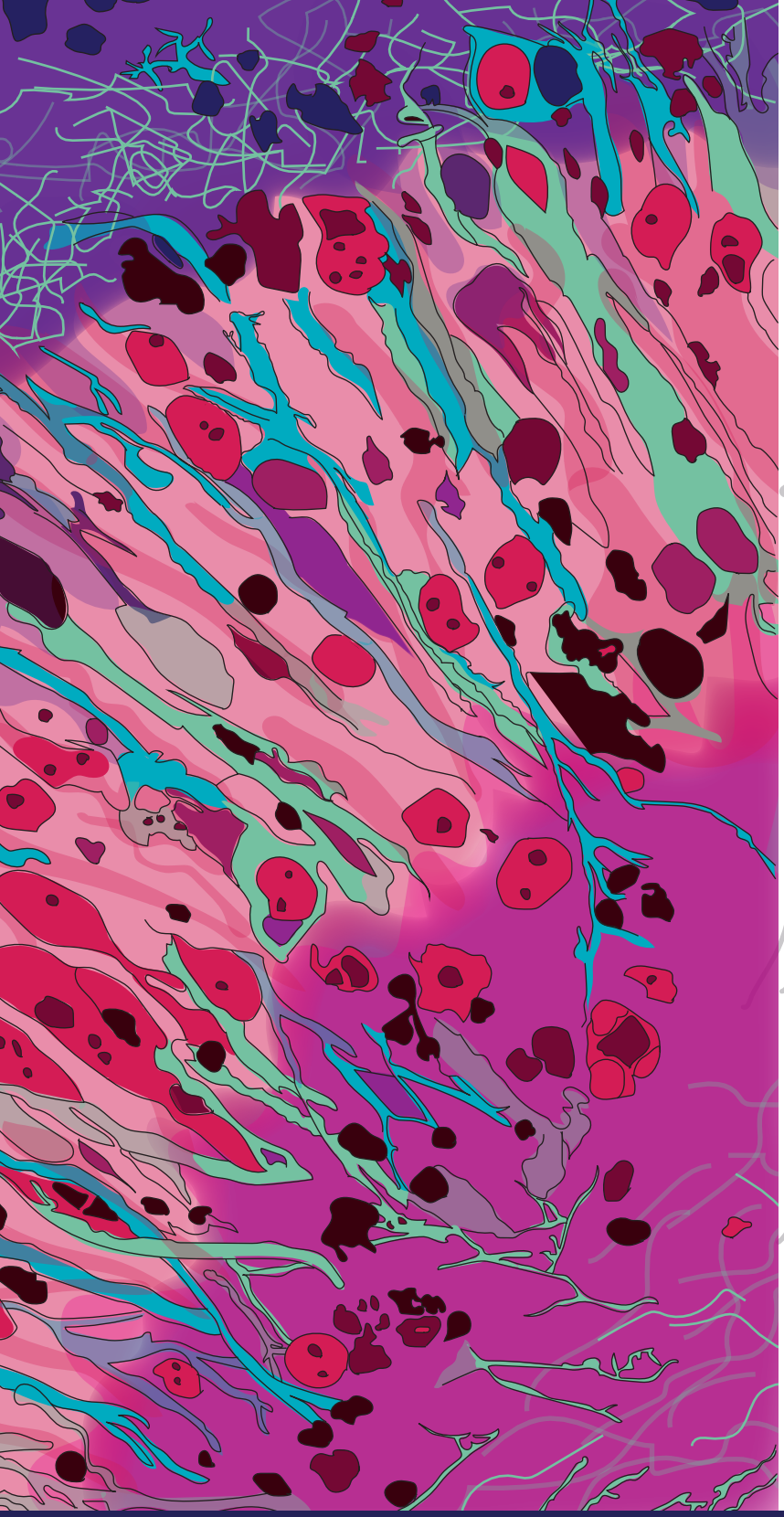

EVELYN F. & WILLIAM L. MCKNIGHT BRAIN INSTITUTE OF THE UNIVERSITY OF FLORIDA

2015 Annual Report

UF | UNIVERSITY of FLORIDA

William L.
Brain Institute

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Message from the Director

NEUROSCIENCE PREEMINENCE INITIATIVE RECRUITS

- **H. Lee Sweeney, PhD**, myology and muscular dystrophy, Director of the Institute of Myology
- **Gordon Mitchell, PhD**, spinal cord injury and respiratory drive, Director of the Center for Respiratory Biology and Rehabilitation
- **Steven Munger, PhD**, smell and taste, Associate Director of the Center for Smell and Taste at UF
- **Carol Mathews, MD**, genetics/environment/culture influence on psychiatric disorders
- **Lisa Scott, PhD**, cognitive/developmental/social psychology
- **Andrew Berglund, PhD**, small molecule biochemistry
- **Glenn Smith, PhD**, dementia and patient-centered outcomes, Chair of the Department of Clinical and Health Psychology
- **Karim Oweiss, PhD**, sensory integration mechanism and brain-machine interface
- **Kevin Otto, PhD**, neural interface engineering

In 1991, the University of Florida decided to establish a brain institute to facilitate research, education and clinical missions in neuroscience. In 1997, William G. Luttge, PhD, then Chair of the UF Department of Neuroscience, obtained a $38 million grant from the Department of Defense, which UF matched to go ahead with this plan. In 1998, UF received a critical additional fund of $30 million ($15 million gift from the McKnight Brain Research Foundation, which was matched by $15 million from the State of Florida), enabling the establishment of the Evelyn F. & William L. McKnight Brain Institute at UF.

Dr. Luttge became the founding Executive Director of the MBI. Since then researchers at the MBI have made significant contributions to the advancement of neuroscience. Subsequent Executive Directors Douglas K. Anderson, PhD and Dennis A. Steindler, PhD, both accomplished neuroscientists, firmly built strong research teams on basic neurosciences. I succeeded the MBI as the fourth Executive Director in 2010 while I was chairing the Department of Neurology. In 2011, the MBI established the current strategic plan, which focuses on five areas of research. These are: Age Related Memory Loss and Cognitive Aging, Brain and Spinal Cord Injury, Brain Tumor, Neurodegenerative Diseases, and Addiction.

Since then, our research portfolio has grown substantially. There was a UF-wide campaign to recruit preeminent investigators in multiple fields of research, and neuroscience turned out to be one of the most successful areas of this preeminence recruitment effort. The preeminence program aims to elevate UF to one of the top 10 public universities in the US. Under the leadership of Michael Perri, PhD, Dean of the Public Health and Health Professions, the neuroscience group recruited nine preeminent scholars. Earlier, Dr. Duane Mitchell was recruited as Co-Director of the Preston A. Wells Jr. Center for Brain Tumor Therapy, and his arrival has resulted in the recruitment of several brain tumor investigators, including David Tran, MD, PhD, as a clinical preeminence scholar. Furthermore, Steven DeKosky, MD, a prominent leader of Alzheimer's disease research and cognitive aging scholar, has joined us as Deputy Director of the MBI. His arrival is timely and strengthened the Alzheimer's Disease Research Center at UF. The NIH recently awarded funding for this center to Todd Golde, MD, PhD. Dr. Golde has been Director of the Center for Translational Research in Neurodegenerative Disease (CTRND) and is now also Director of the ADRC. Lastly, but not the least, UF and the McKnight Brain Research Foundation have established the Evelyn F. McKnight Chair for Clinical Translational Research in Cognitive Aging and Memory for Ronald Cohen, PhD, who directs the Cognitive Aging and Memory Clinical Translational Research Program. The new investigators brought needed expertise as well as almost $4 million of annual federal grant expenditures to the MBI.

With the expansion of the neuroscience research portfolio, the MBI is upgrading its research environment. To accommodate the new investigators, laboratories have been renovated in the open laboratory format. New equipment such as a multiphoton

Message from the Director *(continued)*

confocal microscope have been added to our Cell and Tissue Analysis Core. The Advanced Magnetic Resonance Imaging and Spectroscopy (AMRIS) facility, which is supported by the National High Magnetic Field Laboratory, is planning to install the second 3T Prisma MRI equipment dedicated to human research to accommodate increasing demands. The MBI also houses the animal care facility and an ICBR-operated flow cytometer core.

The MBI administration office, which was significantly downsized in 2010, operates seamlessly with remarkable transparency and accountability. The strategic decision-making process involves discussions with the MBI Executive Committee whose membership consists of key stakeholders. The Executive Director makes operational decisions based on the Executive Committee's advice. The MBI also has established an equipment committee and space committee, which advise the Executive Committee. Thus, the governance of the MBI is well-established and has been going smoothly.

This annual report primarily focuses on the scientific accomplishments of major programs at the MBI, including within the five strategic areas. It also includes a financial summary, which indicates the MBI's financial state is healthy.

After five years as Executive Director, I have decided to step down. I am proud of the current MBI operation and growth. However, the MBI has great opportunities to advance to the next level of neuroscience research in coming years. A national search has been started for the next Executive Director who can make this excellent neuroscience institute one of the very best brain institutes in the world. I look forward to watching that happen.

Best regards,

Tetsuo Ashizawa, MD
Executive Director, McKnight Brain Institute
Melvin Greer Professor of Neurology

MBI Strategic Research Programs

Age-related Memory Loss

Tom Foster, PhD

Investigators of the ARML Program employ a powerful collection of technologies to examine mechanisms for cognitive decline. The technologies depend on the collection and analysis of large data sets in order to identify the relationship between multiple biological measures and variability in the onset and progression of cognitive decline during aging. For example, next generation sequencing employed in the laboratory of Tom Foster, PhD, and the McKnight Brain Institute's Epigenetics Core permits an examination of the expression of several thousand genes. In collaboration with Jennifer Bizon, PhD, and Sara Burke, PhD, animals are characterized on a battery of cognitive tasks examining different forms of memory, sensory processing, and motor function. The transcriptional profile is then examined in brain regions that mediate the cognitive processes characterized by the behavioral battery. This work is identifying changes in signaling, from the synapse to the nucleus, that underlie variability in cognitive aging. Similarly, Dr. Foster and Brandi Ormerod, PhD, employed Multiplex technology to measure multiple proteins in the blood and several brain regions. They recently published a comprehensive characterization of the relationship between cognition and 27 stress hormones, cytokines and chemokines found in the serum and in different brain regions. The results provide biological markers in the blood that can be used predict the onset of cognitive impairment and suggest that brain region specific inflammation underlies the differential decline of specific cognitive processes. This also has led to a well-scored grant proposal that is expected to be funded for Dr. Foster.

Dr. Burke joined the ARML group last year and recently received an outstanding score on a grant to examine connectivity across brain regions using state-of-the-art methodologies in neurophysiology to simultaneously measure the activity of hundreds of cells across brain regions as animals engage in cognitive tasks that are sensitive to age. In collaboration with Andrew Maurer, PhD, and Dr. Bizon, this multidisciplinary research team is uniquely poised to make a significant advancement regarding age-related functional connectivity alterations in memory networks.

The ARML researchers interact with other researchers across campus to develop models of cognitive aging and to test possible therapeutics. Age-related cognitive deficits in elderly humans are particularly apparent during dual task performance, when cognitive processes are examined while individuals engage in simple motor tasks (i.e. walking or finger tapping). Dr. Burke received funding as a Pepper Scholar and is interacting with individuals at the Institute of Aging at the University of Florida in order to develop an animal model of dual task performance.

Drs. Bizon, Foster, and Jason Frazier, PhD, (Pharmacodynamics) collaborate in studying GABAnergic signaling in working memory deficits of aging with molecular, cellular, and behavioral approaches. The team led by Dr. Bizon and Barry Setlow, PhD, in collaboration with Ron Cohen, PhD, Tetsuo Ashizawa, MD, Kevin Felsenstein, PhD, and Glenn Finney, MD, is pushing the frontier in preclinical translational research in development of GABAB receptor antagonist to improve age-related cognitive deficits. A lead compound that shows significant improvement of cognitive impairments in aged Fisher rats has been identified, and a high throughput screening platform has been developed. The translational research has progressed to the optimization phase aiming at identification of compounds that have an acceptable GABAB antagonist activity, allow oral administration and have promising toxicology profiles, in collaboration with the Florida Translational Research Program (FTRP) at the Sanford Burnham Medical Research Institute (SBMRI) with state funding through the Florida Department of Health. This program is expected to produce the first compound developed by the ARML Program that can be tested at the Cognitive Aging & Memory – Clinical Translational Research Program (CAM-CTRP).

