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Dr. Brenner's laboratory studies the molecular biology of astrocytes, the most common cell type in the central nervous system (CNS). Astrocytes are responsible for many of the homeostatic controls in the CNS, such as maintaining the blood-brain barrier and proper neurotransmitter levels. Astrocytes serve as precursors for neurons and oligodendrocytes during development, and also serve as stem cells for the production of these cell types in the adult. CNS injury stimulates astrocytes to undergo a reactive response, which contributes to healing but can also lead to further damage. Dr. Brenner's laboratory studies the transcriptional regulation of the gene encoding an intermediate filament protein specific to astrocytes, glial fibrillary acidic protein (GFAP), and on the biological role of this protein. The GFAP gene is of interest because it is turned on as astrocytes mature, and its activity increases dramatically during the reactive response. Thus, study of GFAP transcription will yield insights into mechanisms governing development, reaction to injury, and cell specificity, ultimately allowing these processes to be manipulated.

Dr. Brenner's laboratory has also discovered that heterozygous coding mutations in the GFAP gene are responsible for Alexander disease, a rare but fatal neurological disorder. Interestingly, although this establishes that the primary genetic defect in this disease is in astrocytes, the infantile form of Alexander disease is marked by massive myelination defects, and the later onset forms by neuronal dysfunction. Thus the study of this disorder not only has direct clinical implications, but also will reveal critical interactions between astrocytes and oligodendrocytes and between astrocytes and neurons that occur throughout the life span.

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While oligodendrocytes (OLs) have the ability to proliferate in inflammatory white matter diseases such as cerebral palsy and multiple sclerosis, they fail to myelinate axons suggesting a disruption in maturation or inability to make functional contacts with axons. Also, there is a substantial decrease in myelin in the aging brain suggesting that with age the brain has a reduced capacity to remyelinate. Therefore, a better understanding of the signaling mechanisms responsible for myelination would allow us to design therapeutic approaches to promote brain repair. The selection of axons to be myelinated, formation of the nodes of ranvier, and regulation of myelin thickness are known to involve axon-glial signaling. One of the emerging molecules in axon-glial signaling is glutamate. Glutamate, as an essential neurotransmitter, exerts its role by activating glutamate receptors on neurons, and is precisely regulated by glutamate transporters. These same constituents of glutamatergic signaling are developmentally regulated throughout the OL lineage. In fact, vesicular release of glutamate from axons induces glutamate receptor mediated currents in postsynaptic OL progenitor cells, underscoring the importance of studying glutamate as a signaling molecule during myelination. Our lab has shown that stimulation of glutamate receptors leads to activation of specific intracellular signaling cascades that enhance myelination and that inflammatory mediators perturb these signaling pathways and disrupt myelination. Using primary cultured cells in an *in vitro* model of myelination as well as *in vivo* animal models, the goal of our lab is to understand the role of glutamatergic axon-glial signaling during myelination and how inflammation and the process of aging dysregulate these pathways.

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Dr. Dobrunz's research program uses electrophysiological approaches to study synaptic transmission and regulation of presynaptic properties at synapses in the hippocampus. Using hippocampal brain slices and cultured hippocampal neurons from rodents, the lab studies short-term plasticity and the cellular and molecular mechanisms underlying the activity dependent modulation of neurotransmitter release. Projects in the lab include the study of mechanisms and

effects of target-cell specific short-term plasticity, including the role of short-term plasticity in the dynamic balance of excitation and inhibition in hippocampus. The lab also studies the changes that occur in presynaptic function during normal postnatal development and during normal aging.

David Geldmacher, M.D., FACP
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David S. Geldmacher, MD, FACP is the Charles and Patsy Collat Endowed Professor of Neurology and Director of the Division of Memory Disorders and Behavioral Neurology at the University of Alabama at Birmingham. Prior to joining UAB in 2011, he held a Harrison Distinguished Teaching appointment as an Associate Professor of Neurology at the University of Virginia. His research has centered on drug development for dementia, including investigator-initiated clinical trials funded by the NIH and pharmaceutical manufacturers. His other research interests include complex visual processing in aging and neurological conditions. Dr. Geldmacher is the author of *Contemporary Diagnosis and Management of Alzheimer's Dementia*, and has published over 100 research articles, chapters, abstracts and reviews.

