Director’s Letter

When people ask me what sets the ZNI apart from other institutes, especially those outside of USC, I have three responses.

One: the people. Our faculty are among the best and brightest in the world, working in a range of disciplines, examining from a wealth of perspectives the underlying biology and potential causes of disorders affecting the brain. But the researchers at ZNI—myself included—are also fortunate to be part of a larger community of science at USC. We are able to expand our range by collaborating with excellent colleagues, leaders in the field of neuroimaging, physician-scientists in neurosurgery, geneticists in psychiatry, pioneers in stem cell science just to name a few, along with outstanding neuroscientists across campuses. Working with smart people from a variety of backgrounds allows us to be challenged in the best possible way, to work outside of our comfort zone, stimulated to creatively reexamine an approach, an idea, a technique, a hypothesis.

Two: the science. Obtaining grants is a highly competitive process in the best of times, but even more so these days, with NIH dollars spread thin and many foundations scaling back on awards. Getting published, especially in a top-tier journal takes patience and perseverance. But ahead of both of these goals is the ultimate achievement: strong science. If the aims are clear, the experiments novel and the supporting data is sound, in the end, good science will prevail. Such is the case with the work being conducted at ZNI. While all researchers experience bumps in the road in funding or have to contend with the occasional negative review, our researchers ride the waves to success. As evidenced by our increased funding and collectively outstanding publication record, ZNI PIs have proven they can weather a storm and come out on top.

Three: the future. Over the past several years, USC has been investing in the health sciences, building upon our strengths and charting a course for the future. I am delighted to count among my colleagues and collaborators, Andy McMahon of the Broad Center for Stem Cell Research, Art Toga of the Stevens Institute for Neuroimaging and Informatics, and Scott Fraser, Provost Professor and Director of Science Initiatives. I am pleased to have participated in the successful renewal of the Alzheimer’s Disease Research Center (ADRC), led by my friend Helen Chui, who is also chair of Neurology. And I applaud the success of junior scientists like William Mack MD, who received his first R01, one of only six classified as an Outstanding New Environmental Science (ONES) Award from the National Institute of Environmental Sciences (NIEHS). I am happy to report that for the first time in some while, several ZNI PIs now hold more than one R01. Working together, we are creating a formula for success.

This is the new math at ZNI: good people + great science = bright future.

All the best,

Berislav V. Zlokovic, MD, PhD
# Table of Contents

- Director’s Letter: 3
- History and Mission: 6
- ZNI Faculty: 8
  - Faculty News: 11
  - Faculty Research Programs: 14
  - Scientific Advancements: 21
  - Academic and Community Activities: 32
  - Collaborations: 34
- FY 15 Faculty Publications: 46
- ZNI Postdoctoral Trainees: 66
- ZNI Graduate Students: 68
  - Zach Hall Travel Awards: 72
  - NRSA Grant Training: 73
- Grants and Contracts: 74
ZNI Events

ZNI Seminar Series

Special Lectures
5th Annual Zach Hall Lecture
2nd Annual Zilkha Symposium on Alzheimer’s Disease & Related Disorders

ZNI Collaborative Events
Joint ADRC ZNI Pilot Program
Los Angeles Brain Bee
Music to Remember – LA Opera/Alzheimer’s Association

ZNI Administration and Operating Budget
ZNI Development
History and Mission

USC Neuroscience is characterized by collaborative interactions between faculty and students working at many different levels of analysis, including research on cell-molecular neurobiology, systems-level analysis of neural circuits, neural engineering, and cognitive and computational neuroscience. Established in 2003 by a generous gift from Selim Zilkha and Mary Hayley and further support from the WM Keck Foundation, the Zilkha Neurogenetic Institute is an integral part of a larger USC Neuroscience Initiative, encompassing researchers throughout the University. The Zilkha Neurogenetic Institute provides a home for a program of interdisciplinary research that builds on USC’s existing strengths in neuroscience and genetics, as well as the clinical expertise of the physician-scientists in the Keck School of Medicine’s clinical departments.

Faculty associated with the ZNI represent a sampling of the broad and interactive biomedical research effort being conducted at USC. More than 30 faculty members from 17 USC departments, institutes, divisions and centers are affiliated with ZNI. These investigators have active federal grants from more than a dozen different institutes across the National Institutes of Health, the National Science Foundation, Department of Defense, the Department of Public Health Services, foundations and industry partners. ZNI is home to 300 researchers, staff and students, including 34 postdoctoral fellows and 56 graduate students.

Scientists at ZNI are from the Departments of Biochemistry & Molecular Biology, Cell & Neurobiology, Molecular Microbiology & Immunology, Neurology, Neurosurgery, Ophthalmology, Otolaryngology, Physiology & Biophysics, Psychiatry & the Behavioral Sciences and Preventive Medicine, the division of Biostatistics, the Alzheimer Disease Research Center, the Institute for Neuroimaging and Informatics as well as the Eli & Edythe Broad CIRM Center for Regenerative Medicine and Stem Cell Research at USC, to which the ZNI is physically connected via bridges on all floors.
An organized research unit of the Keck School of Medicine at the University of Southern California, the ZNI is housed in a five-story, 125,000 sq. ft. building on the Health Sciences Campus, a state-of-the-art facility that allows basic and clinical neuroscientists to concentrate and collaborate. Research programs at the ZNI concentrate on Alzheimer and Related Diseases, Psychiatric Genetics, Genomics, Circuits, Vascular areas, Vision/Eye and Hearing/Ear. Among other research groups, the ZNI is home to the Protein Structure Lab, the Multiphoton Center, the Center for Genomic Psychiatry and the Center for Neurodegeneration and Regeneration.

Over the last 12 years, ZNI has expanded our network of partnerships to become a leader in the field in basic research. With our colleagues, we are on the forefront of explorations to discover the causes and potential remedies for hundreds of different neurodegenerative disorders.

The Zilkha Neurogenetic Institute (ZNI) is the center of basic and clinical neuroscience research across USC.
ZNI Faculty

Alexandre Bonnin, PhD
Assistant Professor
Cell & Neurobiology

Daniel B. Campbell, PhD
Assistant Professor
Psychiatry & the Behavioral Sciences

Karen Chang, PhD
Assistant Professor
Cell & Neurobiology

Hong-Wei Dong, MD, PhD
Associate Professor
Neurology

David V. Conti, PhD
Professor
Preventive Medicine

Robert H. Chow, MD, PhD
Professor
Physiology & Biophysics

Jeannie Chen, PhD
Professor
Cell & Neurobiology

Marcelo Coba, PhD
Assistant Professor
Psychiatry & the Behavioral Sciences

Hong-Wei Dong, MD, PhD
Associate Professor
Neurology
Oleg Evgrafov, PhD
Associate Professor of Research
Psychiatry & the Behavioral Sciences

Rick A. Friedman, MD, PhD
Professor
Otolaryngology

Radha Kalluri, PhD
Assistant Professor of Research
Otolaryngology

James A. Knowles, MD, PhD
Professor
Psychiatry & the Behavioral Sciences

Ralf Langen, PhD
Professor
Biochemistry & Molecular Biology

William Mack, MD
Assistant Professor
Neurological Surgery

Takahiro Ohyama, PhD
Assistant Professor of Research
Otolaryngology

Carlos Pato, MD, PhD
Professor & Chair
Psychiatry & the Behavioral Sciences

Michele Pato, MD
Professor
Psychiatry & the Behavioral Sciences
Throughout the last year, ZNI continued our efforts to expand programs and relationships with various departments throughout USC and happily celebrated a number of milestones.

In December 2014 our support of the so-called ZNI Incubator Lab produced a most fruitful result: William Mack, MD, received a five-year fully funded R01, the first ever in the history of the department of Neurosurgery. His R01 is one of only six in the nation classified as an Outstanding New Environmental Science (ONES) Award from the National Institute of Environmental Sciences (NIEHS); ONES awards are meant to identify the most talented early-stage PIs who intend to make a long-term commitment to research in the Environmental Health Sciences. A neurosurgeon, Dr. Mack will study how particulate matter exposure can be toxic to blood vessels in the brain, and identify risks to cognitive health in vulnerable populations. Dr. Mack’s success reinforces the idea that with some investment and the right amount of support, researchers can achieve worthy goals.

Ansgar Siemer, PhD received in February 2015, his first R01. The five-year award from the National Institute of Neurological Disorders and Stroke (NINDS) is entitled “Orb2, a functional amyloid in long-term memory: Its structure and how it forms.” In addition, Dr. Siemer received a diversity supplement for this grant to support Silvia Cervantes, a graduate student admitted to the Programs in Biomedical and Biological Sciences. Dr. Siemer who is a past recipient of an award from the Whitehall Foundation, is also a co-I on another R01 grant from NINDS, one held by Ralf Langen; that study investigates the molecular mechanisms of protein misfolding in Huntington Disease.

Three ZNI PIs received notice in June 2015 that they would receive a second R01 commencing in July: in addition to his NINDS R01, Ralf Langen, PhD will receive from the National Institute of General Medical Sciences (NIGMS), another five-year grant entitled “Membrane remodeling by alpha-synuclein: implications for function and disease.” Janos Peti-Peterdi, MD, PhD will receive a second R01 from the National Institute of Diabetes and Digestive Disorders (NIDDK), a multi-year award entitled “Multiphoton imaging of the juxtaglomerular apparatus.” In addition to her R01 awarded in July of 2012, Huizhong (Whit) Tao, PhD will receive in July a second R01 from the National Eye Institute to study the synaptic circuitry mechanisms underlying functional development of the visual cortex.
ZNI also continues to work with the department of Microbiology and Immunology and the Dean’s office to explore potential lab space for recruitment of PIs whose research programs are complementary to the Institute’s mission. This past year I-Chueh Huang (MMI) moved his lab to ZNI 501 and in Summer 2015 we will welcome separate new laboratories for Dr. Jae Jung and Dr. Hyungjin Eoh. We have also continued to work with the USC Biosafety Level 3 (BSL-3) facility which had a soft launch in 2014.

Robert Hsiu-Ping Chow, MD, PhD was promoted to Professor in Physiology & Biophysics. A Fellow of the American College of Physicians, Dr. Chow was trained in membrane biophysics and cellular physiology, using real-time electrophysiological and imaging methods in living cells to study the function of cells, organelles, and molecules. His laboratory works to advance our understanding of how hormone and neuronal secretion is controlled in normal and pathological states, and then to translate this knowledge to improve human health. Currently Dr. Chow is co-I with James Knowles, MD, PhD (ZNI/Psychiatry) on a U01 from the National Institute for Mental Health (NIMH), “Evaluation of Cellular Heterogeneity Using Patchclamp and RNA-Seq of Single Cells”. Dr. Chow is also working with Dr. Mark Humayan in Ophthalmology on a National Science Foundation (NSF) Grant to develop the next generation of retinal neuroprosthesis, based on cell membrane-embedded molecules that convert light into electrical signals, as well as an R01 from the National Eye Institute (NEI), which aims to study factors that allow patients to resolve complex shapes with a retinal prosthesis. Dr. Chow recently received a pilot grant from the USC Clinical Translational Science Institute and is co-I with Dr. K. Kirk Shung (USC Biomedical Engineering) on a P41 from the National Institute of Biomedical Imaging and Bioengineering (NIBIB).

In recognition of his pioneering work and cutting edge research on kidney disease, Janos Peti-Peterdi, MD, PhD was elected this Spring to two prestigious honor societies, the American Society for Clinical Investigation (ASCI), and the European Academy of Sciences and Arts (EASA).

Dr Peti-Peterdi was also named the 2015 recipient of the ASN-AHA Young Investigator Award. Co-sponsored by the American Society of Nephrology (ASN) and the council on the Kidney of the American Heart Association (AHA), the annual award recognizes a kidney researcher age 45 or younger with an outstanding record of achievement and creativity. The award was scheduled to be given out in November.
In January 2015, Gregory D Field, PhD relocated his laboratory from ZNI to Duke University. Dr. Field’s research is centered around identifying the functional connectivity between photoreceptors (rods and cones) and approximately 20 distinct retinal ganglion cell types. He maintains an active collaboration with Jeannie Chen, PhD and they plan to submit a grant to the NEI in late 2015.

At the end of FY15, after 10 years as Chair of the Department of Psychiatry and the Behavioral Sciences, Carlos Pato, MD announced he would be relocating his laboratory from ZNI to SUNY Downstate, where he was appointed Dean of the Medical School. As the Genomic Psychiatry Cohort (GPC) grants ended in May 2015, two of his remaining grants will move with him. Michele Pato, MD will retain an adjunct appointment with ZNI so she may transition her grant into a subcontract to Downstate, and maintain her collaboration with James Knowles MD PhD collecting and analyzing data for the obsessive-compulsive disorder cohort portion of the GPC.

In Spring 2015, the USC Alzheimer’s Disease Research Center (ADRC) was awarded a five-year competitive renewal. Drs. Arthur Toga and Berislav Zlokovic have now joined Dr. Helena Chui as part of the administrative core of the new ADRC. Dr. Zlokovic is an Associate Director of the ADRC and he co-directs the Core for Neuropathology and Biomarkers. He is also PI of the ADRC project, “Neurovascular Factors in Alzheimer’s Disease,” a CSF biomarker study that deploys imaging to explore biomarkers of the cerebrovascular system and examine blood-brain barrier integrity.

In late 2015, an ADRC-ZNI pilot program will be announced, which will provide additional opportunities for individual PIs across disciplines to obtain funds for novel projects holding promise for further external funding. By combining forces, the ADRC-ZNI program will be able to fund more research programs, expanding Alzheimer Disease studies at USC. The ADRC receives $11.5M over five years from the National Institute for Aging (NIA).

In May 2015, Dr. Berislav Zlokovic coordinated the preparation and submission of a large, multi-center P01 grant with three cores, “Vascular Contributions to Dementia,” which was preapproved as a special new program of the NIA. If awarded, the USC Center would receive $1.5M in direct costs each year for five years. Partners and Co-Is on the grant include Helena Chui MD, Lon Schneider MD, Meng Law MD, Daniel Nation PhD, Jack McArdle PhD, Art Toga PhD, Paul Thompson PhD, Judy Pa PhD, Terrence Town PhD, Hong-wei Dong PhD (all USC); Michael Harrington MD (Huntington Medical Research Institute); John Ringman MD (formerly UCLA, now USC); John Morris MD, Anne Fagan PhD, Tammie Benzinger MD PhD, Randy Bateman MD (all Washington Univ at St Louis); Eric Reiman MD (Banner Institute); Richard Caselli MD (Mayo Clinic); and Russell Jacobs (Caltech).
Faculty Research Programs

Scientists at the Zilkha Neurogenetic Institute reach across boundaries to embrace methods and techniques from many fields of study. They work to identify new approaches for examining nervous system function, so we may all better understand the underlying causes of neurological and psychiatric disorders. Areas of research overlap considerably (e.g., vision and circuits), and every Principal Investigator (PI) has multiple projects ongoing at any one time. Here is an overview of the various topics of study with current examples:

Alzheimer and Related Diseases

The Protein Structure group (Drs. Ralf Langen, Ansgar Siemer and Tobias Ulmer) investigate the structure of proteins involved in debilitating diseases such as Alzheimer’s disease (AD) but also Parkinson’s and Huntington’s disease. Because many disorders of the nervous system are thought to arise from alterations in the structure of cellular proteins, these studies aim to help us understand the molecular basis of neural pathology, with a look toward devising new treatments for the cure and prevention of these diseases. The interaction of proteins with membranes underlies many important biological processes. Proteins can regulate the structure and function of biological membranes by controlling the composition, fluidity, permeability and curvature of cellular membranes. Membranes, in turn, can have a pronounced effect on the structure and function of proteins and help to promote physiologically important structural reorganizations of proteins. In addition, membrane interaction can also result in protein misfolding which could ultimately cause disease.

Dr. Karen Chang’s lab is currently pursuing two main areas of research: 1) identification of the genotype to phenotype correlations in Down syndrome (DS), and 2) investigation of mitochondrial dynamics in neurons. DS, a complex disorder caused by triplication of chromosome 21, is the leading genetic cause of mental retardation. DS patients have numerous clinical manifestations, including early onset Alzheimer’s disease (AD). The exact mechanisms underlying those anomalies, however, remain unclear. We believe that Drosophila, with its powerful genetics, is an ideal model system for identifying the network of genes responsible for mental retardation and AD in DS. Dr. Jeannie Chen is studying how Annexin A5 modifies disease progression in a mouse model for Alzheimer’s disease. Dr. Hongwei Dong’s lab is studying the organizational principle of the brain wiring and how these circuits are disrupted in mouse models of Huntington’s and Alzheimer’s diseases, using high-resolution gene expression analysis in the mouse brain. The goal is to refine the architectonic delineations of the mouse brain and identify novel candidate genes underlying the wiring diagram of brain structures. As a foundation of this project, Dr. Dong published a standard mouse brain atlas: the Allen Reference Atlas (Dong, 2008, Wiley) which serves as the backbone of one genomic-wide gene expression mapping project, the Allen Brain Atlas (www.brain-map.org).
**Dr. Terrence Town** and his team focus on developing a treatment for Alzheimer’s disease by targeting the body’s immune system. Most therapies targeting the disease are thwarted by the blood-brain barrier, a natural mechanism that protects brain cells from entry of peripheral substances, and by the fact that immune responses in the brain are typically muted. However, in laboratory mice programmed to develop Alzheimer’s-like disease, Dr. Town’s group has shown that certain immune cells can be coaxed into the brain from the circulation, where they attack the damaging sticky plaque buildup that is a defining feature of Alzheimer’s disease. Earlier this year, Dr. Town’s lab revolutionized the field of Alzheimer’s disease research by generating the first rat model of the disease that manifests all of the clinico-pathological hallmarks of the human syndrome. Specifically, the transgenic rats over-express two mutant human transgenes that are each independently causative of familial early-onset Alzheimer’s disease; this makes them an invaluable tool for understanding Alzheimer’s disease etiology and for testing cutting-edge therapeutics preclinically.