Finally, Drs. Foster, Bizon, Ormerod (Biomedical Engineering), Paramita Chakrabarty, PhD, (Center for Translational Research in Neurodegenerative Disease), and Christiaan Leeuwenburgh, PhD, (Department of Aging and Geriatric Research) are developing animal models to examine how low level chronic inflammation, which is characteristic of aging, compromises cells or tissues leading to the onset and progression of age-related diseases.

The ARML Program is in part supported by income from the $30 million endowment from the McKnight Brain Research Foundation, as well as a $4 million Endowed McKnight Chair for Dr. Foster.

Age-related Memory Loss *(continued)*

NIH FUNDING

- Dr. Foster: NIH Merit Award R37AG036800 Signaling Cascades and Memory Deficits During Aging, R01AG049711 Systemic Inflammation in Regulating the Onset and Progression of Brain Aging, and R01AG037984 Estrogen and Cognition over the Lifespan.
- Dr. Bizon: R01AG029421 Neural Mechanisms of Cognitive Decline in Aging.
- Dr. Burke: Her R03 application will be funded for FY16 (R03AG049411 Neurogenesis and Memory Network Dynamics During Normal Aging).

Cognitive Aging & Memory

The ARML's sister program, the Cognitive Aging & Memory – Clinical Translational Research Program (CAM-CTRP) also enjoyed a productive year, publishing numerous manuscripts on topics related to cognitive and brain aging. Additionally, Ron Cohen, PhD, the program's director, submitted an RO1 proposal to the NIDDK on obesity and Type 2 diabetes and the effects of bariatric surgery on brain function and aging, which was funded. The project has major implications for understanding the aging brain, particularly the influence of metabolic factors associated with obesity and diabetes on brain structure and function, and the brain effects resulting from reductions in these factors following bariatric surgery and significant weight loss.

CAM-CTRP faculty have over 20 pending grants in PI and Co-PI roles. The topics span a broad range of important areas for study of the aging brain, such as predicting brain changes, multi-modal brain training for broad cognitive transfers in elders, white matter integrity and ultra-high field neuroimaging of the aging brain, and non-invasive interventions for cognitive aging.

CAM-CTRP has recruited Robert Fieo, PhD, and Damon Lamb, PhD, as new faculty members who conduct research in cognitive aging during this reporting period. Additionally, Stephen DeKosky, MD, an internationally renowned researcher in cognitive aging, has decided to move to UF as Deputy Director of the MBI and a member of the CAM-CTRP.

During the summer of 2015, the McKnight Brain Research Foundation (MBRF) established a new $4 million endowed Chair for clinical translational research in cognitive aging for Dr. Cohen. CAM-CTRP also continues to receive funding from the $30 million MBRF endowment income. Additional support for this program comes from the Institute on Aging's Claude D. Pepper Older Americans Independence Center grant (P30AG028740) and Life Study (U01AG022376).

NIH FUNDING

- Dr. Cohen: R01DK099334 Obesity and Type 2 Diabetes: Bariatric Surgery Effects on Brain Function.
- Dr. Anton: R01AT007564 REVIVE: Resveratrol to Enhance Vitality and Vigor in Elders.
- Dr. Manini: R01AG04525 Metabolic Costs of Daily Activity in Older Adults.

Brain and Spinal Cord Injury

Gordon Mitchell, PhD

Through the Brain and Spinal Cord Injury Research Trust Fund (BSCIRTF), the state's Brain and Spinal Cord Injury Program provided $263,628 to the MBI in fiscal year 2014-15. The MBI has asked investigators interested in relevant fields to conduct cooperative translational research to aim for NIH program project or multiple PI grant applications. These investigators formed groups focused on spinal cord injury (SCI), traumatic brain injury (TBI), and ischemic brain injury (IBI). Along with their own external research funding, the researchers aim to leverage the BSCIRTF support to create synergy.

Spinal Cord Injury

BSCIRTF funding was awarded to David Fuller, PhD, and Paul Reier, PhD, in 2014 and was used in part to add Gordon Mitchell, PhD, to the group as one of the key faculty recruitments of UF's Preeminence Initiative. The BSCIRTF funding has directly led to tangible progress toward two goals: 1) strengthening the spinal cord injury (SCI) research group at UF and 2) enabling collection of preliminary data to support federal (NIH) grant applications. The UF SCI research team has coalesced over the last six months since Gordon Mitchell, PhD, was hired, leading to the establishment of the UF Center for Respiratory Research and Rehabilitation. The center investigators meet weekly to review data and are actively planning submission of two NIH program project grants, an NIH T32 training grant, and multiple NIH R01 grants.

Dr. Mitchell served as chair of the Department of Comparative Biosciences at the University of Wisconsin for 17 years and was one of the founding faculty members of the University of Wisconsin's School of Veterinary Medicine. He was director of the Respiratory Neurobiology Training Program at the University of Wisconsin from 2002 to 2014 and was among the first to recognize the importance of neuroplasticity in respiratory motor control. He is one of the world's top experts in this area.

A preclinical focus of the SCI group is on repair and rehabilitation of the subacute or chronically injured cervical spinal cord and establishment of a compelling basis for future clinical translations aimed at improving respiratory muscle function following cervical SCI. Progress from the 2015 SCI group projects are outlined below:

A. *Epidural spinal cord stimulation modulates phrenic motor output after cervical SCI.* Using an established model of cervical SCI, the group studied how epidural stimulation alters phrenic motor activity. There is considerable current interest in this topic, with recent work from UCLA and University of Louisville showing partial restoration of voluntary leg control in humans with SCI following epidural stimulation. Studies at the MBI aim to examine how epidural stimulation impacts respiratory motor output after incomplete cervical SCI, and builds upon earlier reports in complete SCI. The MBI SCI group's initial study has been completed, and showed that high frequency epidural stimulation of the cervical or thoracic spinal cord potentiates ipsilateral phrenic output, but with a bias towards increased tonic activity. The study established a model, and future work will be aimed at determining stimulus paradigms that can increase bursting without the tonic component (e.g. reduced stimulus frequencies, coupling with serotonergic antagonists, etc.).

B. *The endogenous respiratory rhythm can be used to "trigger" intraspinal stimulation of phrenic motoneurons.* The group developed a "closed loop" stimulation paradigm as follows: In an anesthetized rat, medullary driven respiratory activity was recorded from the genioglossus (tongue) muscle, and this signal was used to trigger intraspinal stimulation of the phrenic motoneuron pool. The method worked in both spinal intact and cervical SCI conditions and unexpectedly showed a potential for restoring some degree of spontaneous inspiratory bursting after SCI. These experiments are completed and are the first proof-of-principle data showing that the host respiratory signal can be "captured" to drive respiratory motoneurons caudal to SCI. The data also suggest possible neurorehabilitative effects of the stimulation.

C. *Intraspinal Transplantation.* Among the SCI group's long-term objectives is to test the hypothesis that grafting interneuronal progenitors, alone or in combination with the use of novel neuroprosthetic devices or gene delivery, will promote significant anatomical/functional neuroplasticity and re-activation of the "silenced" phrenic and intercostal circuits via the formation of novel propriospinal-like relay circuits. A significant part of recent efforts have concentrated on research and development of the injury/transplantation model. Sprague-Dawley intraspinal allografts made at one week and three months following unilateral C3/4 contusion injuries were viable one or several months post-transplantation. Variable functionality of the graft was observed. Although the most informative measure of outcome still remains to be determined, phrenic compound

action potentials revealed several instances of tonic phrenic activity on the side ipsilateral to the graft, suggesting the presence of neural interaction between host and graft. One approach to modulate such an interaction would be a combination of intraspinal microstimulation and transplantation.

From a correlative, anatomical perspective, a clear demonstration of host-graft connectivity is required to support the above interpretation and future demonstration of spinal cord repair via novel relay circuits. To demonstrate the host graft connectivity the group has grafted GFP-expressing donor tissue into Fisher-344 rat recipients, in which a number of trials were necessary to define the optimal injury conditions including chronic hemisection and contusion injury.

Establishment of this model will now facilitate demonstrations of neuronal projections into and out of the interneuronal-enriched spinal tissue transplants for other portions of our current BSCIRTF research. For example, we have proposed to test a gene therapy approach for inducing outgrowth of axons from donor neurons. This transplantation approach will form the core of future PO1/RO1 and other research proposals.

Establishment of the Mitchell laboratory and the UF Center for Respiratory Research and Rehabilitation (CRRR) in the MBI will help advance the research agenda in SCI and motor neuron disease. The Mitchell laboratory has two ongoing NIH-funded projects, and one Department of Defense-funded project, focused on spinal, respiratory motor plasticity and/or respiratory plasticity following cervical SCI. Already, CRRR has expended funds to create a center conference/data analysis room to support SCI research, as well as ordered equipment to create center core facilities including:

- A plethysmography system to measure rodent (mice) breathing after SCI/pathology
- A portion of an EMG telemetry system to measure respiratory muscle activity and EEGs in rats with spinal injuries/pathology
- An intermittent hypoxia system to expose rodents to therapeutic and/or pathogenic intermittent hypoxia to restore motor function following spinal injury (and in other clinical disorders such as motor neuron disease)
- A system designed to deliver therapeutic intermittent hypoxia to humans with SCI and motor neuron disease
- Recruitment of an instrumentation specialist to enable use of these core facilities by center faculty

Additional funds will be expended to research the impact of repetitive acute intermittent hypoxia on respiratory motor function through its effects on spinal, chloride-dependent synaptic inhibition; spinal cell proliferation; and compensatory respiratory plasticity due to spinal, respiratory motor neuron cell death.

NIH FUNDING

- **Dr. Reier: R01NS054025 Plasticity and Repair in the Phrenic Motor System.**
- **Dr. Fuller: R01NS080180 Modulation of Phrenic Motoneuron Plasticity After Cervical Spinal Cord Injury.**
- **Dr. G. Mitchell: R01HL069064 Respiratory Plasticity and Spinal Cord Injury.**

Traumatic Brain Injury

The Traumatic Brain Injury (TBI) Group, led by Russ Bauer, PhD, Kevin Wang, PhD, and Sylvain Doré, PhD, was awarded BSCIRTF funding from the MBI for the following project with a July 1, 2015 start date: The central hypothesis is that mild repetitive close head injuries (rCHI) can trigger long-lasting alterations of the neuro-glia-vascular network in the brain, leading to the manifestations of various structural and functional alternations associated with chronic TBI. To address this problem, the group proposed to use a "Program Project Grant" approach by drawing on the established rat and mouse models of repetitive close head injury and the collective expertise in various neuronal, glial and vascular mechanisms relevant to brain injury from the group's team of PI and Co-PI's. More specially, the group proposed to systemically examine the following research questions regarding chronic TBI using complementary rat and mouse rCHI models:

- Contributions of post-TBI sleep disturbances to anatomical and neurostructural changes and neurological/neurocognitive deficits after TBI (Led by Co-PI Dr. Dore)
- Contributions of the central noradrenergic nucleus locus coeruleus (LC) and five specific neural centers as key neural substrates for cognitive, anxiety, balance, pain, and spasticity disorders following (cTBI) *(Led by Co-PI's Floyd Thompson, PhD / Prodip Bose, MD, PhD)*

Brain and Spinal Cord Injury *(continued)*

- Contributions of impaired reactivity of basilar/carotid arteries and oxidative stress to the neuroglia-vascular alterations and subacute and chronic brain structural and functional changes following rCHI *(Led by Co-PI Nihal Tumer, PhD)*
- Monitoring sustained neural, glial and vascular alterations following rCHI using a set of brain tissue- and biofluid-compatible systems biomarkers *(Led by PI Dr. K. Wang)*
- Monitoring neural structural, vasculature and functional changes by high resolution structural and functional nuclear magnetic imaging *(Led by Co-PI Marcelo Febo, PhD)*

NIH FUNDING

- **Dr. Bauer: I21Rx001730 Developing Process-specific Verbal Memory Interventions for Veterans with TBI.**
- **Dr. Wang: R21NS085455 Elucidate Consequences of Autoimmune Response to Protease-modified GFAP in TBI.**
- **Dr. Thompson: I01RX000502 Neurobiology and Experimental Treatment of TBI Pain and Anxiety.**
- **Dr. Bose: I01RX001005 Therapeutic Potential of Combined Locomotor Training and TMS in SCI.**