His major clinical interests are in the diagnosis and management of dementia, evaluation of behavioral neurologic syndromes, and rational drug treatments of disorders resulting from brain dysfunction.

He is a Fellow of the American College of Physicians and a member of the American Academy of Neurology, American Neurological Association, and the American Society of Neurorehabilitation. Dr. Geldmacher graduated *magna cum laude* from the University of Rochester with his B.A. in Biology and Psychology. He obtained his M.D (with Certificate in Academic Research) from the State University of New York - Health Science Center at Syracuse. He trained in Neurology at Case Western Reserve University and completed a postdoctoral fellowship in Behavioral Neurology at the University of Florida.

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Dr. Hablitz's research is centered on understanding control of activity in local cortical circuits. He is using studies on synaptic transmission to further understand basic biophysical properties of mammalian central neurons, as well as to explore the pathophysiology of experimental epilepsy. Whole-cell voltage-clamp recordings from visually identified neurons are used in *in vitro* brain slice preparations. The goal of these studies is to determine the types of synaptic interactions present among pyramidal cells and interneurons in neocortex and how these patterns change over the lifespan. A particular goal is to understand how hyperpolarization-activated non-specific cation (HCN) channels control neocortical excitability. HCN channels and I_h, the membrane current generated by their activation, have been implicated in a variety of processes including memory, behavior and neurological diseases. HCN channels regulate dendritic integration and affect excitability of individual neurons in prefrontal cortex. Alterations in these processes are potentially important in aging since dendritic integration is altered in spatial learning-impaired aged rats. Additional studies involve the use of imaging techniques to directly visualize activity in presynaptic nerve terminals. These studies examine modulation of neurotransmitter release in normal neocortex and animal models of cortical dysplasia.

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Dr. King received her BS from Purdue University and her MS and Ph.D degrees from the University of Michigan. She did postdoctoral fellowships at Cedars-Sinai Medical Center/UCLA characterizing the immunological mechanisms of tumor regression upon adenoviral expression of TK and Flt3L proteins in rodent models of glioma. She did a second postdoctoral fellowship at Boston University School of Medicine where she identified novel small molecules to elevate Klotho transcription and examined the role of epigenetic modification in the age-downregulation of Klotho protein. She is now an Assistant Professor at the University of Alabama at Birmingham. Work in the King lab will expand upon her postdoctoral work to

characterize the pre and post-transcriptional regulation of Klotho. As well the lab is investigating the role of Klotho at the synapse and as an anti-tumor protein. Klotho knockout animals display a prominent ageing like phenotype and rapidly die from the confluence of syndromes induced by the absence of the protein. Klotho is made mostly in brain and kidney as a transmembrane protein where it functions as a coreceptor. Likewise, it is shed from the membrane and functions as a humoral factor. Although Klotho is generated in the kidney and the brain, the majority of studies have focused on its role in kidney. As Klotho has roles in memory retention, axonal transport, and calcium/phosphate/ Vitamin D homeostasis, understanding its involvement in the brain could impact our understanding of age-related changes that occur in the brain.