**Dr. Berislav Zlokovic**’s laboratory has a long standing interest in understanding the role of cerebral blood vessels and blood-brain barrier (BBB) in pathogenesis of neurodegenerative disorders such as Alzheimer’s disease and more recently amytrophic lateral sclerosis, as foundations for development of new therapies for AD and related neurodegenerative disorders as well as stroke. Using animal models and studying human brain, his laboratory has shown that dysfunction in the blood-brain barrier (BBB) and brain microcirculation can accumulate before neuronal dysfunction and contribute to the onset and progression of different neurological phenotypes and symptoms including cognitive impairment. His research team has identified the cellular and molecular mechanisms in cerebral blood vessels causing disruption of the neurovascular unit, which leads to neurodegeneration in models of Alzheimer’s disease, pericyte-deficient rodents and stroke. His group has also identified molecular mechanisms at the BBB that maintain clearance of Alzheimer’s toxin amyloid-beta from the brain into the circulation, and its influx or re-entry from the circulation into the brain, reflecting an important physiological function of the BBB in maintaining brain amyloid-beta homeostasis. Discoveries of his research team have contributed to the development of clinical trials for Alzheimer’s disease based on clearance of amyloid-beta, and stroke based on activated protein C treatment that is currently under clinical assessment in stroke patients as a neuroprotective agent.
Psychiatric Genetics
The Center for Genomic Psychiatry investigates the role genes play in disorders of the mind. **Dr. Marcelo Coba** uses a systems biology approach to study psychiatric disorders, combining state of the art proteomic assays to define protein complexes and post-translational modifications, together with mouse genetics, CRISPR technology, hiPSC derived neurons, computational biology, and synaptic physiology. These methods are used to integrate psychiatric candidate risk factors into spatio-temporal signaling networks and determine how mutations associated to psychiatric disease regulate common signaling mechanisms. This aim is to define network maps that will allow us to stratify patients by their correspondent pathway signatures. **Dr. Dan Campbell** focuses on defining functional genetic variants that contribute to the etiology and treatment effectiveness of autism and schizophrenia. The long-term goals of these studies are to better understand the causes of the disorders and to improve the ability to treat them on an individualized basis. His continuing work seeks to determine how genetic variants influence RGS4 expression in the brain and what other gene variants may also contribute to prediction of antipsychotic medication effectiveness in individual patients.

**Dr. Alex Bonnin** is working to understand how maternal-fetal interactions affect fetal brain development. The current focus is on the role of serotonin (5-HT) signaling in fetal programming or in other words, how serotonin signaling affects the mechanisms by which maternal and environmental factors shape the fetal brain and influence the development of adult diseases. These studies should ultimately provide new clues into the developmental origin of several mental health-related disorders in humans, such as autism and schizophrenia. These and other disorders of adult brain function have developmental components suggesting a crucial ontogenetic role of neurotransmitter systems. In particular the serotonergic modulation of axon guidance mechanisms is important for the refinement of neuronal circuits formation in utero, suggesting that serotonergic signaling is important for normal fetal brain wiring. We are pursuing a translational approach aiming at understanding and potentially reducing the effects of therapeutic drugs, in particular antidepressants, on fetal brain development.

Both **Drs. Carlos and Michele Pato** have several long-standing studies examining genetic factors behind schizophrenia and bipolar disorders, including a meta-analysis of schizophrenia on more than 25,000 patients and 28,000 controls, which to-date reveals 62 distinct genome-wide significant loci. The overall interest of **Dr. James Knowles**’s laboratory is the genetic basis of behavior, cognition and affect. Most of our studies search for the genetic factors that have an etiological role in psychiatric illness. To do so, we participate in both large genetic studies of the “complex” (non-Mendelian) genetic disorders and in studying several simple or Mendelian disorders. Finding genes for the psychiatric disorders is by necessity a collaborative effort. These are large-scale studies that require multiple sites to collect the sample sizes necessary to have adequate power. These studies also require teams of clinicians, geneticists and statisticians, working together, to make progress. Dr Knowles is the geneticist/molecular biologist on several such teams. His work with these investigators has focused on the anxiety disorders, depression and the addictive disorders. He published the first genome-wide scan for linkage to panic disorder, which ruled out the likely existence of a single major gene for the disorder and demonstrated the need for larger sample sizes in psychiatric genetics.
Genomics

**Dr. Kai Wang** is working on creating an automated bigdata pipeline for whole exome/genome sequencing analysis on Mendelian diseases and cancer, and for RNA-Seq analysis of single neuronal cells. His lab also investigates DNA methylation, gene expression and somatic mutations in the malignant transformation of meningiomas. A chief goal of the Wang lab is to develop data mining algorithms to extract more information from genomic data. He has developed several tools in wide use, including the PennCNV, GenGen and ANNOVAR software packages. **Dr. David Conti** is working to elucidate the genetic contribution of complex diseases from population-based samples, using both applied genetic epidemiologic studies and the development of statistical methods. Presently, Dr Conti’s applied work focuses on elucidating the genetic contribution of candidate genes within the dopamine and serotonin pathways and their role in smoking initiation, progression, and cessation. His research in statistical methodology concentrates on the use of hierarchical modeling and Bayes model averaging as a general framework for the analysis of multiple genetic polymorphisms in genes involved in numerous pathways impacting disease. **Dr. Gabriel Zada** utilizes next-generation genomic and epigenomic profiling (i.e. DNA Methylation analysis) to study the behavior of various brain tumors. In particular, he is interested in studying the process of local tumor invasion and developing molecular classification systems for various skull base tumors, including pituitary tumors and meningiomas. He is also working to develop novel treatment strategies for skull base tumors using intranasal therapy systems.

Vascular

**Dr. William Mack** is focused on translational efforts to treat stroke and cerebrovascular disease. He and his group are interested in inflammation and resultant microvascular failure in a range of experimental and clinical models. Dr Mack has refined an experimental model of bilateral carotid artery stenosis to examine the role of inflammation in the setting of chronic cerebral hypoperfusion. This system has enabled his team to assess the impact of vascular disease on cognition and neurodegeneration. The group has identified the C5 complement protein as a critical effecter of injury through histological and behavioral outcome measures. These findings lend insight into the role of complement in progressive cognitive injury and neurodegenerative conditions such as vascular dementia and Alzheimer’s disease. Dr Mack’s laboratory also studies biomarkers of cerebral vasospasm following subarachnoid hemorrhage and employs novel endovascular delivery platforms in the setting of acute stroke. He utilizes advanced MR permeability imaging sequences and serum analysis to quantify blood brain barrier breakdown in subarachnoid hemorrhage patients. Dr. Mack also currently leads a multicenter phase 2a safety and feasibility study of regional and distal intra-arterial Magnesium delivery during endovascular mechanical thrombectomy procedures for acute stroke. **Dr. Berislav Zlokovic** currently studies how genes that influence AD risk (e.g., APOE4, PSEN1, PICALM, CLU) affect the cerebrovascular system using transgenic models, human inducible pluripotent stem cell-derived neuronal and BBB in vitro models of human neurological disorders, and novel neuroimaging methods and molecular biomarkers in the living human and animal brain to evaluate how BBB function and cerebral blood flow changes influence brain connectivity and cognitive functions. He remains interested in developing advanced approaches with activated protein C therapy for stroke and neurological disorders.
Circuits
The aim of Dr. Robert Chow’s laboratory is to advance our understanding of how neuronal and hormone secretion (exocytosis) is controlled in normal and pathological states; part of the lab focuses on fundamental mechanisms (SNARE-mediated secretion), and the other on disease processes (diabetes, retinal and neuro-degeneration) or how to treat diseases (retinal degeneration). A recent interest of his laboratory pertains to cancer biology. When cancer cells become invasive, they express many neuronal-type proteins, including those involved in electrical signaling, secretion, and motility. Thus, Dr Chow has been studying how these genes are turned on, in an effort to develop approaches to recognize the potential of cancer cells to invade/metastasize, as well as to find ways to stop invasion. The Derek Sieburth studies synaptic signaling pathways that regulate synaptic function, with the goal of understanding how these pathways contribute to the function of neuronal circuits controlling behavioral programs in the nervous system. His laboratory uses C. elegans as a model organism for studying synaptic biology, because of its simple neuronal circuitry, the ability to visualize synapses by fluorescent imaging in live animals, and its powerful genetics. He combines state-of-the-art behavioral, genetic, cell biological, and in vivo neuronal imaging techniques in to study the cellular molecular mechanisms underlying secretion of synaptic vesicles and dense core vesicles.

Dr. Li Zhang’s ultimate research goal is to decipher brain circuits, and to understand how perception and behaviors are generated and controlled, how the brain’s cortex adapts in response to changes in the dynamic external environment, and how specific changes in cortical functions result in neurological and psychiatric disorders. To address these highly challenging questions, Dr Zhang’s approach is to resolve the neural circuitry (how neurons are wired in the brain), i.e. the structural basis underlying the brain functions. In the past years, Dr Zhang and his collaborators have committed substantial efforts toward developing molecular/genetic and electrophysiological/imaging techniques for elucidating the neural circuits for both local neuronal computation and for controlling animal behavior. To this end, he and his group pioneered in applying in vivo whole-cell voltage-clamp recording, to reveal at the synaptic connection level, how the excitatory and inhibitory synaptic interplay determines the sensory response/processing properties. Dr. Huizhong Tao’s work concentrates on how functional visual circuits are established during development (please see Vision/Eye below). The development of visual system not only depends on molecular and genetic programs, but also can be profoundly influenced by the pattern of neural activities along the visual pathways. Early synaptic connections in the developing brain can undergo substantial remodeling in response to patterned electrical activity of neurons. Dr Tao examines how neural activity of various patterns leads to modulations of synaptic connections and shapes the formation of visual circuits. Such studies will provide insights into how abnormal visual experience in early life, such as in the condition of strabismus and visual deprivation, can lead to abnormal wiring in the brain, and how we can correct it.
Vision/Eye

Photoreceptor cells are light sensitive neurons in the retina that initiate the first step in vision. One of the main objectives of Dr. Jeannie Chen’s laboratory is to understand how an intracellular signaling cascade is regulated within rod and cone photoreceptor cells, and how this contributes to the specialized ability of these cells to detect dim light and bright light, respectively, and how mutations within this signaling cascade leads to blindness. Drusen is an extracellular deposit commonly present in aging eyes and eyes affected with age related macular degeneration (AMD). Another goal of Dr Chen’s laboratory is to understand how protein misfolding may participate in the etiology of AMD. Dr. Greg Field is trying to understand how neurons function within circuits; current research in his lab is centered around identifying the functional connectivity between the photoreceptors (both rods and cones) and the approximately 20 distinct retinal ganglion cell types.

Dr. Huizhong Tao is interested in the architecture of visual cortical circuits. To dissect the circuits that consist of excitatory and inhibitory neurons, Dr. Tao’s lab applies in vivo electrophysiology, in particular two-photon imaging guided recording, to target different types of neurons in rodent visual cortex. From the response properties of individual neurons and the pattern of synaptic inputs to these neurons, they attempt to deduce the connectivity rules governing the construction of cortical circuits. The hope is that this work will lead to insights into how diverse visual processing functions are achieved by the cortical circuits. Dr. Tao is also interested in how functional visual circuits are established during development. The development of visual system not only depends on molecular and genetic programs, but also can be profoundly influenced by the pattern of neural activities along the visual pathways. Early synaptic connections in the developing brain can undergo substantial remodeling in response to patterned electrical activity of neurons. The Tao lab examines how neural activity of various patterns leads to modulations of synaptic connections and shapes the formation of visual circuits. The aim is to provide insights into how abnormal visual experience in early life, such as in the condition of strabismus and visual deprivation, can lead to abnormal wiring in the brain, and how we can correct it.
Hearing/Ear

The most common sensory abnormality in the world is age-related hearing loss. The second most common form of hearing loss is noise-induced. Dr. Rick Friedman’s laboratory has demonstrated that both of these traits can be treated as common diseases and can be approached through association mapping. The primary objective of Dr. Friedman’s laboratory is to study these common forms of hearing loss using a genome-wide association approach in mice. Dr. Friedman’s laboratory has begun to define the genetic architecture of age-related hearing loss in mice and has identified several loci leading to susceptibility to noise-induced hearing loss. This work will provide important insights into the mechanisms underlying these common forms of hearing loss and studies in the mouse provide the power to begin to understand gene X environment interactions.

Hearing loss is one of the most common birth defects. Approximately one in five hundred newborns suffer from significant hearing impairment. In addition, once mechanosensory hair cells in the inner ear are damaged and lost by any of a variety of reasons such as aging and loud noises, they never regenerate. Thus, majority of sensorineural hearing loss, such as age-related hearing loss and noise-induced hearing loss is permanent and significantly affect the quality of one’s life. Recently, stem cell research has shed light on the possibility of regeneration of hair cells in humans. The research goal of the Takahiro Ohyama lab is to understand the molecular mechanisms of inner ear development and to explore the possibility of regenerating sensory cells to treat hearing and balance disorders.

Humans can detect eardrum vibrations as small as a picometer as well as those that are nearly a million times larger. This extraordinary ability is made possible by the cochlea, an elegant hydromechanical structure that works to separate sounds of different frequencies and maps them onto a different place on the sensory epithelium (cochlea). This frequency-place map within the cochlea is refined by specialized sensory cells that provide feedback forces to actively amplify local mechanical resonances. This feedback mechanism gives rise to key features of mammalian hearing, including sharp frequency selectivity, sensitivity, large dynamic range, and nonlinearities, all of which have important consequences for encoding the subtleties of speech and music. Dr. Radha Kalluri is interested in understanding the biophysical mechanisms by which the auditory periphery parses frequency and intensity information, and how these functions degrade with hearing loss. Recent work is tackling how biophysical differences between subpopulations of bipolar afferent neurons in the auditory and vestibular systems influence their function and their susceptibility to damage.

Understanding nervous system function and dysfunction requires the combined expertise of outstanding scientists from a variety of disciplines. It is at the Zilkha Neurogenetic Institute where great minds come together, exploring new ways to enhance our understanding of how the brain works, so we may improve the outlook for future patient care.
In the following pages are some of the notable accomplishments by ZNI faculty over the past year.

**Alexandre Bonnin**

Research in the Bonnin lab focused on understanding how adverse events experienced during pregnancy can increase the risk of developing mental disorders in the offspring. Efforts were centered around two common types of adverse prenatal events, i.e. 1) maternal infection during pregnancy, and 2) maternal stress/depression as well as exposure to antidepressant drugs. The Bonnin lab demonstrated that maternal infection directly affects the functioning of an important molecular pathway in the placenta which then specifically alters the development of serotonin neurons in the fetal brain. This is expected to have long term consequences on offspring brain function, such as increased anxiety or depression. The Bonnin lab also characterized how maternal depression and the use of SSRI antidepressants during pregnancy directly affect fetal brain development. In addition, we started to characterize the role of a novel adaptor protein in fetal brain development. The results are under review for publication later this year.

**Daniel Campbell**

The rates of autism continue to rise, creating challenges for an increasing number of children and families. The Campbell lab contributed two important publications toward understanding and treating autism this year. First, we published a review in which we outlined the promise and challenges of targeting noncoding RNAs for autism treatment. Noncoding RNAs are genes that do not code for a protein but instead regulate the expression of other genes during brain development. The review allowed us to propose practical measures to describe how our work with noncoding RNAs can be translated to helping individuals with autism. Second, we published a paper showing the neuronal function of a gene that is frequently mutated in autism. Autism sequencing studies showed that a gene called chromodomain helicase DNA binding protein 8 (CHD8) plays a large role in autism risk. Spontaneous, damaging mutations were found three times more often in the CHD8 gene than in any other gene in individuals with autism. Using state-of-the-art RNA sequencing in human neural progenitor cells, we found that CHD8 regulates the expression of more than 1,000 genes. Concurrently, groups from Harvard and Yale published papers with similar findings about the impact of CHD8 mutations on gene expression. However, our work was distinct in identifying noncoding RNAs as primary targets of CHD8. Our ongoing work seeks to identify the role of CHD8 and its downstream noncoding RNA gene targets in gene-environment interactions that contribute to autism.
Karen Chang
The Chang laboratory discovered: 1) a protein upregulated in both Down syndrome and Alzheimer’s disease rescues APP-induced memory defects in young animals but enhances rate of memory loss during aging, suggesting its upregulation may play a role in progressive dementia in both diseases; 2) a novel ligand of integrin that regulates synaptic development and preserves the stem cell niche in Drosophila. They are continuing to investigate the biological functions of both of these proteins, mechanisms of their actions and contribution to neurological disorders.