Ischemic Brain Injury

The Ischemic Brain Injury (IBI) group, led by Michael Waters, MD, PhD, and Dr. Doré was awarded BSCIRTF funding from the MBI for the following projects with a July 1, 2015 start date:

- Neuroprotective benefits of CO/NO in hypoxic ischemia (HI) in neonates. This project will evaluate the neuroprotective ability of inhaled CO, and NO against HI in vivo using a mouse model of HI injury. The specific aim will determine the duration and concentration of inhalational gas that decreases injury and improves functional outcome following HI in a normothermic mouse model. *(Led by CO-PI's Michael Weiss, MD, and Scott Rivkees, MD)*
- Determine the optimal treatment dose regimen of CO following permanent cerebral ischemia in adult mice. This study aims to test whether treatment with low levels of CO reduces infarct size and improves neurologic function after permanent focal ischemia and to determine whether the Nrf2 pathway is partially responsible for the optimal neuroprotective mechanism of CO. *(Led by Co-PI's Abdullah Ahmad, PhD, and Dr. Doré)*
- Beneficial effects of CO treatment following subarachnoid hemorrhage (SAH). This project focuses on investigating a novel, safe, and efficient non-invasive therapeutic strategy for subarachnoid hemorrhage (SAH) induced cerebral vasospasm (CV) and ischemia using low-dose carbon monoxide (CO). *(Led by Co-PIs Alexander Glushakov, PhD, and Dr. Doré)*

NIH FUNDING

- **Dr. Doré: R01AT007429 Better Understanding of the Neuroprotective Mechanisims of Korean Ginseng in Stroke and R01NS046400 Role of Prostaglandin Receptors in Stroke.**
- **Dr. Candelario-Jalil: R01NS065849 Cyclooxygenase-2 Regulation of Blood-brain Barrier Opening in Ischemic Stroke.**
- **Dr. B. Hoh: R01NS083673 Cerebral Aneurysm Healing: Cellular Mediators, Mechanisms and Downstream Actions.**

Brain Tumor

Duane Mitchell, PhD

As of June 30, 2015, the MBI has provided $2.5 million to the Preston A. Wells Jr. Center for Brain Tumor Therapy in support of the University of Florida Brain Tumor Immunotherapy Program (UFBTIP), with another $500,000 per year committed for the next five years (an additional $2.5 million total).

Clinical Neuro-Oncology

The Department of Neurosurgery and Preston A. Wells, Jr. Center for Brain Tumor Therapy were pleased to welcome David Tran, MD, PhD, and Ashley Ghiassedin, MD, as new faculty to UF Health this past summer.

Dr. Tran, Assistant Professor and Chief of Neuro-Oncology, comes to UF from Washington University in St. Louis, Missouri, where he served as director of the adult neuro-oncology section in the oncology division and assistant professor in the Department of Medicine. He received his PhD in immunology from Mayo Medical School in Rochester, Minnesota, and is board-certified in internal medicine and medical oncology. Dr. Tran is an NCI-funded physician-scientist recruited under the UF cancer preeminence initiative. His research program is focused on understanding the mechanism of cancer metastasis and dormancy. He is an experienced clinical researcher, having functioned as principal investigator on over 17 clinical trials in adult brain tumor patients. As Chief of Neuro-Oncology, Dr. Tran will oversee the integration of the multidisciplinary services involved in the treatment and care of patients with brain tumors, and work coordinately with brain tumor center leadership in the development of innovative clinical trial options for patients with refractory brain cancers.

Dr. Ghiassedin, Assistant Professor, completed his neuro-oncology fellowship training at Duke University Medical Center in 2013 before joining UF Health in July. He completed medical school at the University of Toledo in Toledo, Ohio and neurology residency at Indiana University in Indianapolis, Indiana. Dr. Ghiassedin's interests include quality improvement in the care of patients with malignant brain tumors as well as the development and implementation of novel clinical trials for patients with glioblastoma. Dr. Ghiassedin will work coordinately with Dr. Tran in the expansion of the neuro-oncology practice and in the execution of UF initiated clinical trials for patients with brain tumors.

The growth of the neuro-oncology program has necessitated the recruitment of two additional clinical research coordinators and an oncology nurse practitioner, bringing the brain tumor center faculty and staff to a total of eight primary clinical faculty (department of neurosurgery), 10 associate clinical faculty, and seven associated clinical practice or clinical research staff. Ongoing expansion efforts include the recruitment of a dedicated pediatric neuro-oncologist and associated support staff for our expanding focus in the treatment of patients with pediatric brain tumors.

UFBTIP

Lab

The UFBTIP is a comprehensive translational neuro-oncology program focused on the development of novel immunotherapeutic treatments for pediatric and adult brain tumors. The research program encompasses discovery research within preclinical animal models all the way through first-in human phase 1 and phase 2 clinical trials in patients with malignant brain tumors. In addition to evaluating novel therapeutics for the treatment of brain tumors, the UFBTIP serves as a central immune monitoring laboratory for the National Cancer Institute's Pediatric Brain Tumor Consortium (PBTC) and is currently assisting in the development and evaluation of three multi-institutional immunotherapy clinical trials through the PBTC. Our current research efforts involve the preclinical through clinical evaluation of dendritic cell vaccines, adoptive T cell therapy, RNA-nanoparticle vaccines, and combinatorial approaches with immune checkpoint inhibitors.

Faculty Leadership

The leadership of the UFBTIP is comprised of Duane Mitchell, MD, PhD, who serves as program director, and five other faculty members who lead specific areas of preclinical or clinical research related to the immunologic treatment of malignant brain tumors. The six-member faculty leadership of the UFBTIP meets regularly through joint weekly laboratory meetings and a monthly leadership meeting to ensure that efforts are integrated within the UFBTIP to comprise a coordinated and comprehensive neuro-oncology program. In additional to Dr. Mitchell, other members include:

Brain Tumor *(continued)*

- Catherine Flores, PhD, Assistant Professor and Principal Investigator of Stem Cell Engineering
- Elias Sayour, MD, Assistant Professor and Principal Investigator of RNA Engineering
- Maryam Rahman, MD, Assistant Professor and Principal Investigator of Molecular Imaging
- Jianping Huang, MD, PhD, Associate Research Professor and Director of UFBTIP Clinical Operations
- Jesse Kresak, MD, Assistant Professor and Principal Investigator of Tumor Microenvironment

The six-member faculty leadership of the UFBTIP coordinates the activities of 23 other full-time employees and students that comprise the program's membership. These members include one administrative assistant, two clinical research coordinators, two regulatory administrators, two PhD laboratory scientists, and several laboratory research assistants, graduate and medical students, and postdoctoral fellows. Two undergraduate research fellows also conduct research within our program.

Research Initiatives

UFBTIP programmatic research efforts are divided into preclinical research, translational research and clinical research activities. Spanning the spectrum of these research efforts are laboratory programs of RNA Engineering (PI: Dr. Sayour), Dendritic Cell Engineering (PI: Oleg Yegorov, PhD), T cell Engineering (PI: Dr. Huang), Stem Cell Engineering (PI: Dr. Flores), Molecular Imaging (PI: Dr. Rahman), and Tumor Microenvironment (PI: Jesse Kresak, MD). Regulatory compliant research activities are governed by a programmatic IACUC protocol for animal studies and 10 IRB-approved protocols for research involving human subjects and/or tissues. This includes an IRB-approved, multi-institutional phase II clinical trial (Re-MATCH protocol, UF IFB 128-2013) funded by the Department of Defense in which UF serves as the lead and sponsoring institution (PI: Dr. Mitchell). This trial opened for enrollment on October 1, 2014. To date, we have enrolled 10 pediatric subjects on this clinical trial. Referrals to UF for enrollment have come from throughout the United States (California, Nebraska, North Carolina, etc.). Three subjects have received intravenous infusion of ex vivo expanded tumor-specific lymphocytes combined with intradermal tumor RNA-loaded DC vaccines. Infusions were well-tolerated without immune-associated side effects. Continued enrollment and expansion of this protocol into a multi-institutional trial is underway with subjects being followed for progression-free survival endpoint. A phase II protocol of dendritic cell vaccines for adults with glioblastoma in collaboration with Duke University has been FDA and IRB approved and awarded NCI funding for support starting August 1,2015. This trial will start in September 2015. A third immunotherapy protocol targeting newly diagnosed pediatric high-grade gliomas has been accepted for funding support by the Pediatric Cancer Foundation (PCF) in Tampa, Florida. The PCF awarded a one-year grant (Engineering tumor-specific central memory T cells, PI: Mitchell) in November of 2014 for optimization of the expansion and differentiation of tumor-specific T cells incorporating new methodologies developed within our lab prior to initiation of a phase I clinical trial. The clinical trial is on track to initiate after the completion of these studies in early 2016.

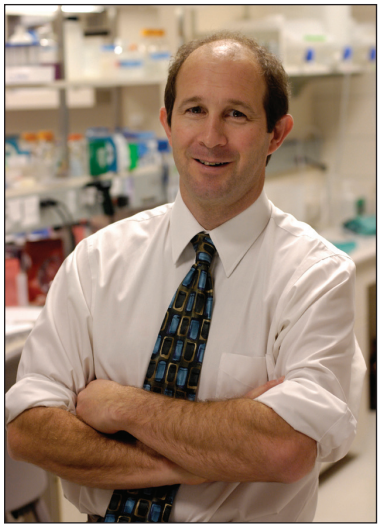
Accomplishments

Over the past year, the Preston A. Wells Jr. Center for Brain Tumor Therapy and UFBTIP have had several accomplishments worth noting. Two new NIH R01s were awarded (1R01CA195563 Enhancing Adoptive Immunotherapy Targeting Pediatric High-Grade Gliomas (PI: Mitchell) and 1R01CA175517 Phase II DC Vaccine (PI: Mitchell) with start dates of July 1, 2015 and August 1, 2015, respectively. Additionally, two FCBTR grants were awarded to UF brain tumor center researchers, Dr. Flores and Ana Tari Ashizawa, PhD. Dr. Flores' grant focused on the novel use of HSCs in adoptive cellular therapy and Dr. Ashizawa's grant focuses on the development of novel nanoparticles for delivery of therapeutic siRNAs to brain tumors. Additional awards received over the past year include a PCF grant (Dr. Duane Mitchell), Alex's Lemonade Stand Young Investigator's Award (Dr. Flores), American Society of Pediatric Hematology/Oncology Young Investigator's Award (Dr. Sayour), UF Program Project Planning Grant (PI: Laurence Morel, PhD, Project Leader: Dr. Duane Mitchell), and FCBTR grants to Drs. Mitchell and Kresak. In total over $7.3 million in new grants were awarded to brain tumor researchers within the Preston A. Wells Jr. Center for Brain Tumor Therapy since July 1, 2014. Twenty peer-reviewed manuscripts were published by investigators from the brain tumor center since July 1, 2014 including a publication featured in Nature *(Mitchell DA and Batich KA et al., epub March 11, 2015)*.

NIH FUNDING

- Dr. D. Mitchell: R01CA195563 Enhancing Adoptive Immunotherapy Targeting Pediatric High-Grade Gliomas and R01CA175517 Efficacy of Dendritic Cell Vaccines Targeting CMV in Glioblastoma (Phase II DC Vaccine).
- Dr. Tran: K08CA160824 Role of Twist1 in EMT Maintenance and Tumor Dormancy.

Neurodegeneration



Todd Golde, MD, PhD

Steven T. DeKosky, MD

Alzheimer's Disease

Florida is an epicenter of the Alzheimer's disease epidemic with approximately 10 percent of all cases of the disease disease in the country. The total economic toll of Alzheimer's in the state is estimated to be $20 billion a year — more than either heart disease or cancer. The toll that Alzheimer's will wreak both socially and economically is only going to increase in coming decades — especially in Florida with its elderly population. Our only hope to reduce these costs is research that will ultimately lead to therapies that modify the disease course or, perhaps more immediately, research that will enable us to better handle patients with dementia within health care systems.