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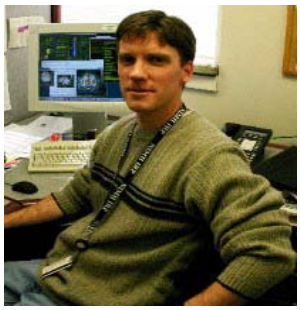

Dr. Knight's research is focused on better understanding the neural substrates of human learning, memory, and emotion using functional magnetic resonance imaging (fMRI). His research employs a Pavlovian fear conditioning paradigm during fMRI to explore changes in human brain activity that occur during this type of associative learning. Findings from these studies are consistent with laboratory animal research in that they indicate the thalamus, amygdala, hippocampus, cingulate, and sensory cortex are important components of the neural circuitry that supports learning and memory of conditional fear in humans. Dr. Knight has been developing methodologies designed to expand the use of autonomic and behavioral measures that are recorded simultaneously with fMRI. The use of such data to extract additional information from functional images may provide more detailed insights into the neural circuitry that mediates certain cognitive processes. Dr. Knight's laboratory is also interested in the role of awareness in the expression of fear-related behaviors, the neural circuitry mediating aware and unaware fear memory processes, and brain regions that process properties of fearful stimuli compared to regions that produce behavioral and autonomic fear responses.

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The central role of CNS nicotinic acetylcholine receptors (nAChRs) in tobacco addiction drives most of the research in the lab. We would like to increase our understanding of the overall function of these receptors in the brain under both physiological and diseased conditions. Our lab has two major goals. The first is to understand how postsynaptic nAChRs contribute to synaptic transmission in the CNS - a mechanism that has remained largely elusive for over 50 years. We propose that nAChRs can be used to sense the overall changes in the level of ambient transmitter, acetylcholine, through diffusion signaling (*volume transmission*) rather than direct point-to-point synaptic communication. Second, we are interested in the molecular and cellular mechanisms that underlie relapse to nicotine after chronic drug abuse. In particular, we have focused on the hippocampus because of its known role in learning and memory, which may couple secondary drug cues/context to the primary nicotine reward. We propose that persistent changes in the neural circuitry as a result of exposure to nicotine may be at least partially responsible for the lasting incentive (*craving*) for nicotine. In addition these same adaptations may underlie the cognitive deficits known to occur after nicotine withdrawal in adults and in offspring of mothers that smoke during pregnancy. Robin A.J. Lester received his Ph.D. in Pharmacology from the University of Bristol, UK in 1988. Following a Research Assistant Professor position at Baylor College of Medicine, he joined UAB in 1995. He is presently an Associate Professor of Neurobiology.

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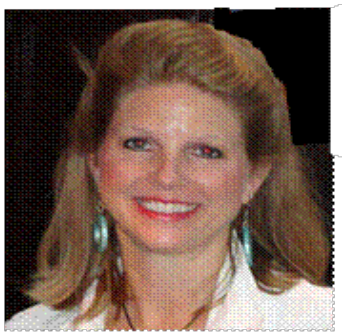
Dr. Lubin's research is primarily directed towards identifying molecular mechanisms that serve to regulate gene expression changes necessary for learning and memory. Currently, Dr. Lubin's lab is focused on characterizing the role of epigenetic mechanisms, such as histone methylation, DNA methylation, and signaling cascades that mediate the interaction of the

nuclear factor-kappa B (NF-kB) transcription factors to chromatin and determine how they participate in the regulation of gene expression as they relate to learning and memory. Dr. Lubin's research program focuses on neurons and synapses in the hippocampus, an area of the brain that plays an important role in memory formation. She is investigating the epigenetic regulation of brain derived neurotrophic factor (BDNF) and early growth response-1 (EGR1/Zif268) transcripts during memory formation. This has lead to the discovery that gene regulation of *BDNF* and *Zif268* transcripts are dynamically regulated by histone methylation and DNA methylation in hippocampus during memory consolidation. Current work also includes an assessment of histone methyltransferase inhibitors and DNA demethylating agents that may be promising in the mitigation or disruption of cognitive disorders.