Jeannie Chen
Excessive light exposure and genetic mutations that acts as “equivalent light” causes photoreceptor cell death and blindness in humans. Rhodopsin is a prototypical G-protein coupled receptor expressed by photoreceptor neurons, and light activation of rhodopsin is the first step in seeing. We found that excessive rhodopsin-driven signaling from the visual G-protein, transducin, induces endoplasmic reticulum stress and the Unfolded Protein Response (UPR), leading to cell death. Our results provide a mechanistic basis for certain form of light-induced blindness and further suggest that manipulation of UPR may prolong photoreceptor cell survival in transducin-induced retinal light damage.

Light activated rhodopsin is rapidly deactivated by addition of phosphate groups onto a cluster of serine and threonine residues on rhodopsin’s carboxyl-terminus, followed by arrestin binding. This rapid deactivation allows for temporal resolution of fleeting images captured by the retina. We found that phosphorylation of threonine sites promoted faster rhodopsin deactivation than serine sites. Our results suggest that coordination of phosphorylation at serine and threonine sites, with arrestin binding, may provide tight control of the duration of the G-protein couple receptor activity.
Robert Chow
We published a paper that identifies a role for a noncoding RNA in the development of cancer invasiveness. Interestingly, this noncoding RNA is derived from the primary transcript of REST protein, one of the major developmental regulators of the neuronal phenotype, supporting our hypothesis that when certain cancers become highly invasive, they are turning on genetic programs related to the development of neurons. The noncoding RNA or its associated pathway may serve as a biomarker of cancer invasiveness, as well as a potential therapeutic target. This work is supported by a provisional patent.

With Jim Weiland and Mark Humayun’s laboratory, we published a paper identifying a new electrical stimulation protocol that improves the visual acuity of patients with the Argus II epiretinal implants. The Argus II is the first FDA-approved epiretinal neuroprosthesis that is surgically implanted in the eye for the treatment of retinitis pigmentosa; it restores low-acuity vision to blind patients. What makes this work exciting is that experiments conducted in the Chow laboratory using an in vitro model of the retinal implant were used to identify the stimulation protocol, and these results were tested out and proved successful in patients who had the retinal implant. This opens the way for further testing and refinements of the epiretinal prosthesis.

With Ralf Langen’s laboratory, we have demonstrated that obesity and exposure to phthalate plasticisers – two major risk factors for type 2 diabetes mellitus – may share a common molecular mechanism leading to the acceleration of amyloid peptide misfolding. Accumulations of amyloid peptides have been implicated in the pathophysiology of a range of cellular degenerative diseases, including Alzheimer’s, Parkinson’s, and, in this case, type 2 diabetes.

Marcelo Coba
Recent technological advances in large-scale human genetics have begun to unveil the genetic architecture of psychiatric disorders such as schizophrenia (SCZ), autism and obsessive compulsive disorders. However, still remains a challenge to determine the signaling landscape where risk factors are integrated. Using in-vivo protein interaction assays, mass spectrometry, peptide arrays, bioinformatics, hiPSC derived neuronal progenitor cells, and mouse genetics, we determined the spatio-temporal profile of SCZ common and rare variants and analyzed their clustering in protein signaling complexes, determining 3360 in-vivo protein interactions. We also determined two major centers for the clustering of SCZ risk factors at embryonic brains and post-synaptic sites of excitatory neurons.

Using mouse genetics and mass spectrometry, we determined that protein associations relevant for SCZ, contained a discrete number of protein domains defining molecular functions that modulate the composition of macromolecular complexes. Mutations in psychiatric disease risk factors can alter the composition of these associations through protein domain interactions. These results were integrated into a software platform, Psychiatric Protein/Pathways Resource (PsyPPRes), which enables the prioritization of SCZ candidate risk factors and places them within their molecular context.
**Marcelo Coba** (continued)
Together with our collaborators we developed a new protocol, for the genome editing of hiPSCs using CRISPR-Cas technology, with increased efficiency and reducing off-target effect. This will allow us an increase in the throughput for the study of SCZ risk factors in hiPSC derived neurons. We continue working with the GO consortium and the Broad Institute in the GO-Synapse consortium, to define the molecular terms and composition of the synapse.

**David Conti**
Recently the Conti group has been focused on methodological advances in three main areas of research in genetic association studies: (1) fine-mapping, (2) integrated analysis, and (3) gene-environment interaction. Motivated by recent applied work in which we examined 67 prostate cancer risk regions in populations of European, African, Japanese and Latino ancestry, we have developed a new and scalable algorithm for the re-analysis of published marginal associations under joint multi-SNP models to better identify a small set of variants for further functional follow-up via laboratory experiments. To leverage the availability of various omics data, we have recently proposed an integrated analysis approach that models the causal relationships of the various data types, such as germline, omic and disease data, to estimate relevant clusters of individuals to better characterize the underlying disease mechanism. Finally, we have expanded our approach to better identify gene-environment interactions by using Bayes model averaging to: (1) balance the robustness of a case-control approach with the power of the case-only approach; (2) leverage marginal SNP effects; (3) allow for the incorporation of prior information; and (4) allow the data to determine the most appropriate model.

**Hong-Wei Dong**
The major direction of our research focuses primarily on the Mouse Connectome Project (MCP) (www.MouseConnectome.org), which aims to create a three-dimensional, Google Earth-like, digital Connectome atlas of the C57BL/6J mouse brain. We have constructed the first comprehensive and precise connectome of the entire cerebral hemisphere and thalamus. The first major milestone, Neural Networks of the Mouse Neocortex, was recently published (Zingg et al., 2014, Cell, 156, 1096-1111), which was selected as top 10 research articles in Cell: Best of 2014, and also listed on the full historical “40 years of Cell” timeline as one of only two landmark papers of 2014 (http://www.cell.com/40/timeline). In the last year, we have been continuously producing, collecting, and processing connectivity data from other parts of brain. We have generated the most comprehensive cortico-striatal projection map (manuscript is under consideration in Nature Neuroscience), and constructed neural networks of the entorhinal cortex, hippocampus, and amygdala. Furthermore, we have developed Connection Lens, a novel informatics algorithm for precisely and reliably processing and analyzing large-scale connectivity data. Finally, we have begun to apply our connectomic approach to systematically characterize “connectopathies” in animal models of neurological diseases, such as Huntington’s and autistic diseases. Overall, we have made tremendous progress in construction of the meso-scale connectome of the mouse brain.
Rick Friedman
The Friedman lab has completed the first GWAS in mice for hearing loss and noise induced susceptibility. They have identified Nox3 as a candidate gene and several new and novel loci. Also, they have begun the first GWAS for vestibular traits and identified Dcc as a novel gene affecting vestibular function. The Friedman lab has generated several transgenic lines and has begun validation of a novel gene for age-related hearing loss, Fhod3.

Radha Kalluri
In the Kalluri lab we study the biophysical processes underlying sensory signaling at the first synapse between the sensory cells of the inner ear and their partner neurons. During the past year we have developed an experimental approach that has allowed us to simultaneously characterizing the ion channel properties and connectivity patterns of developing auditory neurons during a time period preceding the onset of hearing. Our results suggest that some synaptic features that typically serve as markers for functional specificity develop independently from true sensory experience. Other work in the lab focused on defining the biophysical and neuroanatomical basis of sensory organization within the vestibular system. During the past year we’ve identified candidate ion channels whose differential expression within sub-groups of vestibular afferent neurons may serve as the substrate upon which vestibular information is parsed into parallel channels. Ongoing experiments in the laboratory are focused on testing this hypothesis. Finally, in collaboration with the Segil, Ohyama, and Ichida laboratories we have started characterizing the biophysical properties of reprogrammed spiral ganglion neurons using patch-clamp techniques.

James Knowles
The overall theme of the Knowles lab is the identification of genetic risk variants for the neuropsychiatric disorders. During the past year, significant progress has been made towards the discovery of risk genes for obsessive-compulsive disorder (OCD). The Knowles lab has been part of several collaborative international genome-wide association studies (GWAS) on OCD, but definitive findings still are lacking. Thus, our laboratory is conducting additional genotyping studies on some 2,000 new cases and collecting 1,000’s more OCD samples. These data will be contributed to the international effort, increasing the chances of defining susceptibility genes. We are also studying a mouse model of OCD (it lacks the gene encoding the transcription factor BTBD3) which has multiple compulsive behaviors. Over the last year we have begun to examine the structural variation of the brains of these animals and have found that compulsive animals have smaller hippocampi, as region of the brain involved in memory and learning.

We also research the more general question of what genes are expressed in regions, and even individual cells in the human brain throughout development. A related focus of the Knowles lab is to elucidate the DNA sequence variation in the genome that controls the expression of these genes in the brain. This effort, which is part of the PsychEncode Consortium, has made the observation that neuronal cell lines we have derived from individuals with schizophrenic appear the have the proper chromatin marks to control of the expression of a calcium channel gene previously identified through GWAS as a susceptibility gene for schizophrenia, whereas other cell lines lack these marks, making our cell lines a good model for the study of the disorder.
Ralf Langen
During the past year, the Langen lab has continued to investigate what makes proteins take up toxic shapes in protein misfolding diseases including Alzheimer, Parkinson, Huntington disease as well as type 2 diabetes. The focus has been on understanding the structural changes of proteins known to promote the aforementioned diseases with the goal of developing potential therapeutic molecules that can reverse misfolding. One such molecule is humanin, a mitochondrial peptide that can potently inhibit misfolding. The Langen group found that this peptide can protect from the misfolding that occurs in type 2 diabetes as well as other diseases. The Langen group also found that several misfolding protein proteins involved in diseases also have unique ways of disrupting cellular membranes in a manner toxic to cell. They were able to show that the peptides causing diabetes and Parkinson disease can permeabilize membranes by strongly inducing membrane curvature. Based on they data, they now suspect that this mechanism may be more widely applicable to many other neurodegenerative diseases. In addition, the Langen group has made more advances in determining the structures of toxic species present in neurodegenerative diseases.

Bill Mack
During the paThe Mack laboratory was awarded a grant to study the effects of air pollution from vehicular exhaust in the setting of acute stroke. New R01- NIH/NIEHS ONES (Outstanding New Environmental Scientist): The proposed research program seeks to determine the impact of particulate matter (PM) exposure on white matter injury and neurocognitive decline. These associations are further examined in the setting of underlying cerebrovascular disease (chronic cerebral hypoperfusion).

Takahiro Ohyama
The Ohyama Lab is investigating how the cochlea, the auditory organ, develops during embryonic development. They discovered BMP signaling pathway is important for cell fate decision between sensory and non-sensory structure of mammalian cochlea. The Ohyama lab is also analyzing the mechanisms how migrating neural crest cells are incorporated into the non-sensory structure of developing cochlea, which is crucial for proper hearing functions. These projects aim to understand disease mechanisms of hearing impairment and develop translational research such as regeneration of auditory cells.
Janos Peti-Peterdi
The Peti-Peterdi lab investigated the cellular and molecular mechanisms of glomerular kidney diseases and renal tissue repair, and identified several new potential therapeutic targets for future further development. The main focus of our studies last year was the role of a special chief cell type in the kidney called macula densa, and their role in endogenous nephron repair. Our laboratory deployed serial multiphoton microscopy to track the fate and function of individual cells in the same region of the living intact kidney over several days, during physiological adaptive responses, and in disease development. This approach has led to significant advances in understanding the highly dynamic kidney tissue and glomerular environment, and the mechanisms of glomerular injury and regeneration. Ongoing work in the laboratory is studying the fate and function of renal stem cells, and their role in endogenous kidney repair. Based on targeting specific molecular mechanisms within macula densa cells that control a newly discovered tissue repair process, the Peti-Peterdi lab is currently developing a new regenerative therapeutic approach for the treatment of chronic kidney disease. Another focus was the role of a pericyte-like cell type within the glomerulus called podocyte, in the development of glomerulosclerosis and chronic kidney disease. We identified purinergic calcium signaling mediated by the P2Y2 receptor, and the cell membrane calcium channel TRPC6 as the most significant mechanisms of podocyte cell-to-cell communication and propagation of podocyte injury. We are currently testing the effects of various pharmacological approaches that target these podocyte mechanisms, to investigate if they provide benefit in chronic kidney disease.
Derek Sieburth
The Sieburth lab is interested in how environmental cues impact behavior by influencing how neurons communicate with each other at specialized structures called synapses. We use the nematode as a model system for studying synapse structure and function because of its simple nervous system and the ability to visualize proteins in synapses in behaving animals. This year the lab discovered a new cellular signaling pathway that controls when neurons become activated during a rhythmic behavior. The lab also discovered that the cellular response to oxidative stress is regulated by neuroendocrine signaling from the nervous system.

Ansgar Siemer
The Siemer lab has made important progress on its main goal of characterizing the differences between amyloid fibrils that have positive functional roles and amyloid fibrils that are found in disease. We are working on the functional amyloid fibrils formed by Orb2, a protein that is important for long-term memory in fruit flies. Recently, we found a structural explanation for the importance of the N-terminal domain of this protein for its amyloid forming properties and consequently long-term memory. Using a combination of solid-state NMR and EPR spectroscopy, we were able to show that this N-terminal domain can form amyloid fibrils by itself without the glutamine-rich domain originally proposed to play that role. Comparing these data with data of huntingtin exon-1 responsible for Huntington’s Disease brought us a major step forward in differentiating functional from toxic amyloids. We found that fibrils formed by huntingtin exon-1 are very different from Orb2 since the poly-glutamine domain forms the amyloid fibril core and the N-terminal and especially the C-terminal domain are very dynamic and do not contribute to the amyloid core.
Huizhong (Whit) Tao

During FY15, Dr. Tao’s lab made three major discoveries. First, in layer 4 of the mouse primary visual cortex (V1) they revealed synaptic changes induced by monocular deprivation (MD), which is a popular experimental model for studying mechanisms and treatments for amblyopia. They found that in individual neurons of normal mice, inhibition and excitation driven by either eye are balanced, and thus suppressing PV interneurons does not alter ocular preference. MD disrupts the binocular balance of inhibition and excitation in individual neurons, therefore suppression of PV interneurons led to changes their ocular preference. Second, using optogenetics they showed that silencing corticotectal projections from layer 5 of V1 to superior colliculus (SC) significantly reduces an SC-dependent innate behavior (i.e., temporary suspension of locomotion upon a sudden flash of light as short as milliseconds). Interestingly, optogenetic activation of SC-projecting neurons in V1 or their axon terminals in SC sufficiently elicits the behavior, in contrast to other major L5 corticofugal projections. Thus, via the same corticofugal projection, V1 not only modulates the light-induced arrest behavior, but also can directly drive the behavior. Third, using optogenetics, they examined thalamic innervation patterns for excitatory and different types of inhibitory neurons across laminae in visual and auditory cortical slices. Their results reveal that thalamic information can be processed independently and differentially by different cortical layers, in addition to the generally thought hierarchical processing starting from layer 4. In addition, this parallel processing is shaped by feedforward inhibition from PV neurons in each individual lamina.

Terrence Town

My lab’s focus continues to be on developing a treatment for Alzheimer’s disease by targeting inflammation and the immune system. For the first time in 2015, we have shown that ‘re-balancing’ the immune system in pre-clinical Alzheimer’s rodent models halts learning and memory impairment and ameliorates pathological features of the human disease. This work was published earlier this year in two top journals- Neuron and Trends in Neurosciences. Furthermore, we had two additional high-profile papers in The Proceedings of the National Academy of Sciences on our work related to the role of the immune system in cancer. In addition, my lab has revolutionized the field of Alzheimer’s disease research by generating the first rat model of the disease that manifests all of the clinico-pathological hallmarks of the human syndrome. Specifically, we made transgenic rats that over-express two mutant human transgenes that are each independently causative of familial early-onset Alzheimer’s disease: “Swedish” mutant amyloid precursor protein and deltaE9 mutant presenilin-1. Unlike their transgenic mouse cousins that develop ‘senile’ plaques but fail to manifest ‘tangles’ and frank neuronal loss, these transgenic rats-for the first time-develop the full spectrum of Alzheimer pathologies. This makes them an invaluable tool for understanding Alzheimer’s disease etiology and for testing cutting-edge therapeutics, pre-clinically. Using this exciting new Alzheimer rat, we are actively pursuing collaborations with academics and with industry around the world to understand basic mechanisms of Alzheimer’s and to develop a cure for this devastating disease of the mind.
Tobias Ulmer
The Ulmer lab has associated the brain enzyme carnitine palmitoyltransferase 1C with spastic paraplegia in humans. Spastic paraplegia are a group of human neurological disorders with progressive spasticity and weakness of the lower limbs, which is likely a result of distal axonopathy in the corticospinal tract where axons reach lengths of >1 m. At present, the lab is aiming to elucidate the biochemical basis of carnitine palmitoyltransferase 1C action. In extending the understanding of cell-cell adhesion, the Ulmer lab has developed new techniques to study the thermodynamic basis of integrin receptor activation. As a first application of our technological advance, they examined the role of membrane lipid composition on receptor activation and found that negatively charged lipids act to stabilize the receptor in its inactive state. They have collected a large dataset to understand receptor activation for almost all human integrin receptors, which provides insight into the function of this critical and ubiquitous receptor family.

Kai Wang
The Wang lab has developed several computational tools for genome analysis, including (1) PennCNV3, a Hadoop-based system for rapid detection of structural variants from whole-genome sequence data. (2) SeqMule, a software system for automated human genome/exome analysis and disease gene identification.