Over the past six years, 14 new faculty, who study Alzheimer's disease and other neurodegenerative disorders, have joined the MBI and have developed a portfolio of extramural funding of about $10 million/year, which has increased nearly 30 percent from last year. This team includes Todd Golde, MD, PhD, Sylvain Doré, PhD, Jada Lewis, PhD, Nikolaus McFarland, MD, PhD, David Borchelt, PhD, Benoit Giasson, PhD, Edgardo Rodriguez, PhD, Christopher Janus, PhD, Paramita Chakrabarty, PhD, Yona Levites, PhD, David Vallaincourt, PhD, and Meredith Wicklund, MD.

Two very notable additions joined UF this summer. Glenn E. Smith, PhD, an internationally recognized neuropsychologist and dementia researcher, has been named the Elizabeth Faulk professor and chair of the department of clinical and health psychology at the UF College of Public Health and Health Professions.

Dr. Smith joined UF from the Mayo Clinic in Rochester, Minnesota, where he was a professor of psychology in the College of Medicine, the associate director of education resources at the Mayo Clinic Center for Clinical and Translational Science, and deputy director of education at the Kern Center for the Science of Health Care Delivery. In his 25 years at the Mayo Clinic, Smith's dementia research has focused on early diagnosis, outcomes, depression, behavioral issues and successful cognitive aging.

The other major recruitment was Steven T. DeKosky, MD, an international leader in Alzheimer's disease research, who has been named deputy director of the Evelyn F. and William L. McKnight Brain Institute of the University of Florida and a professor of neurology in the College of Medicine.

A UF alumnus, Dr. DeKosky is known around the world as an expert in translational research, which leverages basic scientific findings to produce new treatments for patients. Dr. DeKosky is an emeritus professor of neurology at the University of Virginia and holds an adjunct appointment in neurology at the University of Pittsburgh, where he previously served as director of its Alzheimer's disease center and chairman of the neurology department. Most recently he was a visiting professor of radiology at the

Neurodegeneration *(continued)*

University of Pittsburgh School of Medicine and a visiting professor in the department of medical ethics and health policy at the University of Pennsylvania's Perelman School of Medicine. From 2008 to 2013, he was vice president and dean of the University of Virginia School of Medicine.

His research has focused on understanding the neurochemistry, genetics, neuroimaging, treatment and prevention of Alzheimer's disease. He was funded continuously in basic and clinical research by the NIH for more than 30 years. Dr. DeKosky was the principal investigator in the clinical application of Pittsburgh Compound B, or PiB, a groundbreaking imaging agent invented by colleagues at Pitt. PiB enables visualization of the plaque associated with Alzheimer's disease and aids in definitive diagnosis.

Alzheimer's Disease Research Center

Leveraging additional resources at the University of Florida, the Neurodegenerative Disease Program aims to become the preeminent center in the Southeast for neurodegenerative research and translation to improved clinical outcomes.

Notable advances include receipt of an NIH-funded Alzheimer's Disease Research Center (ADRC). This grant, which is a collaborative effort with Mount Sinai Medical Center in Miami, is funded for five years at $1.5 million per year. This award also involves faculty at Florida Atlantic University, Florida International University and the University of Miami. ADRCs serve a role much like national cancer center designations. This will be the 29th center to receive such designation and the first primarily based in Florida. The UF-MSMC ADRC enables us to create infrastructure that supports clinical care for patients with Alzheimer's disease. ADRCs also serve as hubs of translational science that are necessary to advance the science in order to reach our shared goal of preventing or treating Alzheimer's disease. They are essential to increasing enrollment from industry-sponsored clinical trials and also for ensuring that advances in the science and care of Alzheimer's disease are efficiently and rapidly disseminated to the wider community. By enhancing clinical trial capacity in Alzheimer's disease, we project that we will enroll an additional 200 clinical trial participants per year in the state of Florida resulting in an additional $2 million per year. This increase will ramp up over the course of the grant. The vast majority of these funds for clinical trials would be from the pharmaceutical industry.

These ADRCs serve as hubs for both established STEM employees as well as training centers for those interested in STEM jobs. ADRCs will result in medical tourism, as they represent a sign of clinical and scientific excellence to the outside world. ADRCs also provide a basis for many private-public partnerships in the battle to cure Alzheimer's disease — infrastructure developed for the ADRCs would also be used to compete for other programmatic grants that provide a similar level of extramural funding.

Finally, we have recruited two outstanding clinical AD investigators to UF. With their arrival and our ADRC grant, we can envision future recruitment of faculty in this area to provide the critical mass and intellectual capital to become one of the preeminent centers for Alzheimer's and other neurodegenerative research in the world. Again, state funds will provide critical support for our future efforts in this area.

Overall our efforts in neurodegenerative disease research are thriving. In addition to the ADRC, eight new grants have been awarded to MBI investigators this year, including two R01s.

Parkinson's Disease, Movement Disorders and Neurorestoration

Despite the growing burden of Parkinson's disease and limitations in funding, the UF Center for Movement Disorders and Neurorestoration (CMDNR) has been prospering. The CMDNR is focused on providing care to patients from all over globe. The center features a unique national/international program, where patients may travel to UF stay in the hotel next door and have their needs addressed by a coordinated interdisciplinary care team. Through excellence in care, we aim to fuel research and education for future generations.

Roughly 1.5 million Americans suffer from PD. If the same geriatric population growth rate remains unchanged, by the year 2040, the combined deaths from the three main neurodegenerative diseases (PD, Alzheimer's disease and ALS) will exceed lung cancer, colon cancer, breast cancer, liver cirrhosis and malignant melanoma (if no cure is found for these illnesses). PD alone will disable 10 million worldwide by 2020.

The CMDNR has become one of the largest and most integrated clinical-research centers in the world. The center physically moved in April 2011 to the Orthopedics and Sports Medicine Institute and was transformed into a one-of-a-kind, world class, 15,000 square-foot site for integrated clinical care and research. Located on the University of Florida campus across the street from the Hilton UF Conference Center, the center is designed to offer convenient access to local residents, as well as to patients and visitors from around the world.

Neurodegeneration *(continued)*

The space for the center includes 21 dedicated patient exam rooms, as well as tailored space for clinical trials, research, telemedicine and for one of the world's largest movement disorders databases. The space is equipped with a full physical therapy, occupational therapy, and speech therapy area, with access to an MRI and swallowing disorders suite. The center's staff arranges patient-specific and coordinated rehabilitation programs either within the building, or elsewhere. The CMDNR provides the finest possible coordinated interdisciplinary care for patients, along with an opportunity to participate in research. (Research initiatives are detailed in the Narrative section.)

Accomplishments in the last year:

- Maintained National Parkinson Foundation Center of Excellence status
- Continued year 3 of the Bachmann-Strauss Center of Excellence
- Provided half of the projects for the $2.5 million Tyler's Hope Alignment grant for dystonia
- Named as the hub of the new Tourette Syndrome Association Center of Excellence
- Named a Huntington's Disease Center of Excellence
- Named a Mangurian Foundation Headquarters for Lewy Body Disease and Parkinson's Disease Dementia
- Performed the first closed-loop human deep brain stimulation experiments on human Tourette
- Secured a large grant from the Michael J. Fox Foundation to develop a deep brain stimulation approach to treat freezing of gait in Parkinson's disease
- Secured a new NIH R01 application on DBS mobile computing platforms
- Secured a Blepharospasm Foundation and a NORD grant (orthostatic tremor)
- Secured a grant from the Restless Legs Foundation
- Performed our 1,000th DBS lead operation
- Continue to have over 30 active clinical trials in Parkinson's disease and movement disorders

Amyotrophic Lateral Sclerosis (ALS)

The past year produced several exciting studies that reveal new opportunities in drug development, provide new insights into disease mechanisms, and advance efforts to produce reliable pre-clinical models of ALS. In regard to drug development, the laboratories of Drs. Borchelt, Golde, Chakrabarty, and Levites collaborated to develop new approaches to expressing biotherapeutic molecules in the CNS of mice that model ALS. This effort produced data to indicate that modulating the inflammatory pathways by expressing a molecule termed IL-10 significantly delayed the onset of disease in an established model of ALS. This effort lead to new grant funding from the ALS Association to further develop IL-10 as a therapeutic and investigate the potential other natural immune modulators as therapeutics for this disease. Additionally, Dr. Borchelt's laboratory received a grant from the Department of Defense to develop drugs that target an enzyme termed superoxide dismutase 1 (SOD1). Mutations in SOD1 cause a familial form of ALS by inducing the protein to misfold. The Borchelt lab will be screening for drugs that prevent the misfolding of SOD1 as a new approach in drug development.

The past year also produced multiple studies that provided new insights into disease mechanisms. One of the most perplexing features of ALS is that the disease seems to spread from one set of muscle groups to another. Insight into one mechanism by which this may occur came from a study lead by Jacob Ayers, PhD, and Dr. Borchelt. Dr. Ayers demonstrated that injecting the spinal cords of a particular strain of mice with tissue preparations that contained misfolded SOD1 could produce the symptoms of ALS. This outcome suggests that misfolded protein can move between cells of the nervous system to spread disease. The laboratory of Laura Ranum, PhD, in collaboration with investigators at Johns Hopkins University, determined that a mutation in a gene called C9orf72 causes the production of aberrant proteins that accumulate pathologically in the brain and spinal cords of ALS patients. This finding mechanistically links these two distinct genetic forms of ALS to a common pathology, namely the accumulation of aberrant proteins.

Advances in models ALS came on multiple fronts over the past year. A collaboration by Drs. McFarland and Golde demonstrated that aspects of ALS caused by mutations in a gene termed ubiquilin could be modeled in mice by engineering adeno associated viruses to express the mutant ubiquilin in the brains of mice. The study demonstrated that mutations in ubiquilin that cause disease

Neurodegeneration *(continued)*

generate a protein that aberrant folds and accumulates pathologically in the brains of these mice. With funding provided by the MBI, Drs. Borchelt and Lewis launched an effort to develop new mouse models of ALS by generating transgenic mice that express a gene termed Matrin 3. The MBI also funded efforts by Dr. Ranum to develop mice that model disease caused by mutations the C9orf72 gene.

NIH FUNDING

- **Dr. Golde: R01AG018454 Immune-mediated Mechanisms Underlying CNS Abeta Clearance, U01AG046139 A System Approach to Targeting Innate Immunity in AD, and P50AG047266 UF – Mt. Sinai Medical Center AD Research Center.**
- **Dr. Borchelt: R01AG049456 Proteostasis and Secondary Proteinopathy in AD and FTD, R01NS092788 Modeling the Progression of SOD1-linked Motor Neuron Disease, R21AG046711 Seeded Models of AD Pathology, and R21NS088839 Seeded Transmission of SOD1 Misfolding.**
- **Dr. J. Lewis: R01NS082672 Biological and Pathological Interactions between TAU and LRRK2.**
- **Dr. Giasson: R01NS089622 Mechanisms of Aggregated Alpha-synulcein Induction and Progression.**
- **Dr. E. Rodriguez: R21NS087346 Cell Type Specific Analysis of Mirna Expression and R21NS093400 Somatic Inactivation of the SNCA Locus: A New Approach to the Understanding and Treatment of Parkinson's Disease.**
- **Dr. Vaillancourt: R01NS058487 Role of the Cortex and Cerebellum in Visually-guided Motor Behavior, R01NS075012 Non-invasive Marker of ND in Movement Disorders, and R21NS093695 Pathophysiology of Upper and Lower Limb Motor Control in Spinocerebellar Ataxia.**

Addiction

Addiction research at the MBI included progress from the following investigators:

Adriaan Bruijnzeel, PhD: The Bruijnzeel laboratory has been investigating the neuronal mechanisms that contribute to the development of drug addiction. During the last year we have been investigating the neuronal mechanisms that mediate the rewarding effects of nicotine and nicotine withdrawal. The release of stress peptides plays an important role in the negative mood state associated with nicotine withdrawal. However, recent studies suggest that prolonged overexpression of stress peptides may lead to tolerance to the effects of these peptides. The lab first showed that the viral vector (AAV) mediated overexpression of corticotropin releasing factor (CRF) in the central nucleus of the amygdala increases the expression of the CRF type 2 receptor and diminishes nicotine withdrawal (Qi et al., Translational Psychiatry, 2014). In a follow-up study they showed that the overexpression of CRF in the bed nucleus of the stria terminalis also induced a large increase in CRF2 receptor levels and diminished nicotine withdrawal (Qi et al., manuscript in preparation). The overexpression of CRF did not diminish anxiety-like behavior associated with nicotine withdrawal. In addition to this they investigated the effect of a vasopressin 1b (V1b) receptor antagonist on nicotine withdrawal (Qi et al., Behavioural Brain Research, 2015). We showed that chronic, but not acute, blockade of V1b receptors diminishes the negative mood state associated with nicotine withdrawal. The rewarding effects of nicotine play an important role in the initiation of tobacco smoking, and in collaboration with Dr. Marcelo Febo, they conducted functional imaging studies (fMRI) to investigate the brain sites that are being activated by nicotine (Bruijnzeel et al., Int. Journal of Neuropsychopharmacology, 2014). This study showed that nicotine activates a wide range of brain sites that play a role in reward, compulsive behavior, and

Addiction *(continued)*

cognition. In addition to this, in collaboration with Drs. Setlow and Febo we have established a cannabis smoke exposure setup. The lab's studies show that passive exposure to cannabis smoke leads to the development of cannabis dependence, clinically relevant THC levels, and that passive exposure to cannabis smoke has similar behavioral effects as injections with the main psychoactive component of cannabis (tetrahydrocannabinol) (Bruijnzeel et al., submitted to PLOS ONE). Support for Dr. Bruijnzeel's work is provided through several R21 (R21DA039349, MPI; R21DA039701 Co-PI) and R01 mechanisms (R01DA021274, Co-PI; R01DA023575, PI) from the National Institute on Drug Abuse.