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My lab is currently investigating the role of estradiol in hippocampal synapse density, synaptic plasticity and learning. We are particularly interested in determining how loss of estradiol during aging impacts hippocampal function and whether hormone replacement therapy can activate estradiol-dependent mechanisms to restore normal synaptic function in hippocampus as well as hippocampal dependent learning and memory. Ovariectomized female rats treated with estradiol at various intervals following ovariectomy are used as a model system. Experiments involve electrophysiological measurements of NMDA currents, synaptic transmission, and long-term plasticity in acute brain slices. We have recently reported that estradiol increases NMDA transmission mediated by NR2B containing receptors and that is causally related to the heightened LTP induced by estradiol. Furthermore, we find that the period of hormone deprivation rather than chronological age determines the effectiveness of estradiol replacement to increase hippocampal dependent learning and synaptic function. Determining how estradiol and hormone replacement affects hippocampal function could lead to development of therapies to alleviate hormone-dependent memory loss in aging.

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Dr. Meador-Woodruff received his BS in Chemistry from the University of Richmond, and his MD from the Medical College of Virginia. He then moved to Ann Arbor, and completed a

combined residency in psychiatry and a research fellowship at the University of Michigan. After completing his research training, he joined the faculty of the Department of Psychiatry and the Mental Health Research Institute at the University of Michigan where he remained for nearly 22 years. He left Michigan in April 2006 to become the Heman E. Drummond Professor and Chairman of the Department of Psychiatry of University of Alabama at Birmingham (UAB). He moved his lab largely intact to UAB, and his current research focus is on understanding brain abnormalities in schizophrenia. His research has been continuously funded by NIH since 1989. His laboratory's primary research interest is on understanding how different parts of the brain communicate with other parts via a variety of chemical signals, and how this communication is disrupted in schizophrenia. His current focus is on studying the expression of genes associated with glutamatergic neurotransmission within individual cells in the nervous system. He also has a longstanding interest in teaching and mentorship, including serving on the APA Corresponding Committee on Research Training which he chaired in 2006, is a frequent faculty participant at the annual APA Research Colloquium for Junior Investigators, and was the director of the University of Michigan's Psychiatry Residency Research Track, holding one of the first NIH grants designed to fund such programs. Nearly 100 trainees have rotated through his lab. He is Editor-in-Chief of the journal Neuropsychopharmacology.

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The focus of Michelle’s research is to enhance our understanding of the role of astrocytes in brain and spinal cord function. Astrocytes are the most numerous cells in the central nervous system yet the role of astrocytes in injury, particularly pediatric injury, and neurodevelopmental disorders is highly understudied. Her work focuses on two essential functions of astrocytes; buffering of extracellular K+ and glutamate. These functions are thought to be largely mediated by two astrocytic proteins, Kir4.1, an inwardly rectifying potassium channel and excitatory amino acid transporter, GLT-1. These two proteins function to dampen neuronal excitability. Following injury, persistent alterations in the biophysical properties of astrocytes hinder their ability to perform these basic altruistic functions. The resulting dysregulation of extracellular K+ and glutamate are associated with increased neuronal excitability and changes in synaptic physiology and plasticity in the adult. In the developing central nervous system, loss of these functions may profoundly impact neuronal development and may contribute to seizures and cognitive impairments following injury. Surprisingly, little is known regarding the regulation of either protein in normal brain, following injury or during abnormal development. The current research projects span from understanding the regulation of Kir4.1 and GLT-1 gene transcription in pathophysiology, examining protein expression, function and activity, to understanding how the loss of extracellular K+ and glutamate regulation impact neuronal development.

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Dr. Roberson received his A.B. with highest honors from Princeton University. He then earned his M.D. and Ph.D in neuroscience at Baylor College of Medicine in Houston where he studied molecular mechanisms of learning and memory using a combination of electrophysiology and biochemistry. He completed a residency in neurology at the University of California San Francisco, where he also served as Chief Resident in Neurology. After residency, he completed a clinical fellowship in behavioral neurology with Dr. Bruce Miller at UCSF and resumed basic research in the laboratory of Dr. Lennart Mucke at the Gladstone Institute of Neurological Disease, initiating his current studies of neurodegenerative disease using mouse models. He was appointed as Assistant Professor of Neurology at UCSF in 2005. In 2008, he moved to UAB to establish his independent research laboratory. Dr. Roberson also cares for patients with memory disorders and dementia at the Kirklin Clinic.