Gabriel Zada
The Zada lab focuses translational research pertaining to genomics and targeted, precision molecular therapies for brain tumors. Our lab research focuses on a variety of brain tumors including pituitary adenoma, meningioma, glioma, cerebral metastases, chordoma, and craniopharyngioma, among others. Research in 2014-2015 has focused on performing genome-wide DNA methylation and gene expression analysis of surgically-resected pituitary adenomas and meningiomas. Based on this research and prior work, several promising candidate gene targets have been identified that are now being incorporated into tumor cell line models to test the effects of modulated gene expression on cell survival, invasion, and hormone production.
Li Zhang
The Zhang Lab continued their multiple-aspect investigation of the neural circuits at different auditory processing stages along the central auditory pathway. By integrating a series of cutting-edge techniques, they were able to reveal some new computational mechanisms exploited by the auditory circuits to process acoustic information. In particular, they have recently explored the neural circuitry underlying an auditory-motor behavior, and revealed that sensory cortex can directly drive innate defense behavior through corticofugal projections, a previously unrecognized neural pathway mediated by the inferior colliculus.

Berislav Zlokovic
We have developed an advanced dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) technique to evaluate subtle changes in the cerebrovascular integrity and blood-brain barrier (BBB) permeability in the living human brain that have not been possible to study before (Montagne et al., Neuron 2015). Using this new technique, we showed that BBB breakdown during normal aging begins in the hippocampus, brain’s center for memory and learning, and is worsened in patients with mild dementia, suggesting it may precede the onset of cognitive decline. We next showed that a deficiency in glucose transporter 1 (GLUT1) at the BBB that develops in Alzheimer’s disease (AD) patients accelerates neurodegeneration in a mouse model of AD contributing to BBB breakdown and neurodegenerative changes (Winkler et al., Nature Neuroscience 2015). We then discover a new role for PICALM, a frequently validated genetic risk factor for AD by showing that PICALM has a critical role in clearance of Alzheimer’s toxin amyloid-β across the BBB, and that non-protective allelic variants of PICALM lead to diminished PICALM expression in brain endothelium and faulty Aβ clearance, suggesting a vascular connection between PICALM and AD (Zhao et al., Nature Neuroscience, 2015).
Academic and Community Activities

**Dr. Alexandre Bonnin** taught in the USC Neuroscience Graduate Program as well as Pharmacology to 1st year USC medical students. Additionally, Dr. Bonnin was an invited speaker and session co-chair at national and international symposia (including those held in Paris, France and Milan, Italy). Dr. Bonnin is also a member of the USC Institutional Biosafety Committee.

**Dr. Daniel Campbell**'s contributions to the understanding of the role of noncoding RNAs in psychiatric disorders was recognized by invitations to give lectures at Harvard University, the University of Pittsburgh, the Biotech Connection Los Angeles Minisymposium, and Childrens Hospital Los Angeles. Dr. Campbell was also invited to participate in strategic planning meetings at the University of Missouri Thompson Center for Research on Autism and Neurodevelopmental Disorders and the Environmnet Defense Fund’s Elucidating Environmental Dimensions of Neurological Disorders and Disease.

**Dr. Jeannie Chen** served on the Scientific Advisory Board of the Karl Kirchgessner Foundation.

**Dr. Robert Chow** served as a mentor for the following programs: CIRM summer internship, CIRM Bridges internship, Bridging the Gaps: Bench to Bedside Summer Research Program, Engineering Research Center, and Engineering Health Academy.

**Dr. Hong Wei Dong** was invited to give several domestic and international talks: (1) CHDI’s 10th Annual HD Therapeutics Conference (Feb 23-26); (2) SPIE Photonic 2015 West Conference; (3) a Seminar at UCLA; (4) two other talks in China.

**Dr. Rick Friedman** volunteered for College Bound, a non-profit organization facilitating Shure High School students college preparation. He also served as a Healthy Hearing Physician volunteer for the Special Olympic World games.

**Dr. Ralf Langen** was one of the organizers for the upcoming Protein Society Meeting, a large international meeting for scientists working on proteins.

**Dr. Bill Mack** was elected to the Society of Neurointerventional Surgeons Board of Directors and was an Associate editor for Journal of Neurointerventional Surgery and on the editorial board of World Neurosurgery as the Book Review Section Editor. Dr. Mack was also awarded a 2014 Keck School of Medicine Outstanding Research Scholarly Project Mentor Award at Keck.
Dr. Janos Peti-Peterdi served as the director of the USC Multiphoton Microscopy Core. He also serves on the KSOM Faculty Research Council, and the Faculty Appointments, Promotion, and Tenure Committee. He is elected member of the European Academy of Sciences and Arts, and the American Society for Clinical Investigation. He was selected to receive the 2015 Young Investigator Award of the American Society of Nephrology.

Dr. Huizhong Tao served as the co-director of the Neuroscience Graduate Program core course.

Dr. Terrence Town lectured at National and International venues, including two prestigious lectures at top universities: University of Bonn (Germany), and Yale University.

Dr. Kai Wang reviewed grant applications for a number of agencies, including American Cancer Society - Institutional Research Grant (ACS-IRG) and Wellcome Trust. He also participated in the Program Committee for 2th International Conference on Algorithms for Computational Biology.

Academic and community-based activities that Dr. Gabriel Zada’s laboratory has been involved with include the USC Pituitary Symposium and Chordoma Foundation Community Conference, both hosted here at The USC Norris Comprehensive Cancer Center.

Dr. Li Zhang’s graduate student, Brian Zingg, was awarded NRSA predoctoral fellowship (F31).

Dr. Berislav Zlokovic presented the Chancellor’s Award Lecture in Neurosciences at the Louisiana State University Health Sciences Center in October 2014. He was included in the Thomson Reuters List, ‘The World’s Most Influential Scientific Minds’ 2014 for ranking among the top 1 percent of the most cited authors in the field of Neurosciences over the last 11 years (2002-2012). He was elected as a member of prestigious Dana Alliance for Brain Initiative (DABI) in 2014. Dr. Zlokovic was also elected in 2015 into the European Academy of Sciences – Life Sciences section.

Collaborations

**Alexandre Bonnin**
- Irina Burd of Johns Hopkins University; collaborating on fetal brain imaging studies following maternal exposure to stress and antidepressant drugs.
- Anne Andrews of UCLA; collaborating on fast microdialysis studies to measure offspring neurochemical activity following prenatal exposure to stress and antidepressant drugs.
- Gerard Karsenty of Columbia University, NY; collaborating on a study related to the role of a bone-derived molecule in fetal brain development.
- George Anderson of Yale University; collaborating on fetal, placental and maternal measures of biogenic amines.
- Robert Schwarcz of University of Maryland; collaborating on fetal, placental, and maternal measures of specific biogenic amines.
- Brett Lund of USC Neurology; investigating the effect of maternal infection on fetal cytokine levels.
- Skyla Herod of Azusa Pacific College; studying placental and fetal brain development in serotonin transporter knockout mouse model.

**Daniel Campbell**
- Wange Lu, USC Broad Institute; studying the impact of autism-related genetic variants on neuronal differentiation
- James Knowles of ZNI; studying gene expression changes caused by non-coding RNAs.
- Kai Wang of ZNI; studying gene expression changes caused by non-coding RNAs.
- Gerry Coetzee of USC Department of Urology; studying strategies for following up genome wide association study hits in autism.
- Heather Volk of Johns Hopkins University; investigating gene-environment interactions in autism.

- Kevin V. Morris of Scripps Research Institute; studying the molecular mechanisms of non-coding RNAs.
- Judy Van de Water of UC Davis; studying the genetic basis of altered immune sensitivities in autism
- Lisa Croen of Kaiser Permanente; studying the genetic basis of altered immune sensitivities in autism.
Karen Chang
- Tai Min of UNIST, Korea; investigating common molecular pathways altered in Down syndrome and Fragile X syndrome, two of the most common genetic causes of mental retardation.
- Dion Dickman of USC, Dept. of Neurobiology; studying the role of a novel synaptic kinase in regulating synaptic growth and function.
- Ralf Langen, Zilkha Neurogenetic Institute, USC; examining the effects of post-translational modification on membrane protein functions.

Jeannie Chen
- Alapakkam Sampath of UCLA; investigating the signal transfer from the photoreceptor sensory neurons to bipolar cells during retinal degeneration and during recovery from degeneration.
- Greg Field of Duke University; investigating how changes in retinal ganglion cell receptive fields during retinal degeneration and during recovery from degeneration.
- Amy Lee of USC, Department of Biochemistry and Molecular Biology; investigating the role of endoplasmic reticulum stress in certain genetic mutations leading to blindness.
- Ralf Langen of ZNI; investigating amyloid structures in eyes affected with macular degeneration and exploring therapeutic agents to dissolve these structures.
- M. Carter Cornwall of Boston University; collaborating on the molecular mechanisms that regulate recovery of light sensitivity following bright light exposure.
- King-Wai Yau of Johns Hopkins University School of Medicine; collaborating on the role of calcium-feedback to the olfactory sensory neurons in sensitivity adjustment during odorant adaptation.
- Vsevolod Gurevich of Vanderbilt University; studying function of visual arrestins in the physiology of the photoreceptor cell.
- Gordon Fain of UCLA; collaborating on mechanisms that regulate phototransduction in rod and cone photoreceptors.
- Vladimir Kefalov of Washington University; investigating proteins that regulate calcium concentration in rod and cone photoreceptors.

Robert Chow
- Sivaraj Sivaramakrishnan of University of Minnesota; development of a novel genetically encoded ratiometric calcium indicator
- Oleg Evgrafov of USC; development of a novel 3D culture of differentiated nasal neuroepithelial biopsy cells, in order to test hypothesis that such cells will form synapses, and if derived from schizophrenic patients the synapses will be abnormal.
- Cheng-Ming Chuong of USC; understanding the role of calcium channels in development of chick feather bud morphology.
- Justin Ichida of USC; understanding the gene changes associated with the pathology of SMA and ALS.
Robert Chow (continued)

- Ralf Langen of ZNI; investigating the potentiating effect of free fatty acids in potentiating amyloid peptide cytotoxicity, in the setting of obesity in type 2 diabetes and Alzheimer’s.
- Jeannie Chen of ZNI; Dr. Chen’s lab is using the Chow lab’s new genetically encoded ratiometric calcium indicator to study cytoplasmic calcium of photoreceptors in vivo and in vitro in mouse models of photoreceptor degeneration.
- James Knowles of ZNI; studying transcriptome variability among ostensibly identical and non-identical cells, in order to validate the newest generation of RNA-Seq platforms. We are also collaborating to identify miRNA candidates regulating the switching on of glucose-response genes in stem cells being differentiated to beta-like cells.
- Mark Humayun and James Weiland of USC, Department of Ophthalmology; are collaborating on two projects: 1) Improving performance of the Argus II retinal prosthesis, and 2) Development of a novel photovoltaic nanoswitch for remote optical control of neuron activity.
- Koping Kirk Shung of USC, Viterbi School of Engineering; collaborating on a project to distinguish highly invasive breast cancer cells from less invasive cancer cells, using high-frequency ultrasound stimulation of cytoplasmic calcium elevation.

Marcelo Coba

- Guoping Feng, Stanley Center for Psychiatric Research, Broad Institute, Boston; studying of SHANK3 mutations in psychiatric disorders, and their role in postsynaptic signaling.
- Justin Ichida, Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC; collaborating on hiPSC cells for the study of neurodevelopmental processes in psychiatric disease.
- James Knowles of ZNI; studying the role of synaptic signaling complexes in Obsessive compulsive disorder and Schizophrenia.
- Ted Abel of University of Pennsylvania; studying the role of Shank3 and AKAP signaling mechanisms associated to neurological disease.
- Marco Bortolato of Kansas University; collaborating on the role of NMDAR signaling in the pathophysiological processes underlying impulsive aggression and related neurodevelopmental disorders (autism-spectrum disorder, ADHD, Tourette syndrome).
- Thomas O’Dell of UCLA; collaborating on the role of TNiK and Dlgap1 signaling in synaptic plasticity, learning and memory.
- Chao Zhang of USC; investigating the chemical genomics approaches to the study of protein kinase signaling.
- Fengzhu Sun, Department of Computational Biology and Bioinformatics at USC; analyzing of protein domains and their role in synaptic signaling complexes associated to Schizophrenia.
- Pat Levitt of USC-CHLA; working to determine of the Autism Risk factor MET interactome and its role in the developing synapse
- Stephanie Dulawa of University of Chicago; studying the role of synaptic signaling complexes in Obsessive compulsive disorder
David Conti

- Sylvia Richardson and Paul Newcombe of MRC Biostatistics Unit, Cambridge, UK; developing of Bayesian model selection for functional integration in genetic association studies.
- Graham Casey, Fred Schumacher, Steve Gruber of USC, Department of Preventative Medicine; investigating the role of genetic variants in colon cancer risk using genetic association studies and functional assays.
- Chris Haiman, Fred Schumacher, and Brian Henderson of USC, Department of Preventative Medicine; investigating the role of genetic variants in prostate cancer.
- Marc Tischkowitz of University of Cambridge, Dept. of Medical Genetics, Jonine Bernstein of Dept. of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center; collaborating on WECARE Study (Women’s Environmental, Cancer, and Radiation Epidemiology) which examines genetic susceptibility and radiation exposure in breast cancer.
- Frank Gilliland and Jim Gauderman of USC, Department of Preventative Medicine; examining the role of genetic variation and pollution in asthma and lung function development in over 10,000 children followed for over 10 years in Los Angeles.
- James Knowles and Carlos Pato of ZNI; examining genetic sequence data to identify variants involved in schizophrenia.
- Wendy Cozen of USC, Department of Preventative Medicine; through genetic association studies, they are investigating the role genes play in multiple myeloma and Hodgkin’s lymphoma.
- Neal Benowitz of University of California San Francisco; Rachel Tyndale of University of Toronto; Caryn Lerman of University of Pennsylvania; and Gary Swan and Andrew Bergen of SRI International; as part of the Pharmacogenetics of Nicotine Addiction and Treatment, they are identifying genetic variants involved in smoking cessation and treatment response.
- Duncan Thomas of USC, Department of Preventative Medicine; developing new statistical approaches to the analysis of genes and environmental factors that interact via biological pathways.
- Paul Marjoram, Simon Tavare, Magnus Nordborg and Sergy Nuzhdin of USC, Department of Molecular and Computational Biology; as part of USC Center of Excellence in Genome Sciences, they are investigating how prior biologic knowledge can be used to influence statistical analysis.
- Kiros Berhane of USC, Department of Preventative Medicine; developing new statistical methods that incorporate both age and sex related changes in the dynamic relationship between weight, height and obesity as well as the complex multi-level relationships of determinants of obesity.
- Lilyana Amescua of USC, Department of Neurology; investigating the impact of genetics in Multiple Sclerosis using a Hispanic population sampled in Los Angeles and novel statistical methods.
- Danieli Salinas of USC, Department of Pediatrics; estimating clinical outcomes and classifying CFTR variants of unknown significance in children with a positive newborn screening for Cystic Fibrosis.
Hong-Wei Dong
- Jean Shih, Department of Pharmacology, USC. We collaborate on characterizing disruption of cortico-striatal pathways in the mouse models of Autism.
- X William Yang, Department of Neuropsychiatry, UCLA. We collaborate on characterizing connectopathies in the mouse models of Huntington’s disease.
- Peyman Golshani, Department of Neurology, UCLA. Collaborative project: Optogenetic treatment of social behavior in autism.

Rick Friedman
- Jake Lusis of UCLA; analyzing of transcriptome data and GWAS for hearing traits.
- Eleazar Eskin of UCLA; using of the Efficient Mixed Model Analysis of our GWAS data.
- Hooman Allayee of USC; analyzing GWAS for hearing and balance traits.
- Takahiro Ohyama of ZNI; developing of constructs for transgenics, knockouts, and organ culture for Fhod3 experiments.
- Justin Ichida and Neil Segil of Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research BCC at USC; looking at genetic phenotypes in culture.

Radha Kalluri
- Ruth Anne Eatock of University of Chicago; working on a computation model for defining information transfer in the vestibular sensory periphery.
- Neil Segil, Takahiro Ohyama, Justin Ichida of Departments of Otolaryngology and Broad at USC; studying the molecular basis of neuronal differentiation in directly differentiated neurons.
- Carolina Abdala of Department of Otolaryngology at USC; using otoacoustic emissions to non-invasively probe the status of mechanical transduction in hearing impaired humans.
- Christopher Shera of Harvard Medical School; collaborating on the mechanical basis of low-frequency hearing.
- Raymond Goldsworthy Department of Otolaryngology of USC; linking behavioral and physiological measures of frequency resolution in humans.