Marcelo Febo, PhD: The Febo laboratory continues to work on a number of projects. Some of these are supported by the MBI Neuroimaging and Stroke initiatives. First, the Febo lab has continued research activities funded by the MBI Neuroimaging initiative grants in collaboration with Jasenka Zubcevic, PhD, and Mohan Raizada, PhD. They have also continued to work on a second MBI Neuroimaging initiative with Drs. Yuqing Li and Vaillancourt. These are anticipated to lead to novel and impactful research publications and grant submissions. Dr. Febo submitted an R01 and an R21 as PI to NIDA. The R21 has been funded and the R01 is being resubmitted. With pilot funding from the MBI, Drs. Setlow, Bruijnzeel, and Febo submitted an R21 proposal to investigate the neural and behavioral effects of cannabis smoke (as noted above and below). The grant is now funded. Dr. Febo is Co-Investigator on this proposal and is in charge of collecting and analyzing brain volumetric imaging data in live rats exposed to cannabis smoke during adolescence. In collaboration with Paul Carney, MD, in pediatric neurology, Dr. Febo will start new research on a state of Florida funded project to determine the effects of cannabidiol (Epidiolex) in intractable childhood epilepsy. At the moment, Dr. Febo is preparing a new R01 to be submitted to NINDS as PI (Dr. Carney, Co-PI). Dr. Febo has begun collaborating with Dr. Sylvain Doré in the MBI Stroke group initiative. Dr. Febo also continues to collaborate with Eduardo Candelario-Jalil, PhD, in the Department on Neuroscience as a Co-Investigator on an NINDS R01. From September 2014-July 2015, Dr. Febo published 15 peer reviewed papers, which are divided as 6 research papers and 9 review articles. His postdoctoral research trainee, Luis Colon-Perez, PhD, obtained the MBI fellowship runner up and was awarded the Society for Neuroscience NeuroScholars Postdoctoral Award. Grant information: R21 DA038009 - PI; R21 DA039701 - Co-PI; R21 DA039349 - Co-PI; R01 NS065849 - Co-PI; R01 NS077004 – CoPI).

Drake Morgan, PhD: The Morgan lab is characterizing the behavioral effects of novel serotonergic compounds for the treatment of a variety of psychiatric disorders. The lab recently completed a grant examining the potential use of these compounds for the treatment of amphetamine/methamphetamine addiction (in collaboration with Ray Booth at Northeastern University as a multiple PI on a R01 grant from the National Institute on Drug Abuse). They are currently seeking funding for the use of these drugs in the treatment of ADHD and the cognitive dysfunction that occurs with a number of disorders (e.g. schizophrenia). A separate part of our research program is investigating the behavioral effects of alterations in the microbiome. They are primarily focused on anxiety-related behavior, at this point in time. The primary goals are to identify the mechanisms by which alterations in the microbiome (via pharmacological treatment or diet changes) produce increased anxiety, and how changes in the serotonergic system (both in the periphery and centrally) modulate these behavioral alterations. This work is in collaboration with faculty in Medicine (Gary Wang, MD, PhD), Psychiatry (Drs. Kevin Wang and Febo), and Pathology (Timothy Garrett, PhD). There are several funded grants that are supporting this research (an R21 from NIH National Institute on Mental Health (R21MH106983 - Co-PI) and a UF Opportunity Fund grant; Dr. Gary Wang (PI)). Another goal of the lab is to study the behavioral and physiological effects of drugs that alter "healthspan." For example, they have discovered that particular regimens of rapamycin administration (this is a clinically used drug to prevent organ transplant rejection and potentially cancer) can alter lifespan and a variety of behavioral/functional measures. The lab is currently developing a battery of behavioral and physiological tests to use as a screen for novel compounds. These experiments are funded by an R01 from NIH NIDDK (NIH NIDA R01 DA036534, Philip Scarpace, PhD (PI) and Dr. Morgan Co-PI) and a contract from Sanofi (to Christy Carter, PhD).

Sara Jo Nixon, PhD: Over the past year, the Neurocognitive Laboratory (Nixon) has continued to focus on the neurobehavioral and psychosocial concomitants of substance use and misuse. In the last year, five manuscripts have been accepted or published and several others are nearing completion. This group continues to work on a NIAAA R01 (R01AA022456) focusing on the neurobehavioral processes underlying both cognitive and emotional processing in substance abusers. Additionally, funding is pending for a NIDA R21 (R21DA03828) that is a Phase 2 clinical trial designed to explore the potential of a novel pharmacotherapeutic to aid in smoking cessation. This project is a collaborative effort involving William Kem, PhD, and Roger Papke, PhD, from the Department of Pharmacology and Therapeutics. The Nixon laboratory is also active in a study of neurocognitive integrity and behavioral health interventions (Betsy Shenkman, PhD, MSN, (PI)), and conducts research with the Stewart Marchman Act Behavioral Healthcare system, which has treatment locations in multiple locations and provides transitional housing for inmates). Dr. Nixon is site co-PI (with Linda Cottler, PhD) of a U01 application created in response to the NIH's ABCD initiative Funding decisions remain undetermined, but the application achieved the most favorable score in the country. Analysis

Addiction *(continued)*

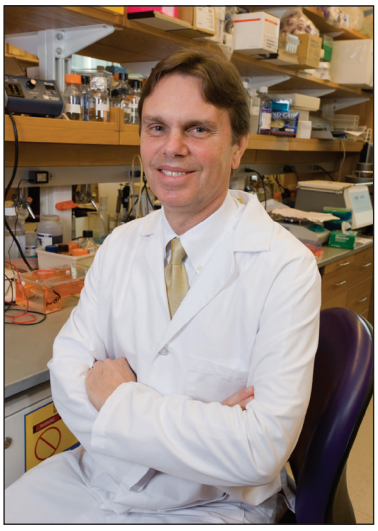
continues on data gathered from the recently completed NIAAA R01 on moderate drinking in preparation for a competitive renewal application in the fall of 2015. Dr. Nixon serves as Co-Director of a NIDA T32 program (T32DA035167L. Cottler, PI), Co-Director of the UF Center for Addiction Research & Education, Director of the CTSI Biobehavior Core, and as a member of the UF Medical IRB. Over the past year, MD-PhD trainee ,Alfred Sklar, was awarded his PhD. Another student successfully defended her PhD qualifying exam and an undergraduate trainee was honored with a University Scholars Program award. In addition to seven posters at national and international meetings, Dr. Nixon has given talks at the Research Society on Alcoholism (San Antonio, TX), the 2015 Science of Change Conference (San Antonio, TX), the Frank M. Norfleet Forum for the Advancement of Health (Memphis, TN), the Meeting of the Collaborative Initiative on Fetal Alcohol Spectrum Disorders (Rockville, MD), and the International Convention of Psychological Science (Amsterdam, Netherlands). This year, Dr. Nixon was elected to a three-year term on the American Psychological Association's Board of Scientific Affairs (2015-2017). She was also an active reviewer for NIAAA, chairing reviews for both training grants and research centers. In May, 2015, Dr. Nixon was named a University of Florida Research Foundation Professor for the period of 2015-2017.

Barry Setlow, PhD: In the past year, research in the Setlow lab has focused on neurobehavioral consequences of chronic exposure to drugs of abuse, as well as on neural mechanisms of decision-making. Additional research (in collaboration with Dr. Jennifer Bizon) has focused on neural and behavioral mechanisms of cognitive aging. They published seven peer-reviewed papers and one book chapter pertaining to this work, and have several more under review or in preparation. Members of the lab have also given numerous oral and poster presentations (approximately 15 in total) at national and international meetings. To support this research, the lab continues to receive funding from an R01 grant from the National Institute on Aging (Dr. Bizon PI, funded through 2019). In addition, the lab received a new R01 grant from the National Institute on Drug Abuse (R01 DA036534, Dr. Setlow PI, funded through 2020) to continue research on interactions between risky decision-making and cocaine use. In addition to this R01 funding, Dr. Setlow is a co-PI (multiple PI mechanism) on two new R21 grants (R21 DA039701; R21 DA039349; both funded through 2017) from the National Institute on Drug Abuse, one with Dr. Bruijnzeel and one with Dr. Maurer. Both of these grants follow up on the cannabis smoke exposure research project that was begun with a grant from MBI, and the preliminary data obtained with MBI funding was critical for their success. In addition to these grants, Dr. Setlow is a co-I on a new R21 grant (R21 DA038009) awarded to Dr. Febo to study a class of drugs of abuse commonly known as "bath salts." Dr. Setlow also sponsored the successful application for a Thomas H. Maren Post-doctoral Fellowship by a member of his lab, Caitlin Orsini, PhD, (funded through 2017) and he has sponsored or co-sponsored several additional NIH training award applications for members of his lab or other MBI/UF trainees (two F31s, one F32, one K01, and one K99/R00). Finally, Dr. Setlow is a co-investigator on several additional NIH grant applications (three R21s and one R01) that are pending review or funding decisions.

NIH FUNDING

- **Dr. Febo: R21DA038009 Imaging In Vivo Neural Mechanisms of Synthetic Cathinones (Bath Salts).**
- **Dr. Nixon: R01AA022456 Neurobehavioral and Emotional Deficits in Male and Female Alcoholics and R21038286 Effects of GTS-21 on Smoking Behavior and Neurocognitive Function.**
- **Dr. Setlow: R01DA035534 Risk Taking and Cocaine Use: Interactions, Mechanisms, and Therapeutic Targets, R21DA039349 Lasting Behavioral and Neuroimaging Consequences of Adolescent Exposure to Cannabis Smoke, and R21DA039701 Development of a Rat Model of Cannabis Smoke Self-administration.**

Neuromuscular Disease



H. Lee Sweeney, PhD

The Department of Pharmacology welcomed H. Lee Sweeney, PhD, to its faculty. Dr. Sweeney joined the department as The Thomas H. Maren, MD, Eminent Scholar Chair. Dr. Sweeney's world-renowned research on neuromuscular diseases has led to the development of the first drug approved in Europe for the treatment of Duchenne muscular dystrophy, the most common form of muscular dystrophy in children. While his research on treatments for muscular dystrophy continues, so does his parallel work on myosin motors. His myosic research is directed toward understanding the fundamental chemo-mechanical transduction mechanism used by these nano-machines. Dr. Sweeney is using this knowledge towards developing novel approaches to fight cancer cells.

In February 2015, the MBI and College of Medicine completed a major renovation of 1,283 square feet of animal housing and wet lab in the MBI for Dr. Sweeney and Elisabeth Barton, PhD (Applied Physiology and Kinesiology).

In addition to his research, Dr. Sweeney established the Myology Institute at UF. The mission of the Myology Institute is to unravel the causes and pathophysiology of neuromuscular diseases and myopathies, perform preclinical studies to evaluate novel therapeutics, conduct clinical studies/trials for neuromuscular diseases, and to unite investigators and clinicians at the University of Florida and other institutions who are committed to understanding the basic biology and pathophysiology of muscle and developing treatments for neuromuscular disorders.