The Roberson lab studies the neurobiology of two common neurodegenerative disorders, Alzheimer's disease (AD) and frontotemporal dementia (FTD), with a focus on understanding the underlying cellular and molecular mechanisms that will lead to better treatments. Lab members use modern neuroscience approaches to study animal models of these conditions. One area of interest is pursuing the discovery that tau reduction makes the brain resistant to AD-related neuronal dysfunction and seizures, to determine how the protective effects of tau reduction might be harnessed as a treatment for these conditions. Other members of the lab work on determining how mutations in tau and progranulin cause the social and behavioral dysfunction seen in FTD.

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Dr. Sweatt's research program focuses on molecular mechanisms underlying learning and memory. Dr. Sweatt uses knockout and transgenic mice to investigate signal transduction

mechanisms in the hippocampus, a brain region known to be critical for higher-order memory formation in animals and humans. His laboratory also uses a large number of genetically engineered mouse models for human learning and memory disorders in order to investigate the molecular and cellular basis of human memory dysfunction. His laboratory has discovered a number of new roles and mechanisms of gene regulation in memory formation, focusing on studies of transcription factors, regulators of chromatin structure, and other epigenetic mechanisms such as chemical modification of DNA. Overall his work seeks to understand the role of regulation of gene expression in synaptic plasticity and long-term memory formation and storage. His laboratory also is interested in using what they have learned about the molecular basis of hippocampal synaptic plasticity and memory formation to generate insights into human pathological conditions associated with aging-related memory dysfunction.

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Lindsey Vedder is a graduate student under the mentorship of Dr. Lori McMahon. Lindsey's studies investigate the ability of 17β-estradiol (E2) to enhance hippocampal dependent learning and memory and synaptic plasticity in aged rats that have experienced long-term ovarian hormone loss. During her thesis work, Lindsey has found that E2-enhanced hippocampal function, including enhanced long-term potentiation at CA3-CA1 synapses, dendritic spine density, current mediated by NR2B-containing NMDA receptors and object recognition learning, is absent after 19 months of ovarian hormone loss. This loss in E2-enhanced hippocampal function is due to the length of time of ovariectomy as aged-matched ovary intact rats still exhibit the E2-enhanced hippocampal function. The last part of Lindsey's thesis will investigate whether chronic replacement of E2 will protect against the loss of E2-enhanced hippocampal function seen with long-term ovariectomy. These studies will further characterize the window of opportunity during which E2 replacement remains beneficial to hippocampal plasticity and will better inform the clinical community to treat hormone related cognitive decline during menopause.

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Dr. Visscher is interested in characterizing what brain mechanisms underlie the human ability to flexibly process inputs from the environment. We often process the same information in different ways at different times. For example, sometimes we may hear a string of numbers (e.g. a phone number on a commercial from the radio) and try to remember it, while at another time, the same string of numbers may be irrelevant, and we may ignore it. Dr. Visscher uses a variety of tools to better characterize how human brain activity before a stimulus is presented may impact the ways in which that stimulus is processed. Behavioral measurements (psychophysics and eye movements), measurement of electrical activity in the human brain using EEG, and measurement of neural activity through fMRI allow insight into this question.
Dr. Visscher started at the University of Alabama at Birmingham in April 2009, after a postdoctoral fellowships at Harvard University, where she worked with Randy Buckner and studied how connectivity among brain areas (as measured with functional MRI) change with experience. She used psychophysical and EEG techniques to examine how brain activity before a stimulus influences whether a stimulus will interfere with items in working memory during a previous postdoctoral fellowship at Brandeis University working with Robert Sekuler. She received her Ph.D. in Neuroscience from Washington University in St. Louis in 2004, where, with Steve Petersen, she studied how techniques of fMRI can be used to examine different time courses of neural activity.