James Knowles
- The Knowles lab is highly collaborative. Projects range from investigations of animal models of human anxiety disorders to large scale international efforts to identify genetic risk factors for complex neuropsychiatric disorders (e.g., schizophrenia, bipolar disorder, depression, autism, and obsessive-compulsive disorder) to smaller studies of genetic predisposition to congenital disorders (e.g., congenital heart disease; non-syndromic hearing loss) to projects that build computer workflow pipelines to handle petabytes of genetic data. The following are either ongoing collaborations or newly established alliances that were formed to further these research projects.
• Carlos and Michele Pato, Oleg Evgrov, Robert Chow, Derek Sieburth, Kai Wang, Li Zhang, Marcelo Coba, David Conti, Dan Campbell, Chris Haiman, William Mack of ZNI. ONGOING. Various projects with ZNI investigators on studies of genetic expression and genetic variation in health and disease (e.g., autism, schizophrenia)
• Ting Chen, Ewa Deelman, Jonathan Buckley, Graham Casey, Colin Dias, Mike Kahn, Carl Kesselman, Helena Mederios, Jerold Shinbane, Justin Ichida, Arthur Toga, Paul Thompson, Yonggang Shi, Gerry Coetze, Peggy Farnham and Brad Peterson of USC; collaborating on various projects including the identification of susceptibility genes for complex diseases. ONGOING
• Dan Stein of University of Capetown, Gerry Nestadt and Jack Samuels of Johns Hopkins University, Abby Fyer of Columbia University, Ben Greenberg and Steve Rasmussen of Brown University, James McCracken and John Piacentini of UCLA, David Pauls, Scott Rauch and Dan Geller of Harvard University, Dennis Murphy and Yin Shugart of NIH, Carol Matthews of UCSF, and Stephanie Dulawa of University of Chicago, Russel Jacobs of CalTech; studying Obsessive compulsive disorder (OCD). ONGOING
• Mohammad Ayub of Queens University, Kingston, ONT; Jim Fallon, Fabio Macciardi and Biff Bunney of UC Irvine; Barbara Lipska of the NIMH Intermural Program; working on Early-onset major depression. ONGOING
• Steven McCarroll of Harvard University/Broad Institute, Mike Boehnke and Goncalo Abecasis of the University of Michigan; Ayman Fanous of the Veterans Administration, Washington DC; Mohammad Ayub of Queens University, Kingston, ONT; studying Schizophrenia. ONGOING
• Ned Kalin, Pat Rosebloom, Jonathan Oler, and Drew Fox of the University of Wisconsin, Madison; genetic studies of anxiety in primates. ONGOING.
Ralf Langen
- Harvey McMahon of Laboratory of Molecular Biology in Cambridge; investigating mechanisms of membrane curvature induction by proteins.
- Alasdair Steven of the NIH; using a cryo electron microscopy to look at mechanisms of membrane curvature and protein misfolding in neurodegenerative diseases.
- Tobias Ulmer of ZNI; combining NMR and EPR-based approaches to determine structures of amyloidogenic proteins involved in neurodegeneration.
- Ansgar Siemer of ZNI; combining solid state and NMR and EPR-based approaches to determine structures of amyloidogenic proteins involved in neurodegeneration.
- Martin Kast of USC, Department of Molecular Microbiology & Immunology; investigating membrane-bound annexin A2 complexes as receptors for HPV entry.
- Ian Hawaorth of USC, Department of Pharmacy; combining EPR and computational methods for determining protein structures.
- Jonah Chan of UC San Francisco; studying control of membrane curvature during myelin formation and its role in multiple sclerosis.
- Oliver Daumke of University of Berlin; investigating control of membrane curvature by EHD-2.
- Songi Han of UC Santa Barbara; using novel EPR and NMR-based methods to monitor water exposure and its application to protein misfolding and membrane interaction.
- Julio Camarero of USC, Department of Pharmacy; engineering cyclotides in order to make them misfolding inhibitors that could be used as drugs against Alzheimer’s disease, Parkinson’s disease and type-2 diabetes.

Bill Mack
- Caleb Finch of USC Gerontology and Constantinos Sioutas of USC Environmental Engineering; collaborating on studies of the effects of particulate matter exposure from vehicular exhaust on the progression of stroke and cerebral hypoperfusion.
- Kai Wang of ZNI; collaborating on studies characterizing genetic and epigenetic signatures of Meningiomas.
- James Knowles of ZNI; working on a large study designed to evaluate cellular heterogeneity of temporal and cerebellar cells using patchclamp and RNA-Seq of single cells.
- Robert Chow of ZNI; collaborating on a large study designed to evaluate cellular heterogeneity of temporal and cerebellar cells using patchclamp and RNA-Seq of single cells.

Takahiro Ohyama
- Neil Segil and Justin Ichida of Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC; researching factors that directly transform somatic cells into auditory sensory cells.
- Pinchas Cohen of USC Davis School of Gerontology; testing protective effects of mitochondria-derived peptides on drug-induced hair cell damage.
- Rick Friedman of ZNI; testing molecular functions of genes identified through genetic screening of mouse hearing disease model.
Janos Peti- Peterdi
- Michael Caplan of Yale University and Jennifer Pluznick of Johns Hopkins; collaborating on the role of olfactory receptors in the kidney.
- Andrew McMahon of USC; analysis of the macula densa cell molecular fingerprint.
- Genevieve Nguyen of College de France, Paris; studying the role of the prorenin receptor in macula densa cells.
- Dominique Eladari and Regine Cambrey of INSERM, France; working novel electrolyte transport mechanisms in the distal nephron.
- Paola Romagnani of University of Florence; studying Intrarenal stem cells.
- Andrew Salmon of University of Bristol; studying the role of the glomerular glycocalyx.
- Thomas Benzing of University of Cologne; researching calcium imaging of podocytes in vivo.
- Akira Nishiyama of Kagawa University; studying glomerular filtration of renin and prorenin.
- Peter Deen of University of Nijmegen; investigating the role of GPR91 in distal nephron ion transport.
- Attila Szabo and Agnes Prokai of Semmelweis; studying multiphoton imaging of the effects of calcineurin inhibitors in the kidney.
- Laura Perin of Children's Hospital Los Angeles; studying the role of amniotic fluid-derived stem cells in kidney repair.
- Valter Longo of USC; studying the mechanism of liver regeneration.
- Alicia McDonough of USC, Dept. of Neurobiology and Romer Gonzalez-Villalobos of Cedars Sinai Medical Center; studying the role of the intra-renal rennin-angiotenisn system.
- Rudy Ortiz of UC Merced; studying the role of mitochondrial factors in cell and tissue metabolism.
- Stuart Shankland of University of Washington, Seattle; studying the mechanisms of glomerular dysfunction and repair.
- Katalin Susztak of University of Pennsylvania; studying podocyte function in health and disease.
- Giuseppe Remuzzi of University of Bergamo; collaborating on a clinical study of a new therapeutic approach to kidney regeneration.
- Jochen Reiser (Rush University) and Sanja Sever (Harvard University); studying the effects of suPAR on the glomerular filter.
- Inderbir Gill (USC KSOM Urology); human translational studies on the macula densa renal tissue repair mechanism.
- Chaim Jacob (USC KSOM); studying the role of glomerular immune cells in lupus nephritis.

Derek Sieburth
- James Knowles of ZNI; sequencing entire genomes of the nematode C. elegans to identify mutations that cause defects in synaptic transmission and profiling changes in gene expression patterns in the nematode C. elegans in response to oxidative stress.
- Robert Chow of ZNI; examining how calcium regulates the release of neurotransmitters in real time from living tissue (using Total Internal Reflection Fluorescence Microscopy).
Ansgar Siemer
- Ralf Langen of ZNI; studying the structure and dynamic of toxic huntingtin fibril
- Kausik Si of Stowers Institute for Medical Research; studying the structure of the functional amyloid Orb2 responsible for long-term memory
- Dr. Siemer continued to serve on USC’s PIBBS (Programs in Biomedical and Biological Sciences) admission committee. He is teaching graduate level Molecular Biology and Protein Chemistry cases and co-coordinating the graduate level Protein Chemistry course.

Huizhong Tao
- Christiaan Levelt of Netherlands Institute for Neuroscience, Royal Academy of Arts and Sciences, Amsterdam, Netherlands; studying how monocular deprived induces disruption of the balance between excitatory and inhibitory inputs.
- Jonah Chan of University of California at San Francisco; studying how retinal activity through vision changes the maturation status of myelin wrapping on optic nerve fibers.
- Josh Z. Huang of Cold Spring Harbor; researching on the functional properties of cortical inhibitory neurons.
- Li Zhang of Zilkha Neurogenetic Institute; studying common inhibitory mechanisms underlying visual and auditory cortical processing.

Terrence Town
- John Breitner, MD, MPH and Judes Poirier, PhD (McGill University, Canada) We are working as a group to determine safety and efficacy of non-steroidal anti-inflammatory drugs for the prevention of Alzheimer’s disease.
- Tarek Fahmy, PhD (Yale University Department of Biomaterials) Collaboration to evaluate a next-generation nanoparticle drug delivery system for prevention and treatment of Alzheimer’s disease and pediatric brain cancer.
- Li-Huei Tsai, PhD (Harvard University HHMI Investigator) Collaboration to investigate aberrant cyclin-dependent kinase activation in our novel transgenic Alzheimer rat model.
- Erol Fikrig, MD (Yale University HHMI Investigator) Collaboration to interrogate neuro-immune mechanisms of West Nile encephalitis
Terrence Town (continued)

- Richard A. Flavell, PhD (Yale University HHMI Investigator and National Academy member), Collaboration on developing mouse models with human immune systems as a critical tool to examine stem cell graft tolerance vs. rejection.
- Pasko Rakic, MD (Yale University National Academy member and winner of the ‘new Nobel’ Kavli Prize in Neuroscience), whose wide-reaching expertise in neurobiology has been invaluable for understanding cellular biological aspects of our rodent models of neurodegenerative disease.
- Eliezer Masliah, MD (UCSD; ranked as one of the top 10 AD researchers) Collaboration on developing and characterizing rodent models of Alzheimer’s disease.
- Caleb ‘Tuck’ Finch, PhD (University of Southern California) has made major contributions to our understanding of aging biology and we are working together to understand the role of pollution on brain inflammation and Alzheimer’s disease pathology in pre-clinical animal models.
- Helena Choi, MD (University of Southern California) is an internationally recognized neuropathologist who plays a key role in the USC ADRC, and we are validating observations that my group has made in mouse models using human Alzheimer patient samples.
- Betza Zlokovic, PhD (Director, ZNI, University of Southern California) has made fundamental contributions to our understanding of pericyte biology in the central nervous system and in Alzheimer’s disease. We are actively collaborating to extend his findings with the blood-brain-barrier into our novel Alzheimer transgenic rat model.

Tobias Ulmer

- Mark Ginsberg of UC San Diego; collaborating on the integrin receptor cell biology
- Raymond Stevens of USC; collaborating on G protein-coupled receptor structure
- Woojin An of USC; collaborating on histone protein structure and interactions
- Ralf Langen of ZNI; collaborating on the role of huntingtin in Huntington’s disease

Kai Wang

- Gary Chen of USC Department of Preventive Medicine; working to develop a copy number variation calling algorithm called PennCNV3 for whole-genome sequencing data.
- James Knowles of ZNI; evaluating biological and technical noises of single-neuron RNA-Seq data and benchmarking different bioinformatics algorithms on these data.
- Peter Robinson of Charité - Universitätsmedizin Berlin; developing variant annotation and prioritization software tools that incorporate phenotype information and model organism information.
- Yufeng Shenof Columbia University; investigating the genetic similarity between cancer and neurodevelopmental diseases, and developing methods to use somatic mutation information to predict causal de novo mutations in neurodevelopmental diseases.
**Gabriel Zada**
- Collaborations in 2015 include leading a nationwide collaborative group called the Pituitary Adenoma Genomic and Epigenetic (PAGE) consortium and applying for national support for a consortium-based, multi-institutional study focusing on these tumors. In addition, we have launched a collaborative research study with Dr. Joshua Neman at USC focusing on meningioma research. Additional collaborations at USC have been established with the Farnham laboratory.

**Li Zhang**
- Hongwei Dong and Jean Shih; studying corticostriatal projection and movement control
- Huizhong Whit Tao of ZNI; investigating imaging processing in the visual cortex.
- Berislav V. Zlokovic of ZNI; investigating the impact of brain vascular defects on the functional cortical circuitry

**Berislav Zlokovic**
- Arthur Toga of USC, Institute of Neuroimaging and Informatics; Paul Thompson, USC, Depts. of Neurology, Psychiatry & Behavioral Sciences and Engineering; Scott Fraser of USC, Depts. of Biological Sciences and Biomedical Engineering; Helena Chui of USC, Dept. of Neurology and USC Alzheimer’s Research Disease Center; Lon C. Schneider of USC Alzheimer’s Research Disease Center and Clinical Center and the Pharmacology program of USC NIH Alzheimer’s Disease Research Center; Terrence Town of ZNI; Hong-Wei Dong of ZNI; Roberta Brinton of USC, Depts. of Pharmacology & Pharmaceutical Science, Biomedical Engineering, and Neurology; and Russell Jacobs of Beckman Institute at Caltech; working on the USC Collaborative Initiative in Alzheimer’s Disease.
- David M. Holtzman of Washington University in St. Louis; working on amyloid-beta metabolism and clearance in brain via LDLR receptors and role of apoE in amyloid-beta clearance.
- John Griffin of Scripps Institute; working on new APC variants for stroke.
- William Mack of ZNI; collaborating on hypoperfusion injury to white matter.
- Meng Law of USC, Dept. of Neuroradiology and Helena Chui of USC, Dept. of Neurology; working on MRI imaging of blood-brain barrier permeability in neurologically normal and MS patients and patients at risk for Alzheimer’s disease.
- Collins Liu of USC, Dept. of Neurology and Helena Chui of USC, Dept. of Neurology; studying cerebrospinal fluid and plasma biomarkers of the blood-brain barrier damage in individuals at risk for Alzheimer’s disease.
- Scott Fraser of USC, Depts. of Biological Sciences and Biomedical Engineering and Andy McMahon of USC, Broad CIRM Center; working on serial two-photon tomography, cutting-edge technique that allows for fully automated brain imaging.
Berislav Zlokovic (continued)

- Scott Fraser of USC, Depts. of Biological Sciences and Biomedical Engineering and Russell Jacobs of Beckman Institute at Caltech; collaborating on imaging white matter damage in small rodents due to pericyte loss using high field MRI and blood-brain barrier permeability longitudinal studies in mouse models of stroke.
- Li Zhang of ZNI; collaborating on pericyte degeneration and cortical information processing.
- Justin Ichida of USC, Broad CIRM Center; working on iPSC and fibroblasts from Alzheimer’s patients conversion into neurons and in vitro trials with 3K3A-APC in human ALS models as well as on brain organoids.
- Washington University Alzheimer’s Disease Research Center; collaborating on CSF biomarkers of blood-brain barrier damage in individuals at risk for Alzheimer’s as well as individuals with mild cognitive impairment and Alzheimer’s with apoE4 allele vs. non-apoE4, as well as on postmortem brain tissue analysis and effects of apoE4 on blood-brain barrier integrity.
- Nunzio Pomara and Blas Frangione of New York Medical Center; examining CSF biomarkers of blood-brain barrier injury in cognitively normal individuals at risk for Alzheimer’s.
- Antonio Damasio of USC, Brain Creativity Institute; studying the molecular basis of feelings.
- Terrence Town of ZNI; studying pericytes in the rat model of Alzheimer’s disease.
- Pat Lyden of Cedars Sinai; working on Phase 2 clinical trial for stroke with 3K2A-APC.
- Caleb Finch of USC; examining the blood-brain barrier permeability in 5FAD mice on different apoE genotype.
- Jae Jung of USC; working on brain-specific TRlpartite Motif protein 9
- Michael Harrington of Huntington Hospital and USC; collaborating on imaging blood-brain barrier integrity in apoE4 individuals and CSF biomarkers.
- Daniel Nation of USC; working on CSF and imaging biomarkers in individuals at high risk for hypertension.
- John Morris of Washington University in St. Louis; collaborating on imaging and CSF biomarkers and apoE genotype.
- Anne Fagan of Washington University in St. Louis; collaborating on CSF biomarkers and apoE genotype.
- Tammie Benzinger of Washington University in St. Louis; working on imaging vascular biomarkers in mild cognitive impairment.
- John McArdle of USC; working on longitudinal data and dynamic analysis methods, statistical analysis.
- Judy Pa of USC; working on structural and functional connectivity, neuroimaging, AD and MCI.
- John Ringman of USC; collaborating on AD, PSEN1, ADAD, imaging and biomarkers.
- Eric Reiman of Banner Alzheimer’s Institute, AZ; collaborating on neuroimaging, genomics, biomarkers, APOE, PSEN1.
- Richard Caselli of Mayo Clinic, AZ; collaborating on neuroimaging, genomics and biomarkers.
- Francisco Lopera of University of Antioquia, Columbia; collaborating on neuroimaging, PSEN1 and biomarkers.
One of the most common ways for scientists to formally share their research is to publish an article in a scientific journal focused on a particular area of study. A typical scholarly, scientific journal article is peer-reviewed, discusses the authors’ original research, offers thoughtful analysis of the results, and cites relevant papers from other authors that relate to the research. Scientists (and editors of these publications) rely on their colleagues, the reviewers, to ensure a critical review of the science is conducted, with all aspects of the approach and techniques used, conclusions reached are empirically sound. This process, which takes place as discoveries are made, takes many months of back-and-forth responses between authors and editors and in rare cases, can exceed a year’s time.

A journal’s impact factor is a measure of the frequency with which the average article in a journal has been cited in a particular year. The impact factor is calculated by dividing the number of citations in the current year to articles published in the two previous years by the total number of articles published in the two previous years. While the expectation is that all peer-reviewed publications move science forward, in some areas of study coverage is not as widespread and thus the impact factor of a journal in a highly specialized field will not necessarily have the same impact factor as the broader journals like Science and Nature. How many papers an institution has in high-impact journals is just one of several measures of productivity.