In late 2014, the MBI and Center for Neurogenetics hosted a two-day symposium for Myotonic Dystrophy and the Brain. Twenty-five speakers from UF shared their research and ideas on molecular, pathological and imaging lessons from other neurological disorders, as well as therapeutic strategies.

NIH FUNDING

- Dr. Ashizawa: R01NS083564 RNA-Gain-of-function Pathogenesis in SCA10.
- Dr. Ranum: P01NS058901 Myotonic Dystrophy: Molecular Pathophysiology and CNS Effects and R37NS040389 Molecular Genetic Characterization of SCA8.
- Dr. Sweeney: U54AR052646 Failed Regeneration in the Muscular Dystrophies: Inflammation, Fibrosis and Fat, R01DC009100 Structure and Function of Myosin VI.

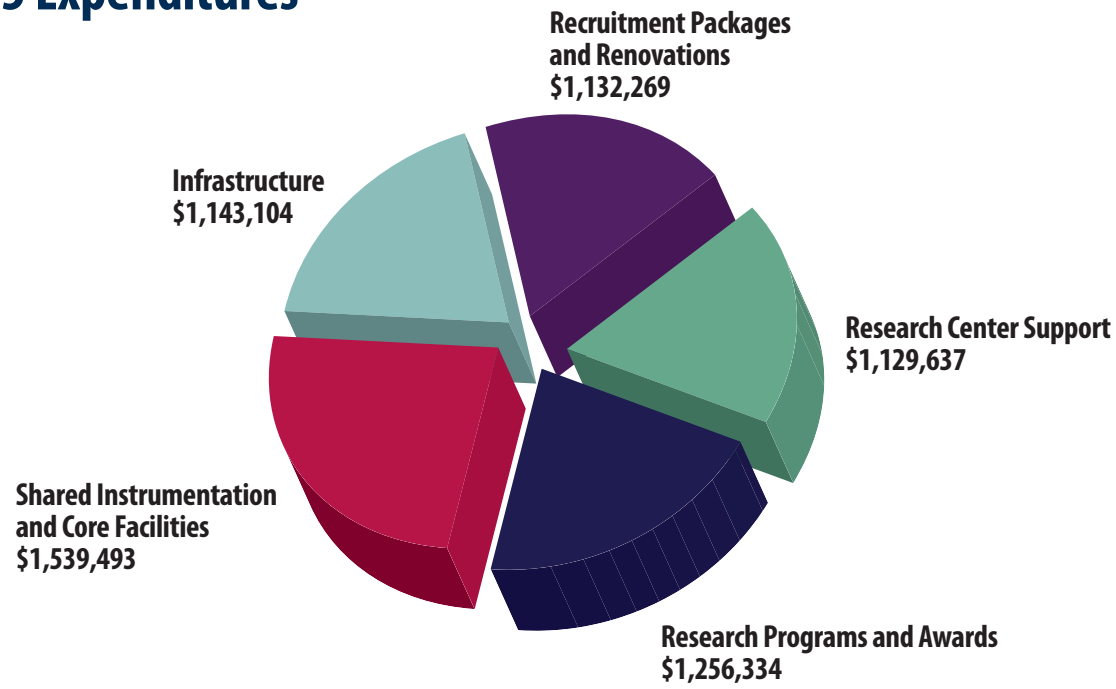
MBI Labs

Principal Investigator/Department

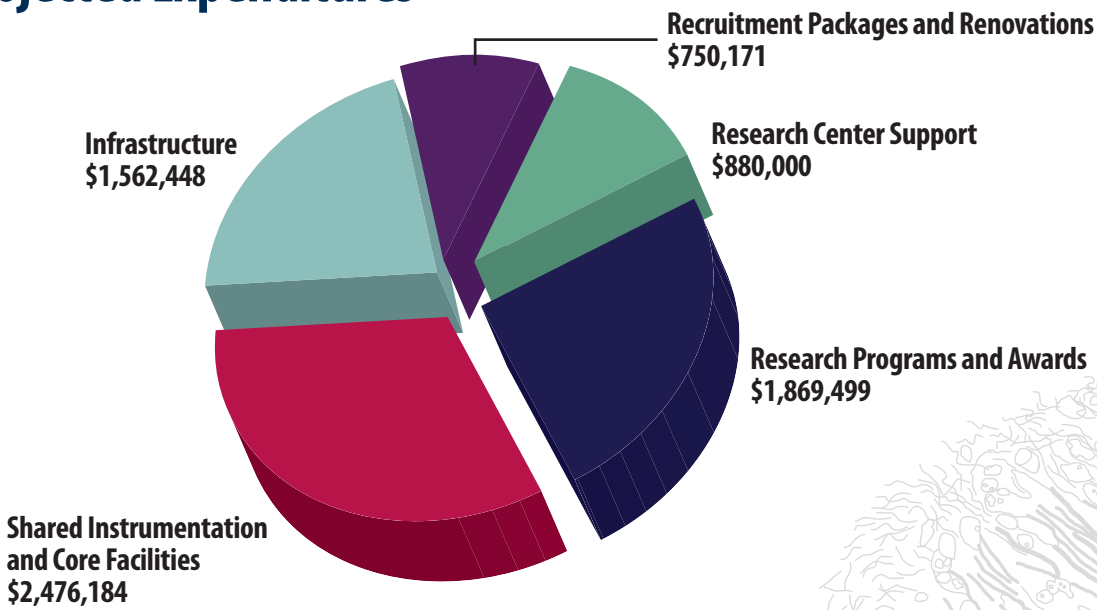
- Ache, Barry – Biology, Center for Smell & Taste
- Agbandje-Mckenna, Mavis/McKenna, Robert – Biochemistry
- Ashizawa, Tetsuo – Neurology
- Bizon, Jennifer L./Setlow, Barry – Neuroscience/ Psychiatry
- Blackband, Stephen – Neuroscience
- Bova, Frank J. – Neurosurgery, Radiosurgery Lab
- Bruijnzeel, Adriaan – Psychiatry
- Burke, Sara – Neuroscience
- Byrne, Barry – Pediatrics, Human Applications Lab
- Candelario Jalil, Eduardo – Neuroscience
- Dotson, Cedrick Deshawn/Heaton, Marieta – Neuroscience
- Febo Vega, Marcelo – Psychiatry
- Fernandez-Funez, Pedro/Rincon-Limas, Diego – Neurology
- Forder, John R. – Radiology
- Foster, Thomas C. – Neuroscience
- Fuller, David – Physical Therapy
- Hoh, Brian – Neurosurgery
- Hoh, Daniel – Neurosurgery
- Khoshbouei, Habibeh – Neuroscience
- King, Michael A. – Pharmacology
- Lai, Song – Radiation Oncology
- Lewis, Mark – Psychiatry
- Long, Joanna R. – Biochemistry
- Mandel, Ronald – Neuroscience
- Mareci, Thomas H. – Biochemistry
- Mathews, Carol – Psychiatry
- Miller, Brooke H. – Psychiatry
- Mitchell, Duane – Neurosurgery, Brain Tumor Immunotherapy Lab
- Mitchell, Gordon – Physical Therapy
- Muehlmann, Amber – Psychiatry
- Notterpek, Lucia – Neuroscience
- Petitto, John – Psychiatry
- Raizada, Mohan K. – Physiology
- Reier, Paul J. – Neuroscience
- Reynolds, Brent A. – Neurosurgery
- Rhoton, Albert L. – Neurosurgery
- Sarkisian, Matthew R. – Neuroscience
- Streit, Jake – Neuroscience
- Sumners, Colin – Physiology
- Sweeney, H. Lee/ Barton, Elisabeth – Pharmacology/Applied Physiology
- Tran, David – Neurosurgery
- Vandenborne, Krista/Walter, Glenn – Physical Therapy/Physiology
- Wang, Kevin W. – Psychiatry
- Waters, Michael F. – Neurology

MBI Expenditures and Commitments

MBI FY15 Expenditures

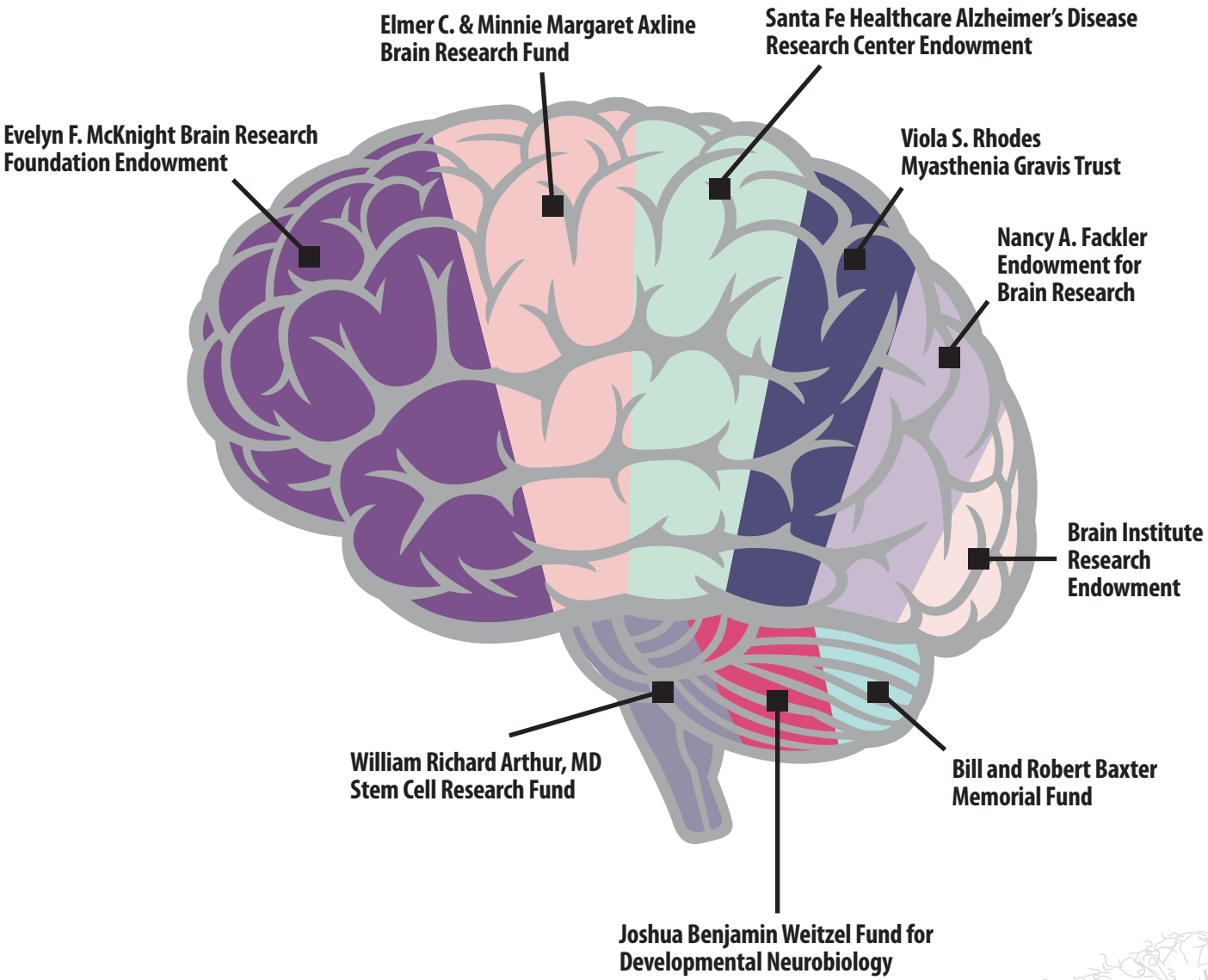


MBI FY16 Projected Expenditures



Philanthropic Gifts

The McKnight Brain Institute has over $42 million in endowed philanthropy funds.



MBI Fellowships

The McKnight Brain Institute awards fellowships each year to recognize and support students and fellows conducting research in the neurosciences in MBI-affiliated laboratories. We received 21 applications this year and awarded two full fellowships and three secondary awards.

Predoctoral Fellow Awardee:
Michael Massengill, Department of Molecular Genetics and Microbiology
Mentor: Alfred Lewin, PhD
AAV2 Delivery of an Nrf2 Derived Peptide to Enhance Neuroprotection in Autosomal Dominant Retinitis Pigmentosa

Predoctoral Fellow Runner-up:
Danielle Sambo, Department of Neuroscience
Mentor: Habibeh Khoshbouei, PharmD, PhD
Sigma-1 Receptor Modulation of Methamphetamine-induced Behavioral Responses and Neuronal Adaptations of Dopaminergic Neurons

Postdoctoral Fellow Awardee:
Kaustuv Saha, Department of Neuroscience
Mentor: eh Khoshbouei, PharmD, PhD
How Does Alpha-synuclein Regulate the Excitability of Dopamine Neurons?

Postdoctoral Fellow Runner-up:
Luis Colon-Perez, Department of Psychiatry
Mentor: Marcelo Febo, PhD
Perinatal Cannabis Smoke Exposure and Development of Brain Network Connectivity

Adj. Clinical Post Doc Fellow Runner-up:
Leli Shahgholi, Department of Neurology & UF CMDNR
Mentor: Michael Okun, MD
An Antidote for Botulinum Neurotoxin/A

MBI Managed Core Facilities

Advanced Magnetic Resonance Imaging and Spectroscopy (AMRIS)

The AMRIS facility is a core facility housed in the MBI that supports nuclear magnetic resonance (NMR) and magnetic resonance imaging (MRI) studies of chemical compounds, biomolecular systems, tissues, small animals, large animals, and humans. We currently offer nine systems with different magnetic fields and configurations. AMRIS has nine professional staff members to assist users, maintain instrumentation, build new coils and probes, and help with administration. In addition to supporting faculty research at the University of Florida, the AMRIS facility supports national and international scientific research as a user facility within the NSF-funded National High Magnetic Field Laboratory (NHMFL). The partnership of the MBI and the NHMFL enables the facility to offer many unique capabilities including a research-dedicated 3T human MRI scanner used in studies ranging from brain cognition to treatment of genetically transmitted diseases, a 17.6T magnet for noninvasive microimaging of excised tissues and small animals; an 11.1T horizontal MRI magnet which is the largest field strength magnet in the world with a 400 mm bore; and ultrasensitive cryoprobes which are the most mass-sensitive NMR probes in the world for 1H and 13C detection, respectively, and are ideal for natural products research. The 3T scanner has 32 channels for rapid parallel imaging and is the only whole body instrument in northern Florida dedicated to research. A unique 5T DNP polarizer enables both fundamental studies of DNP mechanisms as well as in vivo metabolism measurements when coupled to either the 4.7 T or 11.1 T systems. Our systems support a broad range of research studies from natural product identification to solid-state membrane protein structure determination to cardiac studies in animals and humans to tracking stem cells and gene therapy in vivo to functional MRI in humans. The AMRIS facility operates year round as a fee-for-service auxiliary under federal cost accounting standards. Local and NHMFL-affiliated users pay for magnet time from federally funded projects; the NHMFL funds magnet time for users from outside the UF system and development projects.

Facility Developments

With funding from the NHMFL, in 2014 we were able to accomplish three important goals within the AMRIS facility: 1) upgrade our 11.1 T MRI/S system with much stronger, more stable gradients, 2) begin offering dissolution dynamic nuclear polarization (dDNP) capabilities for in vivo studies on the 4.7 and 11.1 T MRI/S systems and 3) enhance in vivo MRI/S capabilities on the 750 MHz system. The upgrade of the 11.1 T system has enabled us to increase the available resolution for MRI/S studies while mitigating vibration issues resulting from Lorentz forces during strong gradient pulses. In concert with the installation of the gradients, next-generation coils and a cantilever/positioning system were developed by the RF support staff and are now available through the user program. The installation in 2013 of a dissolution DNP polarizer realized a major part of the DNP initiative, as outlined in our renewal proposal to the NSF for 2013-2017. This polarizer is able to achieve significant polarization of NMR active nuclei in the polarizer, translating to a 10-20,000 gain in SNR on dissolution and injection into our 4.7 T or 11.1 T MRI/S scanners and enabling the study metabolic flux in vivo. In 2014 we added the polarizer to our user program and expanded the RF coils available on the MRI/S scanners for 13C detection ex vivo and in vivo. Through a development grant awarded to Tom Mareci, PhD, and external users/collaborators, we completed a new probe for in vivo imaging at 17.6 T on both rats and mice with multi-resonance and quadrature detection capabilities; coils for this probe will continue to be developed in response to user requests. The modular design of this probe enables ease of new coil integration with tailoring of coil geometries to maximize filling factor and SNR for the samples interrogated.

Major research activities and discoveries

This year we saw growth in three new user areas. The first area was in offering DNP capabilities to external users. With these new users we have been able to fine-tune operations of the polarizer in concert with the 4.7 and 11.1 T MRI/S scanners and enable users to collect polarizer data at fields higher than is commercially available (Figure 1). We also saw growth in the area of metabolomics through support of the NIH-funded SECIM grant which provides comprehensive and complementary resources for clinical and

MBI Managed Core Facilities *(continued)*

basic science metabolomics studies and has enabled us to expand our user program. A third area of growth was in the area of fMRI studies utilizing rodent models. Dr. Febo, faculty member in the department of psychiatry at UF, has brought new capabilities to the 4.7 and 11.1 T MRI/S scanners, which have enabled us to support fMRI studies in awake rodents.

FIGURE 1. Postdoctoral research associate Bimala Lama is funded through the University of Florida matching support to the NHMFL and assists users with DNP experiments in addition to her own research.

Facility Plans and Directions

In spite of the continued challenging budgetary climate, our users have consistently successfully pursued federal funding to support their research programs and assisted the AMRIS facility in writing proposals to upgrade instrumentation. The successful partnership of the NHMFL user program with individual investigator research grants as well as program project grants provides constant scientific motivation for our technology development. After several years of growth in usage at an annual rate of 5-10%, our 3T human MRI has reached maximum capacity. We recently submitted a high end instrumentation grant seeking funds to add a second research-dedicated 3T to the AMRIS facility. Through UF funds provided in support of faculty hires, we are going to add new digital electronics and multi-receive capabilities to the 11.1 T MRI/S system to enhance the image acquisition capabilities for rodent brain imaging studies. This will help researchers capitalize on the SNR benefits of this ultra high field and attain the extent of spatiotemporal capacity provided in part by the recently installed high power spatial encoding gradients. Given the limitations of applying invasive techniques in combination with human brain imaging, animal brain imaging studies offer an important bridge to investigate and translate novel mechanisms involved in human brain diseases.

Cell & Tissue Analysis Core (CTAC)

The CTAC research facility provides access to and training on imaging and histological equipment that may be too specialized and unique, or potentially cost-prohibitive for an individual researcher to purchase. Making these vital tools available as a community asset maximizes the utilization of resources and helps facilitate research campus-wide. Since CTAC was first established in 2007, we have partnered with well over 800 individual students and researchers from almost 300 different labs throughout the MBI and greater UF community. We continue to strive to increase our visibility, knowledge base, services, and instrument offerings.

By far the biggest news for fiscal year 2014-15 is that funding for an NIH Shared Instrumentation Grant for a multiphoton confocal microscope was awarded this spring. The MBI congratulates Habibeh Khoshbouei, PhD, the grant's PI, for submitting the successful proposal and helping to bring this advanced microscopy technology to UF. The new Nikon A1R Multiphoton microscope has been specified and ordered, and should be installed this coming October. We expect to begin user training on the new system in early November.

This Nikon A1R Multiphoton system will be heavily equipped for numerous imaging techniques, including standard filter-based and spectral confocal, 3 channel multiphoton, and super-resolution. 2-Photon excitation on the system will be provided by a Spectra-Physics Mai-Tai HP DS tunable wavelength IR pulse laser. Additional funds were provided by the UF College of Medicine in order to equip the system with state-of-the-art N-STORM Super-Resolution capability. This will provide researchers with the ability to acquire fluorescent images below the traditional "diffraction barrier" down to a resolution of approximately 20nm.

As part of our ongoing effort to increase awareness of the CTAC core across UF we once again held our annual CTAC Imaging Expo in May. This springtime tradition gathers all of our local imaging-related vendor representatives together for a two day mini exposition which allows UF students and researchers to learn about the latest advances in bio-research imaging technology. The free yearly expo event includes technical lectures, software training classes, equipment demonstrations, and about 25 vendor tables. Funding for this event is provided by a small table fee charged to each of the attending vendors.

MBI Managed Core Facilities *(continued)*

In order to make way for some of the many lab-space renovations going on in the McKnight building, the CTAC Histology Resource Lab was relocated to a new location on the third floor this year. We were able to successfully complete the move into the new location with minimal disruption to ongoing histology services.

This coming year will see several changes to the CTAC Imaging facility. Two of our existing in-vivo imaging systems are to be relocated into the fifth floor animal facility to make way for the incoming Nikon multiphoton microscope. A second Olympus spinning disk confocal microscope, similar to our current Olympus DSU system, will now be added to the CTAC Imaging suite. This second spinning disk confocal will add additional user capacity and capabilities to what has been our most popular microscope over the last several years.

In order to reduce costs under the current operating model, CTAC does not maintain service contracts for any of its existing systems. We make every effort to maintain, and whenever possible, effectively repair the various CTAC systems in house. The subsequent cost of annual equipment repairs for CTAC is a small fraction of what we would pay if we maintained annual service contracts. The incoming Nikon multiphoton system has four years of factory service included in the initial purchase package. At the end of that period we may decide whether or not to maintain the factory service contract or self-insure as we do with most of our other systems.

MBI Leadership

In 2015, we welcomed Steven DeKosky, MD, as deputy director of the MBI. A noted cognitive aging, memory, and Alzheimer's disease researcher, Dr. DeKosky is a former vice president and dean at the University of Virginia College of Medicine and former chairman of neurology and head of the Alzheimer's center at the University of Pittsburgh.

Dr. DeKosky has received National Institutes of Health research funding consistently for three decades, and is expected to boost the already active cognitive aging and memory and Alzheimer's disease research programs at the MBI, the Institute on Aging, and the Center for Movement Disorders and Neurorestoration.

His experience includes clinical research into an imaging agent that colleagues at Pitt invented to diagnose Alzheimer's and a report on the dementia tied to traumatic brain injuries in former professional football players.