Last year, ZNI faculty published 139 papers, and 14% of these were in high impact journals. Congratulations to all the ZNI scientists who had their work published in FY15.


Industrious members of any laboratory, postdoctoral trainees continue their training and education by conducting their own experiment under the guidance of an established faculty member. Working on multiple projects provides key support for the faculty member while establishing the postdoctoral research scientist’s interests. Listed below are ZNI’s postdoctoral trainees, (their mentors), and the titles of their research projects.

**Yen Chan** (Alexandre Bonnin): “Maternal stress and antidepressants effects on fetal brain development”

**Patrick Hecht** (Daniel Campbell): “Identification and Functional Characterization of Non-Coding RNAs in Autism Spectrum Disorder”

**Inmaculada Ballesteros Yanez** (Daniel Campbell): “Non-Coding RNAs in the Transcriptional Landscape of Human Neural Progenitor Cell Differentiation”

**Tian Wang** (Jeannie Chen): “Phototransduction in Dark Adaptation and Retinal Degeneration”

**Reymundo Dominguez** (Robert Chow): “Single-cell analysis”

**Ming-Yi Sonya Lin** (Robert Chow): “Single-Cell Analysis” and “Photovoltaic Nanoswitches for Remote Optical Control of Neurons”

**Andrew Weitz** (Robert Chow): “Imaging Platform for Determining Tumor Invasiveness”

**Lan Yue** (Robert Chow): “Photovoltaic Nanoswitches for Remote Optical Control of Neurons”

**Houri Hintiryan** (Hong Wei Dong): (1) Identify Neuroendocrine genes that are vulnerable to chronic psychological stress; (2) the Mouse Connectome Project.

**Michael Bienkowski** (Hong Wei Dong): “The Mouse Connectome Project”

**Pezhman Salehi Dermanaki** (Rick Friedman): “Novel genes involved in age-related and noise-induced hearing loss in mice”

**Mario Isas** (Ralf Langen): “Structural Studies of huntingtin misfolding”
Toru Miwa (Takehiro Ohyama): “Molecular analysis of developmental mechanisms of developing mouse inner ear”

Anne Riquier-Brison (Janos Peti-Peterdi): “The role of macula densa cells in chronic kidney disease”

Kengo Kidokoro (Janos Peti-Peterdi): “Tracking podocyte fate in nephrotic syndrome”

Ina Schiessl (Janos Peti-Peterdi): “Intravital imaging of cell death dynamics in the kidney”

Ju-Young Moon (Janos Peti-Peterdi): “Novel tissue remodeling mechanism in the diabetic kidney”

Toshiki Doi (Janos Peti-Peterdi): “Macula densa-mediated tissue remodeling in renovascular hypertension”

Sungjin Kim (Derek Sieburth): “Regulation of synaptic function by stress signaling”

Mingxi Hu (Derek Sieburth): “Control of rhythmic behaviors by neuropeptide signaling”

Marie-Victoire Guillot-Sestier (Terrence Town): “The Anti-Inflammatory Cytokine Interleukin-10 in Innate Immune Response to Amyloidogenesis in Alzheimer’s Disease”

Tara M. Weitz (Terrence Town): “Pharmacological Blockade of TGF-β Signaling in Peripheral Macrophages in the TgF344-AD Rat Model of Alzheimer’s Disease”

Kevin Doty (Terrence Town): Modulating Microglial Activation in Alzheimer’s Disease by Deleting Innate Immune STAT3 Signaling”

JiHong Kim (Kai Wang): “Comparative Analysis of Multiple RNA-Seq Quantification Tools for single-cell RNA-Seq data”

Gil Carvalho (Berislav Zlokovic): “Cellular Basis of Feelings and Sentience”

Kassandra Kisler Elliott (Berislav Zlokovic): “Pericyte Regulation of Neurovascular Coupling and Local Brain Oxygen Supply”

Axel Montagne (Berislav Zlokovic): “Quantitative Dynamic Contrast-Enhanced Magnetic Resonance Imaging to Evaluate Blood-Brain Barrier Integrity in Alzheimer’s Disease and Related Disorders”

Amy Nelson (Berislav Zlokovic): “The Role of Pericytes in Hippocampal Function”
The robust graduate student population at ZNI comes from a variety of USC programs and departments: Neuroscience, Preventive Medicine, Biostatistics and Physiology & Biophysics, and PIBBS (Programs in Biomedical and Biological Sciences), which includes degrees in Cancer Biology & Genomics; Development, Stem Cells & Regenerative Medicine; Medical Biology; and Molecular Structure & Signaling). Each graduate student works with a ZNI faculty mentor for up to 5 years. Below is a current list of students at ZNI, (their mentors), and their projects.

**Nick Goeden** (Alexandre Bonnin): “Placental Tryptophan Metabolic Dysfunction: A Potential Pathway for the Developmental Programming of Mental Disorders”

**Juan Velasquez** (Alexandre Bonnin): “Effects of Maternal Depression and Antidepressant Treatments on Fetal Neurodevelopment”

**Jennifer King** (Alexandre Bonnin): “Investigation of the role of a new adaptor protein in fetal brain development”

**Jessica DeWitt** (Daniel Campbell): “Neurobiological Impact of Non-Coding RNAs with Genome-wide Significant Association with Autism”

**Jillian Shaw** (Karen Chang): “A Role for Nebula/DSCR1 in Ameliorating Axonal Transport Defects Associated with Alzheimer’s Disease”

**Joo Yeun Lee** (Karen Chang): “A Novel DnaJ Domain Protein Regulates Synaptic Development and Maintains Stem Cell Niche in Drosophila”

**Liping Wang** (Karen Chang): “Regulation of synaptic vesicle endocytosis by the minibrain kinase”

**Jung Hwa Cho** (Robert Chow): “Calcium Sensitivity of Large-dense Core Vesicle Exocytosis in Complexin 2 Knock-out Mouse Chromaffin Cells”

**Jason Lou** (Robert Chow): “Improving performance of Argus II retinal prosthesis”

**Steven Walston** (Robert Chow): “Improving performance of Argus II retinal prosthesis”
Madison Zitting (Robert Chow): “Calcium Sensitivity of Large-dense Core Vesicle Exocytosis in Complexin 2 Knock-out Mouse Chromaffin Cells”

Ting Fu (Robert Chow): “Targeted photovoltaic nanoswitch delivery peptide”

Brent Wilkinson (Marcelo Coba): “Synaptic Signaling Networks”

Zhao Yang (David Conti): “Integrated analysis of germline, omic and disease data”

Lilit Chemenyan (David Conti): “Bayesian model selection for functional integration in genetic association studies”

Kan Wang (David Conti): “Multiethnic fine-mapping in genetic association studies”

Nicholas Foster (Hong Wei Dong): “Mouse brain connectome mapping of cortical and striatal long-distance axon projection deficits in Huntington’s Disease mouse models”

Marshall Ge (Rick Friedman): “Nox3 and noise induced hearing loss”

Christopher Ventura (Radha Kalluri): “The role of hyperpolarization-activated inward currents in shaping neuronal function in the vestibular nerve”

Alex Markowitz (Radha Kalluri): “Ion channel properties of spiral ganglion neurons during development”

Photo Caption: A photo of Hong Wei Dong lab members
Emily Chen (James Knowles): “Investigating Major Depressive Disorder by Next-Generation Sequencing and Differential Gene Expression in Brains of Suicide Completers”

JaeMun (Hugo) Kim (James Knowles): “Single Cell RNA Sequencing”

Edder Lopez (James Knowles): “Differentiation of Neural Progenitors in 2D and 3D Cultures”

Chris Armouskus (James Knowles and Kai Wang): “Statistical Analysis of Genetic Variation Predisposing to Schizophrenia” / “Comprehensive Detection of Expression QTLs in CNON cells”

Mark Ambroso (Ralf Langen): “Curvature Driven Myelination by Myelin Basic Protein”

Alan Okada (Ralf Langen): “Understanding and Preventing Misfolding in Neurodegeneration and Diabetes”

Natalie Kegulian (Ralf Langen): “Identifying toxic conformations in huntingtin”

Urvi Shroff (Janos Peti-Peterdi): “Development of a macula densa cell line”

Jackey Qi (Derek Sieburth): “Regulation of oxidative stress response by neuroendocrine signaling”

Ukjin Choi (Derek Sieburth): “An Innexin family member negatively regulates neuronal excitability”

Silvia Cervantes (Ansgar Siemer): “Structural characterization of Orb2A by EPR

Sandy Falk (Ansgar Siemer): “Interaction of Orb2 isoforms A and B”

Maria Conrad (Ansgar Siemer): “Oligomer formation and membrane interaction of Orb2A”

Brain Zingg (Huizhong Tao): “Using Optogenetics to Dissect a Circuit for Innate defense Behavior”

Xiaolin Chou (Huizhong Tao): “Fear Conditioning Induced Cortical Synaptic Plasticity”

Leena Ibrahim Marosh (Huizhong Tao): “Cross-Modality Sharpening of Visual Cortical Processing through a Top-Down Circuit”

Lingyun Li (Huizhong Tao): “How Inhibitory Circuits Mediate Lateral Refinement of Auditory Cortical Processing”
**Brian P. Leung** (Terrence Town): “C1q Signals through TREM2 to Control Aβ Phagocytosis in Alzheimer’s Disease”

**Kwok (Chris) Im** (Terrence Town): “T cell TGF-beta Signaling as a Therapeutic Target for Pediatric Brain Tumors”

**Diana Schall** (Tobias Ulmer): “Structural basis of brain carnitine palmitoyltransferase 1 function”

**ChengLiang Dong** (Kai Wang): “iCAGES: genome-guided precision medicine for cancer treatment”

**Yunfei Guo** (Kai Wang): “SeqMule: An Automated Pipeline for Whole Genome/Exome Analysis on Mendelian Diseases”

**Hui Yang** (Kai Wang): “Phenotype-based detection of causal SNPs and CNVs from next-generation sequencing data”

**Young Joo Kim** (Li Zhang): “Molecular Mechanisms for the Development of Auditory Cochlear Innervation Pattern”

**Lukas Mesik** (Li Zhang): “Functional Characterization of Inhibitory Interneurons During Development”

**Qi Fang** (Li Zhang): “visual cortical processing in awake mice”

**Pan Kong** (Berislav Zlokovic): “Glut1 and Picalm”

**Divna Lazic** (Berislav Zlokovic): “Understanding the role of Mfsd2a Transporter in the Blood-Brain Barrier Dysfunction in Alzheimer’s Disease”

**Anita Ramanathan** (Berislav Zlokovic): “The Cell-specific Influence of PICALM in AD Pathogenesis”

**Melanie Sweeney** (Berislav Zlokovic): “APOE ε4 Allele Modulates Risk for CSF Biomarkers of Neurovascular Injury in Alzheimer’s Disease”
Zach Hall Travel Awards

Through a generous donation from Zach Hall and Julie Giacobassi, ZNI is able to offer each year, travel awards to qualified graduate students working with ZNI Investigators, which allow a student to attend a scientific meeting, collaborative trip or research training opportunity. The competitive application process requires students to submit a mini-grant proposal, including a description of their research project, CV and letter of nomination from their mentor. The Zach Hall Travel Awards program aims to make a positive difference in the training of our graduate students.

In 2014, the awardees attended a diverse group of meetings, presenting posters and papers across the globe: Jung-Hwa Cho (laboratory of Dr Robert Chow) presented a poster at the Biophysical Society Annual Meeting in Baltimore, MD; Lingyun Li (laboratory of Dr Huizhong Tao) displayed her poster at the Society for Neuroscience annual meeting in Washington DC; David Gate (laboratory of Dr Terrence Town) shared his work at the 12th International Conference on Alzheimer’s and Parkinson's Diseases and related neurological disorders (AD/PD) in Nice, France; Chengliang (Coco) Dong (laboratory of Dr Kai Wang) presented her research at the American Society for Human Genetics meeting held in San Diego; and Xiaorui (Ray) Xiong (laboratory of Dr Li Zhang) prepared a poster the Society for Neuroscience annual meeting in Washington DC.

Each graduate student also participates in the poster session following the Zach Hall lectures, sharing their work with USC colleagues. In addition, all the recipients are invited to attend a celebratory lunch with Dr Zach Hall on the day of the event. Congratulations again to all the awardees!
In conjunction with the USC Program in Neuroscience, ZNI again in FY15 hosted workshops for graduate students who might be interested in submitting proposals under the National Institute of Health (NIH)’s Ruth L. Kirchstein National Research Service Awards (NRSA). The NRSA programs are a family of grants provided by the NIH for training researchers in the behavioral sciences and health sciences. They are highly selective and very prestigious source of funding for doctoral and postdoctoral trainees and notably difficult to obtain. Only applications with very good impact scores are funded, based on budget cutoffs determined by each individual NIH institute.

The two-day workshops are team taught at ZNI by M. Carter Cornwall, MD, PhD, Professor of Physiology & Biophysics at the University of Utah; Alapakkam Sampath, PhD, former member of ZNI and currently Associate Professor at Jules Stein Eye Institute of UCLA; and Jeannie Chen, PhD, ZNI member and Professor of Cell & Neurobiology. The workshops cover tips and tricks, sample successful applications, writing critiques but also have students submit their draft applications for an in-depth and critical review. Individuals who avail themselves to this opportunity dramatically increase their success rate when submitting final NRSA grant applications. In FY15, a number of graduate students submitted NRSA applications and we expect to hear positive results in the months to come.
ZNI PIs had a busy FY15. The number of grant submissions averaged 7-8 per month, in addition to roughly 30 progress reports prepared each year. We had 83 sponsored projects during the reporting period, many from 11 different NIH institutes. Despite the difficult funding climate, ZNI investigators managed to increase total project costs by 20% over the prior year. Most significantly, the percentage of new grants received (vs. submitted) rose in FY15 from 14% to 25%.
Direct Costs | F&A Costs | Total Costs
--- | --- | ---
FY13 $12,613,663 | $5,833,907 | $18,447,570
FY14 $13,841,591 | $6,269,721 | $20,111,312
FY15 $17,308,999 | $7,692,518 | $25,001,517

Total number of active grants increased from 69 in FY14 to 85 in FY15. Total dollars received also rose.

**Total Number of Active Grants for FY15**

<table>
<thead>
<tr>
<th>Source</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Federal Grants (includes 1 DOD, 1 NSF)</td>
<td>55</td>
</tr>
<tr>
<td>Federal Fellowships</td>
<td>1</td>
</tr>
<tr>
<td>Foundation/Private Grants</td>
<td>24</td>
</tr>
<tr>
<td>Non-Federal Fellowships</td>
<td>2</td>
</tr>
<tr>
<td>Industry</td>
<td>2</td>
</tr>
<tr>
<td>California Institute for Regenerative Medicine</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>85</strong></td>
</tr>
</tbody>
</table>
### Active Awards - Fiscal Year 2015

<table>
<thead>
<tr>
<th>ZNI Investigator</th>
<th>Funding Agency</th>
<th>Direct Costs</th>
<th>F&amp;A Costs</th>
<th>Total Costs</th>
<th>Project Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bonnin, Alex</td>
<td>Autism Science Foundation Fellowship</td>
<td>$25,000</td>
<td>$0</td>
<td>$25,000</td>
<td>The impact of maternal inflammation during pregnancy on placental tryptophan metabolism, and downstream</td>
</tr>
<tr>
<td>Bonnin, Alex</td>
<td>Childrens Hospital of Los Angeles SubK (National Institute of Mental Health R01)</td>
<td>$15,350</td>
<td>$9,900</td>
<td>$25,250</td>
<td>Enduring Effects of Early-Life Serotonin Signaling</td>
</tr>
<tr>
<td>Bonnin, Alex</td>
<td>Department of Defense</td>
<td>$400,000</td>
<td>$135,699</td>
<td>$535,699</td>
<td>Altered Placental Tryptophan Metabolism: A Crucial Molecular Pathway for the Fetal Programming of Neurodevelopmental Disorders</td>
</tr>
<tr>
<td>Bonnin, Alex</td>
<td>University of Maryland SubK (National Institute of Mental Health R01)</td>
<td>$30,418</td>
<td>$19,582</td>
<td>$50,000</td>
<td>Kynurenic Acid and Cognitive Abnormalities</td>
</tr>
<tr>
<td>Campbell, Daniel</td>
<td>Kaiser Permanente SubK</td>
<td>$22,623</td>
<td>$2,262</td>
<td>$24,885</td>
<td>Air Pollution, MET Genotype and ASD Risk: GxE Interaction in the EMA Study</td>
</tr>
<tr>
<td>Campbell, Daniel</td>
<td>National Institute of Mental Health R21</td>
<td>$125,000</td>
<td>$80,365</td>
<td>$205,365</td>
<td>Non-Coding RNAs in Autism</td>
</tr>
<tr>
<td>Campbell, Daniel</td>
<td>National Institute of Mental Health R01</td>
<td>$252,384</td>
<td>$164,049</td>
<td>$416,433</td>
<td>Biology of Non-Coding RNAs Associated with Psychiatric Disorders</td>
</tr>
<tr>
<td>Chang, Karen</td>
<td>Lejeune Foundation</td>
<td>$47,974</td>
<td>$2,398</td>
<td>$50,372</td>
<td>Systematic analysis of genes contributing to synaptic defects in Down Syndrome</td>
</tr>
<tr>
<td>Chang, Karen</td>
<td>Alzheimer's Association</td>
<td>$272,730</td>
<td>$27,270</td>
<td>$300,000</td>
<td>Functional Protein Interactions in Alzheimer's Disease and Down Syndrome</td>
</tr>
<tr>
<td>Chang, Karen</td>
<td>National Institute of Neurological Disorders &amp; Stroke R01</td>
<td>$216,562</td>
<td>$139,683</td>
<td>$356,245</td>
<td>Role of DYRK1A/MNB in synaptic growth and function</td>
</tr>
<tr>
<td>Chen, Jeannie</td>
<td>National Eye Institute R01</td>
<td>$376,557</td>
<td>$242,566</td>
<td>$619,123</td>
<td>Phototransduction in dark adaptation and retinal degeneration</td>
</tr>
<tr>
<td>Chow, Bob</td>
<td>California Endowment</td>
<td>$250</td>
<td>$0</td>
<td>$250</td>
<td>Bridging the Gaps Research Mentor</td>
</tr>
<tr>
<td>Chow, Bob</td>
<td>National Eye Institute R01 (Ophthalmology Satellite)</td>
<td>$107,629</td>
<td>$69,780</td>
<td>$177,409</td>
<td>Experimental and Clinical Investigations of Retinal Stimulation</td>
</tr>
<tr>
<td>Chow, Bob</td>
<td>National Science Foundation</td>
<td>$135,308</td>
<td>$87,517</td>
<td>$222,825</td>
<td>Retinal Nanophotoswitch</td>
</tr>
<tr>
<td>Chow, Bob</td>
<td>National Institute of Mental Health U01</td>
<td>$253,045</td>
<td>$163,123</td>
<td>$416,168</td>
<td>Evaluation of Cellular Heterogeneous National Eye Institute Using Patchclamp and RNA-Seq of Single Cells</td>
</tr>
<tr>
<td>Chow, Bob</td>
<td>National Institute of Biomedical Imaging and Bioengineering (BMES Satellite)</td>
<td>$27,116</td>
<td>$17,501</td>
<td>$44,617</td>
<td>A Resource on Medical Ultrasonic Transducer Technology</td>
</tr>
<tr>
<td>Coba, Marcelo</td>
<td>University of Kansas SubK (National Institute of Mental Health R01)</td>
<td>$143,579</td>
<td>$92,908</td>
<td>$236,487</td>
<td>Deciphering gene-environment interactions in pathologically reactive agression</td>
</tr>
<tr>
<td>Conti, David</td>
<td>National Cancer Institute R01</td>
<td>$318,153</td>
<td>$203,405</td>
<td>$521,558</td>
<td>Incorporating intermediate biomarkers of folate with colorectal cancer</td>
</tr>
<tr>
<td>Evgrafov, Oleg</td>
<td>SENS Research Foundation</td>
<td>$3,200</td>
<td>$0</td>
<td>$3,200</td>
<td>Whole genome sequencing of S. aleutianus: The fish with the highest longevity</td>
</tr>
<tr>
<td>Evgrafov, Oleg</td>
<td>National Institute of Mental Health R01</td>
<td>$404,134</td>
<td>$244,983</td>
<td>$649,117</td>
<td>Transcriptome Sequencing of Neuronal Cell Lines from Patients with Schizophrenia</td>
</tr>
<tr>
<td>ZNI Investigator</td>
<td>Funding Agency</td>
<td>Direct Costs</td>
<td>F&amp;A Costs</td>
<td>Total Costs</td>
<td>Project Title</td>
</tr>
<tr>
<td>--------------------</td>
<td>-----------------------------------------</td>
<td>--------------</td>
<td>-----------</td>
<td>--------------</td>
<td>-------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Evgrafov, Oleg</td>
<td>Brain &amp; Behavior Research Foundation</td>
<td>$46,296</td>
<td>$3,704</td>
<td>$50,000</td>
<td>In Vitro Modeling of Altered Brain Development in Schizophrenia</td>
</tr>
<tr>
<td>Field, Greg</td>
<td>Whitehall Foundation</td>
<td>$206,400</td>
<td>$18,600</td>
<td>$225,000</td>
<td>Mapping the connectivity of the mammalian retina</td>
</tr>
<tr>
<td>Field, Greg</td>
<td>National Eye Institute R01</td>
<td>$250,000</td>
<td>$161,250</td>
<td>$411,250</td>
<td>Light adaptation and circadian modulation of parallel processing in retina</td>
</tr>
<tr>
<td>Field, Greg</td>
<td>Karl Kirchgessner Foundation</td>
<td>$50,000</td>
<td>$0</td>
<td>$50,000</td>
<td>Vision Research Grant</td>
</tr>
<tr>
<td>Knowles, James</td>
<td>National Institute of Mental Health R01</td>
<td>$66,179</td>
<td>$41,031</td>
<td>$107,210</td>
<td>Genome-Wide Screen for Linkage Disequilibrium to Obsessive Compulsive Disorder</td>
</tr>
<tr>
<td>Knowles, James</td>
<td>National Institute of Environmental Health Sciences R01</td>
<td>$396,000</td>
<td>$245,520</td>
<td>$641,520</td>
<td>Discovery of genetic variation influencing schizophrenia using next generation DNA sequencing</td>
</tr>
<tr>
<td>Knowles, James</td>
<td>National Human Genome Research Institute R01 (Satellite from Biomedical Engineering)</td>
<td>$39,374</td>
<td>$25,363</td>
<td>$64,737</td>
<td>Robust and Portable Workflow-based tools for MRNA and Genome re-sequencing</td>
</tr>
<tr>
<td>Knowles, James</td>
<td>National Institute of Mental Health U01</td>
<td>$797,335</td>
<td>$506,606</td>
<td>$1,303,941</td>
<td>Evaluation of Cellular Heterogeneity Using Patchclamp and RNA-Seq of Single Cells</td>
</tr>
<tr>
<td>Knowles, James</td>
<td>International OCD Foundation</td>
<td>$43,629</td>
<td>$0</td>
<td>$43,629</td>
<td>Replication of Genome-Wide Association Findings</td>
</tr>
<tr>
<td>Knowles, James</td>
<td>University of Wisconsin SubK (National Institute of Mental Health R01)</td>
<td>$34,576</td>
<td>$22,301</td>
<td>$56,877</td>
<td>Brain Mechanisms Mediating Genetic Risk for Anxiety and Depression</td>
</tr>
<tr>
<td>Knowles, James</td>
<td>National Institute of Mental Health R01</td>
<td>$395,437</td>
<td>$254,563</td>
<td>$650,000</td>
<td>The USC PsychENCODE Project</td>
</tr>
<tr>
<td>Knowles, James</td>
<td>National Institute of Mental Health R01 (Supplement)</td>
<td>$98,510</td>
<td>$63,990</td>
<td>$162,500</td>
<td>The USC PsychENCODE Project - supplement</td>
</tr>
<tr>
<td>Langen, Ralf</td>
<td>John Douglas French Alzheimer's Foundation</td>
<td>$100,000</td>
<td>$6,000</td>
<td>$106,000</td>
<td>Alpha-Synuclein Misfolding in Dementia</td>
</tr>
<tr>
<td>Langen, Ralf</td>
<td>National Multiple Sclerosis Society</td>
<td>$96,767</td>
<td>$9,677</td>
<td>$106,444</td>
<td>Initiating myelination: a matter of membrane curvature</td>
</tr>
<tr>
<td>Langen, Ralf</td>
<td>Batey Family Research Fund</td>
<td>$30,000</td>
<td>$0</td>
<td>$30,000</td>
<td>Prevention of Misfolding and Membrane Permeabilization in Parkinson's and Other Neurodegenerative Diseases</td>
</tr>
<tr>
<td>Langen, Ralf</td>
<td>CHDI Foundation</td>
<td>$412,864</td>
<td>$61,930</td>
<td>$474,794</td>
<td>How structure and dynamics of monomeric huntington are modulated by post-translational modifications and polyQ length</td>
</tr>
<tr>
<td>Langen, Ralf</td>
<td>National Institute of Neurological Disorders &amp; Stroke R01</td>
<td>$205,520</td>
<td>$133,352</td>
<td>$338,872</td>
<td>Molecular mechanisms of huntingtin misfolding</td>
</tr>
<tr>
<td>Mack, William</td>
<td>Brain Aneurysm Foundation</td>
<td>$25,000</td>
<td>$0</td>
<td>$25,000</td>
<td>MRI Perfusion Permeability and Matrix Metalloproteinase 9 Levels associated with cerebral vasospasm following aneurysmal</td>
</tr>
<tr>
<td>Mack, William</td>
<td>American Heart Association</td>
<td>$49,206</td>
<td>$2,673</td>
<td>$51,879</td>
<td>Intra-arterial Magnesium Therapy in Acute Stroke</td>
</tr>
<tr>
<td>ZNI Investigator</td>
<td>Funding Agency</td>
<td>Direct Costs</td>
<td>F&amp;A Costs</td>
<td>Total Costs</td>
<td>Project Title</td>
</tr>
<tr>
<td>------------------</td>
<td>----------------</td>
<td>--------------</td>
<td>-----------</td>
<td>-------------</td>
<td>---------------</td>
</tr>
<tr>
<td>Mack, William</td>
<td>National Institute of Environmental Health Sciences R01 (ONES Award)</td>
<td>$299,500</td>
<td>$179,812</td>
<td>$479,312</td>
<td>Neurotoxicity of Airborne Particles: Role of Chronic Cerebral Hypoperfusion</td>
</tr>
<tr>
<td>Mack, William</td>
<td>National Institute for Aging (Neurology Pilot)</td>
<td>$8,642</td>
<td>$0</td>
<td>$8,642</td>
<td>The Role of the C5 Complement Protein in Chronic Cerebral Hypoperfusion</td>
</tr>
<tr>
<td>Pato, Carlos</td>
<td>National Institute of Mental Health R01</td>
<td>$2,438,975</td>
<td>$967,182</td>
<td>$3,406,157</td>
<td>Genomic Psychiatry Cohort (GPC)</td>
</tr>
<tr>
<td>Pato, Carlos</td>
<td>National Institute of Mental Health R01</td>
<td>$100,529</td>
<td>$64,925</td>
<td>$165,454</td>
<td>Whole Genome Sequencing for Schizophrenia and Bipolar Disorder in the GPC</td>
</tr>
<tr>
<td>Pato, Michele</td>
<td>National Institute of Mental Health R01</td>
<td>$18,251</td>
<td>$1,825</td>
<td>$20,076</td>
<td>Role of 5-alpha Reductase 2 and Androgens in Tourette Syndrome</td>
</tr>
<tr>
<td>Pato, Michele</td>
<td>National Institute of Mental Health R01</td>
<td>$50,000</td>
<td>$32,187</td>
<td>$82,187</td>
<td>1/2 Targeted Sequencing and Functional Evaluation of Mutations in Schizophrenia</td>
</tr>
<tr>
<td>Pato, Michele</td>
<td>National Institute of Mental Health R01</td>
<td>$449,805</td>
<td>$291,436</td>
<td>$741,241</td>
<td>Addition of OCD to the Genomic Psychiatry Cohort</td>
</tr>
<tr>
<td>Pato, Michele</td>
<td>National Institute of Mental Health R01</td>
<td>$1,375,149</td>
<td>$448,463</td>
<td>$1,823,612</td>
<td>African Ancestry Genomic Psychiatry Cohort</td>
</tr>
<tr>
<td>Peti-Peterdi, Janos</td>
<td>American Heart Association Fellowship</td>
<td>$96,000</td>
<td>$0</td>
<td>$96,000</td>
<td>Tracking the Fate and Function of the Renin Cell</td>
</tr>
<tr>
<td>Peti-Peterdi, Janos</td>
<td>National Institute of Diabetes and Digestive and Kidney Diseases R01</td>
<td>$225,000</td>
<td>$145,125</td>
<td>$370,125</td>
<td>Novel imaging approach to study podocyte function in vivo</td>
</tr>
<tr>
<td>Peti-Peterdi, Janos</td>
<td>Amgen</td>
<td>$137,931</td>
<td>$62,069</td>
<td>$200,000</td>
<td>Validation of Prodocyte TRPC6 as a Target in Glomerular Pathology</td>
</tr>
<tr>
<td>Peti-Peterdi, Janos</td>
<td>American Heart Association</td>
<td>$63,636</td>
<td>$6,364</td>
<td>$70,000</td>
<td>The role of macula densa cells in renovascular disease</td>
</tr>
<tr>
<td>Peti-Peterdi, Janos</td>
<td>American Diabetes Association</td>
<td>$100,000</td>
<td>$15,000</td>
<td>$115,000</td>
<td>Novel tissue remodeling mechanisms in diabetic kidney disease</td>
</tr>
<tr>
<td>Sieburth, Derek</td>
<td>National Institute of Neurological Disorders &amp; Stroke R01</td>
<td>$212,231</td>
<td>$131,583</td>
<td>$343,814</td>
<td>Stress Regulation of synaptic transmission</td>
</tr>
<tr>
<td>Sieburth, Derek</td>
<td>National Institute of Neurological Disorders &amp; Stroke R01 (Gerontology Satellite)</td>
<td>$7,460</td>
<td>$4,840</td>
<td>$12,300</td>
<td>Oxygen Radical Toxicity and Protein Degradation</td>
</tr>
<tr>
<td>Siemer, Ansgar</td>
<td>Whitehall Foundation</td>
<td>$66,903</td>
<td>$8,097</td>
<td>$75,000</td>
<td>The Function of Amyloid Proteins in Long-Term Memory</td>
</tr>
<tr>
<td>Siemer, Ansgar</td>
<td>National Institute of Neurological Disorders &amp; Stroke R01</td>
<td>$40,230</td>
<td>$26,079</td>
<td>$66,309</td>
<td>Molecular mechanisms of huntingtin misfolding</td>
</tr>
<tr>
<td>Siemer, Ansgar</td>
<td>National Institute of Neurological Disorders &amp; Stroke R01 Diversity Supplement</td>
<td>$32,201</td>
<td>$20,931</td>
<td>$53,132</td>
<td>Molecular mechanism of huntingtin misfolding - diversity supplement</td>
</tr>
<tr>
<td>Tao, Huizhong</td>
<td>National Eye Institute R01</td>
<td>$288,948</td>
<td>$184,926</td>
<td>$473,874</td>
<td>Inhibitory Synaptic Mechanisms underlying visual cortical processing</td>
</tr>
<tr>
<td>Tao, Huizhong</td>
<td>Kirchgessner (Karl) Foundation</td>
<td>$50,000</td>
<td>$0</td>
<td>$50,000</td>
<td>The Karl Kirchgessner Foundation Vision Research Grant</td>
</tr>
<tr>
<td>ZNI Investigator</td>
<td>Funding Agency</td>
<td>Direct Costs</td>
<td>F&amp;A Costs</td>
<td>Total Costs</td>
<td>Project Title</td>
</tr>
<tr>
<td>-----------------</td>
<td>----------------</td>
<td>--------------</td>
<td>-----------</td>
<td>-------------</td>
<td>---------------</td>
</tr>
<tr>
<td>Tao, Huizhong</td>
<td>National Eye Institute R21</td>
<td>$125,000</td>
<td>$80,000</td>
<td>$205,000</td>
<td>Inhibitory circuity mechanisms underlying visual cortical development and plasticity</td>
</tr>
<tr>
<td>Town, Terrence</td>
<td>National Institute of Neurological Disorders &amp; Stroke F31 Fellowship (Gate)</td>
<td>$36,276</td>
<td>$0</td>
<td>$36,276</td>
<td>Targeting Abeta phagocytosis by blocking IRAK-M innate immunity in Alzheimer mice</td>
</tr>
<tr>
<td>Town, Terrence</td>
<td>National Institute for Aging R21</td>
<td>$26,848</td>
<td>$17,196</td>
<td>$44,044</td>
<td>An iPSC Disease-In-a-Dish Model of Familial Alzheimers</td>
</tr>
<tr>
<td>Town, Terrence</td>
<td>National Institute of Neurological Disorders &amp; Stroke R01</td>
<td>$216,562</td>
<td>$139,863</td>
<td>$356,425</td>
<td>Peripheral TGF-beta Pathway Inhibitor Therapy in Alzheimer's Rats</td>
</tr>
<tr>
<td>Town, Terrence</td>
<td>California Institute for Regenerative Medicine</td>
<td>$335,073</td>
<td>$18,176</td>
<td>$353,249</td>
<td>Role of HLA in Neural Stem Cell Rejection using Humanized Mice</td>
</tr>
<tr>
<td>Town, Terrence</td>
<td>Alzheimer's Association</td>
<td>$139,067</td>
<td>$12,642</td>
<td>$151,708</td>
<td>Macrophage TGF-beta-Smad 2/3 Inhibitor Therapy in Transgenic Alzheimer Rats</td>
</tr>
<tr>
<td>Town, Terrence</td>
<td>American Federation for Aging Research</td>
<td>$311,423</td>
<td>$29,142</td>
<td>$340,565</td>
<td>Re-balancing National Cancer Institute's peripheral TGF-beta signaling in aged Alzheimer's rats</td>
</tr>
<tr>
<td>Ulmer, Tobias</td>
<td>American Heart Association</td>
<td>$63,636</td>
<td>$6,364</td>
<td>$70,000</td>
<td>Ectodomain-Transmembrane Domain Coupling in Integrin Receptor Signaling</td>
</tr>
<tr>
<td>Wang, Kai</td>
<td>National Human Genome Research Institute R01</td>
<td>$215,600</td>
<td>$138,702</td>
<td>$354,302</td>
<td>Integrated variation detection annotation and analysis for high-throughput sequencing National Cancer Institute's data</td>
</tr>
<tr>
<td>Wang, Kai</td>
<td>Vanderbilt SubK (National Human Genome Research Institute R01)</td>
<td>$14,621</td>
<td>$9,420</td>
<td>$24,041</td>
<td>Integrative Statistical Models for Pathway Analysis of GWAS Data</td>
</tr>
<tr>
<td>Wang, Kai</td>
<td>UCSD SubK (National Human Genome Research Institute R01)</td>
<td>$7,709</td>
<td>$4,972</td>
<td>$12,681</td>
<td>Accelerating Curation of GWAS Catalog by Automatic Text Mining</td>
</tr>
<tr>
<td>Zhang, Li</td>
<td>National Institute on Deafness &amp; Other Communication Disorders R01</td>
<td>$74,881</td>
<td>$47,175</td>
<td>$122,056</td>
<td>Synaptic Circuitry Mechanisms for Auditory Cortical Processing</td>
</tr>
<tr>
<td>Zhang, Li</td>
<td>National Institute on Deafness &amp; Other Communication Disorders R01</td>
<td>$250,035</td>
<td>$161,376</td>
<td>$411,411</td>
<td>Inhibitor circuity mechanism for auditory cortical processing</td>
</tr>
<tr>
<td>Zhang, Li</td>
<td>Packard Foundation</td>
<td>$157,516</td>
<td>$17,484</td>
<td>$175,000</td>
<td>Structure of Synaptic Circuitry Underlying Cortical Function</td>
</tr>
<tr>
<td>Zlokovic, Berislav</td>
<td>National Institute for Aging R01</td>
<td>$51,604</td>
<td>$6,305</td>
<td>$57,909</td>
<td>Caloric Restriction and Alzheimer's Aβ Clearance Pathway</td>
</tr>
<tr>
<td>Zlokovic, Berislav</td>
<td>National Institute of Neurological Disorders &amp; Stroke R01</td>
<td>$412,491</td>
<td>$186,251</td>
<td>$598,742</td>
<td>Alzheimer's Aβ: Apolipoproteins and Blood-Brain Barrier</td>
</tr>
<tr>
<td>Zlokovic, Berislav</td>
<td>National Institute for Aging R01</td>
<td>$300,211</td>
<td>$192,386</td>
<td>$492,597</td>
<td>Cerebrovascular Beta-Amyloidosis: A-β CNS Transport Pathways</td>
</tr>
<tr>
<td>Zlokovic, Berislav</td>
<td>National Institute for Aging R01</td>
<td>$205,000</td>
<td>$133,250</td>
<td>$338,250</td>
<td>The Role of Pericytes in the Adult and the Aging Brain</td>
</tr>
<tr>
<td>Zlokovic, Berislav</td>
<td>National Institute of Neurological Disorders &amp; Stroke R01</td>
<td>$461,505</td>
<td>$205,747</td>
<td>$667,252</td>
<td>Activated protein C system in Stroke Models</td>
</tr>
</tbody>
</table>
# Active Awards - Fiscal Year 2015