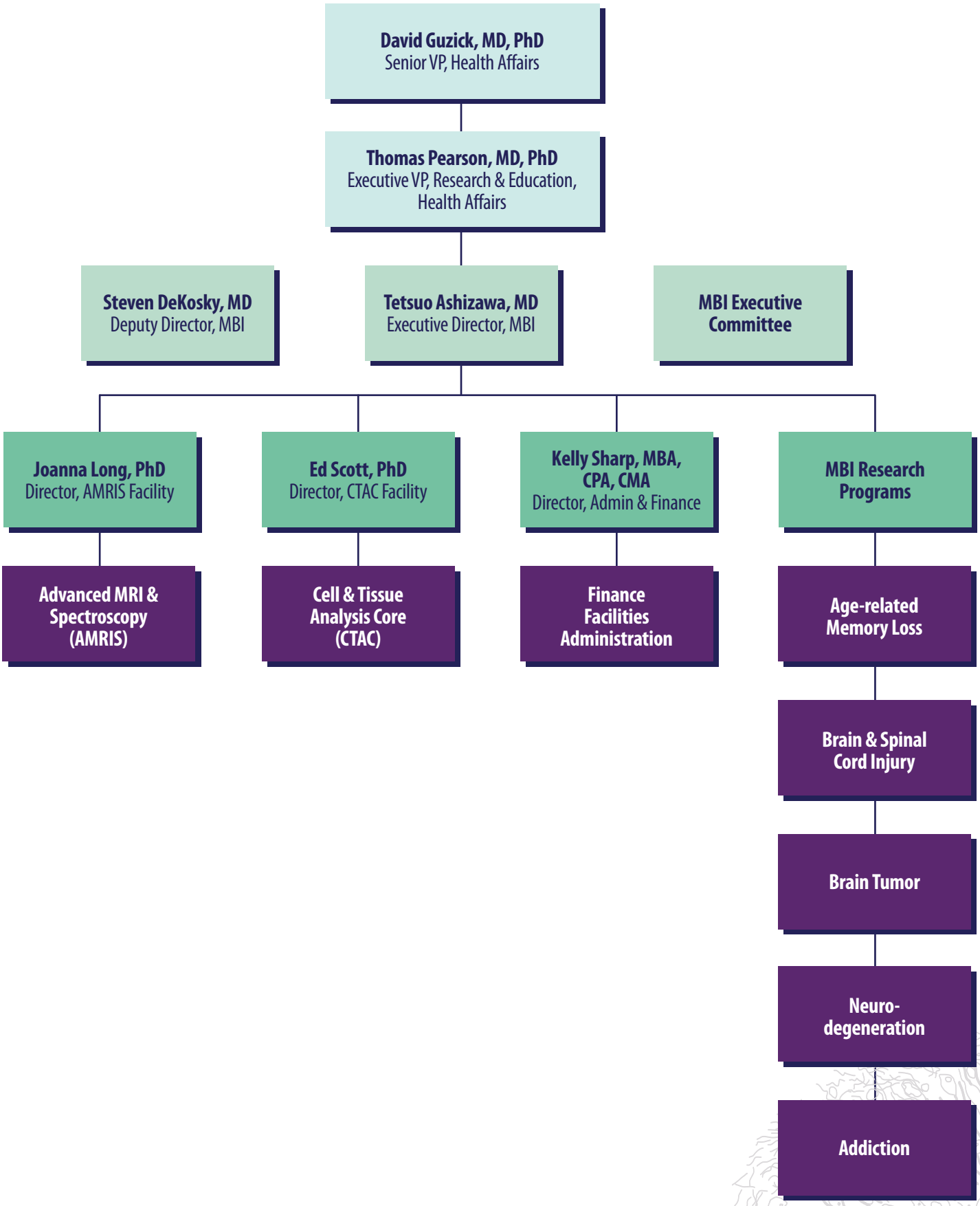
FISCAL YEAR 2014/2015 MBI EXECUTIVE COMMITTEE:

- **Tetsuo Ashizawa, MD**, Executive Director, McKnight Brain Institute; Professor, Department of Neurology
- **Regina Bussing, MD, MSHS**, Interim Chair, Department of Psychiatry
- **Steven T. DeKosky, MD**, Deputy Director, McKnight Brain Institute; Professor, Department of Neurology
- **Thomas Foster, PhD**, McKnight Research Chair for Age Related Memory Loss (ARML); Professor, Department of Neuroscience
- **William A. Friedman, MD**, Chair, Department of Neurological Surgery
- **Todd E. Golde, MD, PhD**, Director, Center for Translational Research in Neurodegenerative Disease (CTRND); Professor, Department of Neuroscience
- **Lucia Notterpek, PhD**, Chair, Department of Neuroscience
- **Michael S. Okun, MD**, Interim Chair, Department of Neurology; Co-Director, Center for Movement Disorders and Neurorestoration (CMDNR)
- **Marco Pahor, MD**, Chair/Director, Department of Aging/Institute on Aging

EX OFFICIO MEMBERS:

- **Ronald Cohen, PhD**, Director of Cognitive Aging and Memory (CAM)
- **Stephen Figueroa**, Director of Development, Neuroscience and Neuromedicine
- **Thomas A. Pearson, MD, PhD**, Executive Vice President for Research and Education, UF Health
- **Kelly Sharp, MBA, CPA, CMA**, Director of Finance and Administration, McKnight Brain Institute
- **Stephen P. Sugrue, PhD**, Senior Associate Dean of Research Affairs, College of Medicine

MBI Organizational Chart



MBI Events

The Florida Brain Project

The Florida Brain Project (FBP) is a consortium effort by Florida universities and research institutions to make the State of Florida known within the United States as the "State of Brain Research," through well-coordinated brain research collaborations across diverse disciplines.

The inaugural conference was held in the Florida capital city of Tallahassee, on July 28-29, 2014, at the DoubleTree (by Hilton) Hotel. The conference included presentations from 40 brain researchers and neuroscientists from across the state. Participating institutions included:

- University of Florida
- Florida State University
- University of Miami
- Scripps Research Institute of Florida
- University of South Florida
- Mayo Clinic of Jacksonville
- Max Planck Florida Institute for Neuroscience
- National High Magnetic Field Lab
- Sanford-Burnham Medical Institute
- Roskamp Institute
- University of Central Florida

This event was made possible by donations to the MBI from Drs. Martin and Sandra Fackler.

Brain Awareness Week

The magnificence, complexities and medical challenges of the remarkable brain were in the spotlight during National Brain Awareness Week at the University of Florida during March 16-20, 2015. Brain Awareness Week featured a series of events, including activities for Alachua County school students, lectures, panel discussions and a local neuroscience conference.

Brain Awareness Week is a worldwide event that aims to increase public awareness about the progress and benefits of brain research. The University of Florida events are sponsored by UF's Evelyn F. and William L. McKnight Brain Institute and organized by the North Central Florida Chapter of the Society for Neuroscience.

MBI Events *(continued)*

A group that included UF undergraduates and graduate students as well as research assistants and postdoctoral fellows from UF's College of Medicine brought brain-related events to 19 elementary, middle and high schools in Alachua County. Students in seventh grade and above received lessons in neuroscience and brain anatomy. Younger students learned about sensory functions and did "brain art" exercises.

A group of homeschooled students from Alachua County visited the McKnight Brain Institute to learn about the brain's sensory processing ability through hands-on activities such as taste strips and by using special goggles that demonstrated how the brain interprets vision.

Brain Awareness Week also featured a conference sponsored by the North Central Florida Chapter of the Society for Neuroscience. On March 20, the conference's keynote speech was given by David Sweatt, PhD, a neurobiology professor and director of the Evelyn F. McKnight Brain Institute at the University of Alabama-Birmingham. Sweatt spoke about "Epigenetic Mechanisms in Memory Formation." His research focuses on the molecular mechanisms related to learning and memory.

William G. "Bill" Luttge, PhD

William G. Luttge Lectureship in Neuroscience

In 2012, the McKnight Brain Research Foundation endowed the University of Florida with $300,000 to establish a permanent annual lectureship as a memorial tribute to the late William G. "Bill" Luttge, PhD, the first director of UF's MBI. Held each year, the William G. Luttge Lectureship in Neuroscience explores inventive ideas and approaches to ensure healthy cognitive aging and to counter brain diseases.

Dr. Luttge spearheaded efforts to organize the vast amount of brain research conducted at the University of Florida into a comprehensive program, eventually resulting in the establishment of the $60 million Brain Institute on the UF Health Science Center campus that was dedicated in 1998. He passed away March 24, 2012, after being diagnosed with multiple myeloma.

On May 4, 2015, renowned neuroscientist and University of Florida alumnus Fred H. Gage, PhD, returned to campus to deliver this year's lecture. Dr. Gage, who received a bachelor's degree in psychology in 1972, is a professor and researcher in the Laboratory of Genetics at the Salk Institute for Biological Studies in La Jolla, California. His lecture, titled "Neuronal Plasticity and Genomic Diversity," was delivered to a standing-room crowd of more than 150 people at the MBI.

Gage's lecture focused on the evolutionary impact of mobile DNA, which can cause a host of genetic variations and mutations by changing places in the genome. More broadly, mobile DNA may influence normal brain function, contribute to some neurological disorders and have a role in genome evolution.

Brain and Machine Cognition Symposium

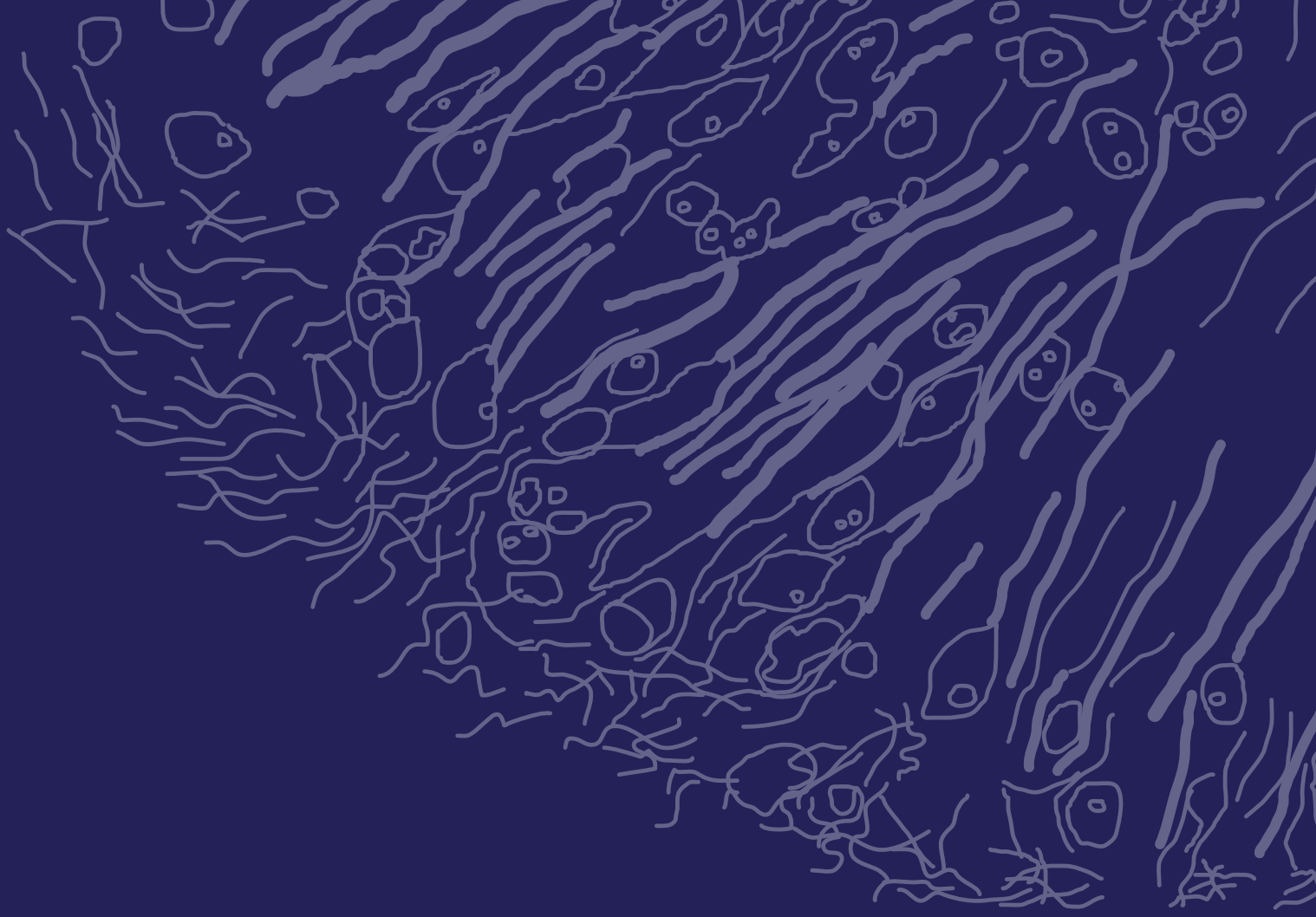
On April 27, 2015, the MBI hosted the Brain & Machine Cognition Symposium at the DeWeese Auditorium to explore collaboration opportunities between UF and the Florida Institute for Human and Machine Cognition (IHMC). This all day event featured in-person and remote presentations from researchers associated with MBI and with IHMC, followed by a brainstorming session and a tour of the MBI facilities. This very informative event's topics included brain prosthetics and interfaces, neuro cognitive and health assessment opportunities, neuron repair, and interventions for cognitive aging, neurodegeneration, and epilepsy.

This event was made possible by donations to the MBI from Drs. Martin and Sandra Fackler.

Myotonic Dystrophy and the Brain Symposium

Hosted by the MBI and the Center for Neurogenetics, this day-and-a-half-long symposium covered clinical, molecular and imaging studies of Myotonic Dystrophy (DM) with a focus on the central nervous system (CNS). The symposium was held at the MBI on December 15-16, 2014. With 25 speakers, this conference included discussions on molecular, pathological and imaging lessons from other neurological disorders, as well as therapeutic strategies.

This event was made possible by donations from the Marigold Foundation.



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