<table>
<thead>
<tr>
<th>ZNI Investigator</th>
<th>Funding Agency</th>
<th>Direct Costs</th>
<th>F&amp;A Costs</th>
<th>Total Costs</th>
<th>Project Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zlokovic, Berislav</td>
<td>National Heart, Blood &amp; Lung Institute R01</td>
<td>$342,868</td>
<td>$134,376</td>
<td>$477,244</td>
<td>Regulation of Brain Thrombosis in Stroke Models</td>
</tr>
<tr>
<td>Zlokovic, Berislav</td>
<td>Cedars Sinai Medical Center SubK (National Institute of Neurological Disorders &amp; Stroke U01)</td>
<td>$11,932</td>
<td>$7,696</td>
<td>$19,628</td>
<td>Safety evaluation of 3K3A-APC in Ischemic Stroke</td>
</tr>
<tr>
<td>Zlokovic, Berislav</td>
<td>Cure Alzheimer's Fund</td>
<td>$250,000</td>
<td>$0</td>
<td>$250,000</td>
<td>The Role of PICALM in Vascular Clearance of Amyloid-beta</td>
</tr>
<tr>
<td>Zlokovic, Berislav</td>
<td>Fidelity Biosciences, Inc.</td>
<td>$200,000</td>
<td>$0</td>
<td>$200,000</td>
<td>Blood-Brain Barrier Pericytes: Safeguards Against Amyloid-Beta Brain Degeneration</td>
</tr>
<tr>
<td>Zlokovic, Berislav</td>
<td>National Institute for Aging R01</td>
<td>$395,012</td>
<td>$214,042</td>
<td>$609,054</td>
<td>Cerebrovascular beta-Amyloidosis: A-beta CNS Transport Pathways</td>
</tr>
<tr>
<td>Zlokovic, Berislav</td>
<td>Alzheimer's Disease Research Center (National Institute for Aging)</td>
<td>$29,960</td>
<td>$19,436</td>
<td>$49,396</td>
<td>ADRC Biomarker Core</td>
</tr>
<tr>
<td>Zlokovic, Berislav</td>
<td>Alzheimer's Disease Research Center (National Institute for Aging)</td>
<td>$92,674</td>
<td>$60,122</td>
<td>$152,796</td>
<td>ADRC Project 1: Neurovascular Factors in Alzheimer's Disease</td>
</tr>
</tbody>
</table>

**TOTAL** $17,308,999 $7,692,518 $25,001,517

---

## 2015 Annual Sponsored Awards

<table>
<thead>
<tr>
<th>Type</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Federal Awards</td>
<td>$21,288,542</td>
</tr>
<tr>
<td>Private Foundation Awards</td>
<td>$3,312,975</td>
</tr>
<tr>
<td>Industry</td>
<td>$400,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$25,001,517</strong></td>
</tr>
</tbody>
</table>
ZNI Events

Every year, ZNI offers a multitude of academic activities that range from our monthly seminar series to more interactive workshops and meetings as well as chalk talks. We pride ourselves in inviting some of the best minds in the field to come and share their expertise and latest findings through our seminar series. Some of the offerings from FY 15 are below.

ZNI Seminar Series

September 2014

“Visualizing and Ablating Endogenous Synaptic Proteins In Vivo”
**Don Arnold, PhD**, Professor of Biological Sciences, USC Dornsife College of Letters, Arts & Sciences

“Attentional Neurons and Circuits”
**Julius Zhu, PhD**, Associate Professor of Pharmacology and Neuroscience, University of Virginia

“Using Quantitative Genetic Studies to Understand the Brain”
**Abraham Palmer, PhD**, Associate Professor of Human Genetics, University of Chicago

October 2014

“Mouse Genetic Approach to Dissect Neuronal and Molecular Targets for Huntington’s Disease”
**X. William Yang, PhD**, Professor of Psychiatry & Biobehavioral Sciences, David Geffen School of Medicine, UCLA

“Functional Genomic Investigation of Neuropsychiatric Disease”
**Dan Geschwind, MD, PhD**, Director of the Neurogenetics Program, Director of the UCLA Center for Autism Research and Treatment, Gordon and Virginia MacDonald Distinguished Chair in Human Genetics, and Professor of Neurology, Psychiatry & Biobehavioral Sciences, UCLA

November 2014

“Rapid High Resolution Brain Mapping with Light Microscopy”
**Raju Tomer, PhD**, Postdoctoral Fellow, HHMI Research Specialist, Stanford University
January 2015

“Vascular Contribution to Brain Aging”
Kevin King MD, MSCS, Assistant Professor of Clinical Radiology, Division of Neuroradiology, Keck School of Medicine of USC

“A Fast Endophilin-Dependent, Clathrin-Independent Endocytic Mechanism”
Harvey McMahon, PhD, Research Scientist, MRC Laboratory of Molecular Biology, Cambridge, UK

February 2015

“Cerebrovascular Reactivity MRI in Aging and Alzheimers Disease”
Hanzhang Lu, PhD, Associate Professor of Radiology & Radiological Sciences, Johns Hopkins University School of Medicine

“Cross-modal Cortical Adaptation to Sensory Loss”
Hey-Kyoung Lee, PhD, Associate Professor of Neuroscience, Mind/Brain Institute, Johns Hopkins University

“Live Imaging of Functional Circuitry from Alzheimer’s Disease to Post-Traumatic Stress Disorder with a Neuropathologist’s Eye”
Elaine Bearer MD, PhD, FAAAS, Harvey Family Professor of Pathology, Vice Chair for Research, Department of Pathology, School of Medicine, University of New Mexico Health Sciences Center

March 2015

“Impact of Antenatal Glucocorticoids on the Developing Brain”
Donald DeFranco, PhD, Professor & Vice Chair of Medical Education, Associate Dean for Medical Student Research, University of Pittsburgh

“ON-OFF Cells of the Auditory System”
Larry Trussell, PhD, Professor of Otolaryngology, Senior Scientist, Vollum Institute, Oregon Health and Science University

“3D Genome Organization and Gene Transcription Regulation in Human Diseases”
Yijun Ruan, PhD, Professor and Director, Genomic Sciences, The Jackson Laboratory for Genomic Medicine
April 2015

“Molecular Mechanisms Underlying the Demise of Neurons”
**Hugo Bellen, DVM, PhD**, Investigator, Howard Hughes Medical Institute, Professor of Molecular and Human Genetics, Director of Developmental Biology, Baylor College of Medicine

“The Anatomical Distribution of Genetic Risk in the Brain”
**Joseph Dougherty, PhD**, Assistant Professor of Genetics and Psychiatry, Washington University in St. Louis School of Medicine

May 2015

“Smells, Worms and Turns: Dissecting *C. elegans* Neural Circuits”
**Sreekanth Chalasani, PhD**, Assistant Professor of Molecular Neurobiology, Helen McLoraine Developmental Chair in Neurobiology, Salk Institute for Biological Sciences

“Subdiffusive Encounter of Membrane Receptors: A Functional Role for Plasma Membrane Heterogeneity”
**Edward Lyman, PhD**, Assistant Professor of Physics & Astrophysics and Chemistry & Biochemistry, University of Delaware

“Synapses, Brain Disorders and Muscular Dystrophy”
**Lin Mei, PhD**, Professor and Chair of Neuroscience & Regenerative Medicine, Medical College of Georgia, Georgia Regents University

“The Kynurenine Pathway of Tryptophan Degradation: Links to Schizophrenia and Other Major Brain Diseases”
**Robert Schwarcz, PhD**, Professor of Psychiatry, Pharmacology and Pediatrics, Maryland Psychiatric Research Center, University of Maryland School of Medicine

June 2015

“Assembly and Function of Chromatic Circuits in Drosophila”
**Chi-Hon Lee, MD, PhD**, Senior Investigator and Head, Section on Neuronal Connectivity, Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), National Institutes of Health (NIH)
The Zilkha Neurogenetic Institute hosted the 5th Annual Zach Hall Lecture on 2 December 2014 in the Herklotz Seminar Room at ZNI. The lecture—named in honor of ZNI’s inaugural director Zach W. Hall, PhD—is a day-long affair, featuring scientific reports, seminars, a poster session featuring the work of over 25 labs, as well as opportunities for graduate students and postdoctoral fellows to have direct contact and conversations with established scientists and senior faculty in formal and informal ways.

The afternoon began with a presentation by Huizhong (Whit) Tao, PhD, Associate Professor in the Department of Neurology and ZNI faculty. Her talk was entitled “Dissecting Neural Circuits for Visual Processing and Behavior.” Dr Tao was followed by Justin Ichida, PhD, Assistant Professor of Stem Cell Biology and Regenerative Medicine, who explored the question “Can Cellular Reprogramming Decode Human Disease? Dissecting ALS Mechanisms Using Induced Neurons”. Both talks preceded the keynote lecture “Neuronal Migration and Brain Map Formation” delivered by Pasko Rakic, MD, PhD, who is the Dory McConnell Duberg Professor of Neuroscience, Professor of Neurology and Chair of Neurobiology, as well as the Director of the Kavli Institute for Neuroscience at Yale University School of Medicine.

Among his many research contributions, Dr Rakic and his colleagues discovered the hidden abnormalities of neuronal positioning that cannot be discerned by routine postmortem examination of the human brain. This provides new insight into possible developmental origin of disorders of higher brain functions, such as childhood epilepsy, autism, schizophrenia and forms of mental retardation. Dr Rakic is a member of the National Academy of Sciences, the Institute of Medicine, American Academy of Arts & Sciences and he is a past president of the Society for Neuroscience.
The seminars were followed by a scientific poster session featuring over 40 displays across multiple disciplines from 25 ZNI laboratories. The range of work speaks to the depth and breadth of the types of research conducted at ZNI. The poster session always affords time for spontaneous yet valuable discussions among the students and researchers at ZNI and USC as well as other members of the broader scientific community.

As one of our signature events, the annual Zach Hall lecture brings substantial recognition to the scientific advances underway at ZNI and USC.
2nd Annual Zilkha Alzheimer Symposium

The 2nd Annual Zilkha Alzheimer Symposium, “Building on Progress: New Developments in Genetics, Neuronal, Glial and Vascular Biology” was held on 10 April 2015, with national and international leaders in the field convening at USC to share their work: Christer Betsholtz, MD, PhD, Uppsala Univ (Sweden); David M Holtzman, MD, Wash U Medical School; Costantino Iadecola MD, Weill Cornell Medical College; Justin Ichida, PhD, Stem Cell Biology & Regenerative Medicine (USC); Daniel Nation, PhD, Psychology (USC); Maiken Nedergaard, MD, DMSc, Univ Rochester Medical Center; Judy Pa, PhD, Laboratory of Neuro Imaging (USC); Dominik Paquet, PhD, NYSCF Druckenmiller Fellow, Rockefeller Univ; Sangram Sisodia, PhD, Univ of Chicago; Rudolph Tanzi, PhD, Harvard; Arthur Toga, PhD, Stevens Institute for Neuroimaging and Informatics (USC); Cheryl Wellington, PhD, Univ of British Columbia (Canada); Berislav Zlokovic, MD, PhD, Zilkha Neurogentic Institute (USC). Session chairs included Maria Carrillo, PhD, VP, Medical & Scientific Relations, Alzheimers Association; Roderick Corriveau, PhD, Program Director, NINDS (NIH); Dr. Helena Chui (USC Neurology) and Dr. Caleb (Tuck) Finch (USC Gerontology). Co-organizers for the symposia with Dr. Zlokovic were David M Holtzman MD (Wash U) and Rudi Tanzi, PhD (Harvard). Opening remarks were given by USC Provost Michael Quick and Mr. Selim Zilkha. The day-long event was underwritten by a generous gift from Eva and Marc Stern.

Planning is now underway for the 3rd Annual Zilkha Alzheimer Symposium, scheduled for 15 April 2016.
(Right) Maiken Nedergaard asking a question following one of the presentations at the Zilkha Alzheimer Symposium.

Photo credit: Steven Cohn

(Left) The attendees of the symposium.

Photo credit: Steven Cohn

(Right) Mr. Selim Zilkha and the many attendees of the symposium.

Photo credit: Steven Cohn
Joint ADRC - ZNI Pilot Project Program

The USC Alzheimer Disease Research Center (ADRC) and Zilkha Neurogenetic Institute (ZNI) are excited to announce that we have combined resources and efforts to form a joint ADRC-ZNI pilot project program.

Each Fall, the ADRC-ZNI Pilot Project Program invites clinical and basic science investigators to submit letters of intent for 12-month pilot projects. The ADRC focuses on mild cognitive changes related to Alzheimer’s, cerebrovascular disease, and their interactions in diverse communities. Now working with the ZNI, we seek new basic, clinical and psychosocial approaches to the pathogenesis, prevention, and treatment of early cognitive impairment in humans and animal models. We encourage the development of new approaches to intervention and translational research from preclinical to early phase trials. Projects that use data available through the National Alzheimer’s Coordinating Center or the USC ADRC are strongly encouraged.

The ADRC-ZNI Pilot Project Program grants are designed for junior faculty level investigators, but may be awarded to a more senior investigator who has experience in areas other than AD research, and who wants to work in the AD research field or who wants to try a new hypothesis, method, or approach that is not an extension of ongoing AD research. Postdoctoral fellows may apply with a faculty sponsor. Successful applicants will receive direct costs up to $30,000 for one-year pilot projects.

This new collaboration between the ADRC and ZNI enables the support of additional pilot projects, using the same integrated solicitation and review process.
Los Angeles/Irvine Brain Bee 2015

The 2015 Los Angeles/Irvine Brain Bee took place on 30 January 2015 and was hosted at the University of California at Irvine for the first time. The event was co-organized by USC, UCI, UCLA, Los Angeles City College (LACC) and InterAxon, the neuroscience-centered graduate student groups of USC and UCLA. Fifty-five high school students from 21 different area high schools competed for the regional title, which qualifies the winner to attend the National Brain Bee in Washington DC. Shyam Chandrasekar, the 2014 winner, assisted with the Jeopardy round. This year’s guest lecturer was Bradley Voytek, PhD, an Assistant Professor at UCSD and a self-proclaimed zombie expert, whose talk was entitled, “A Neuroscientific View of the Zombie Brain”.

The USC liason for the Bee was Amy Nelson, PhD, a postdoctoral scholar in the laboratory of Dr. Berislav Zlokovic; she was assisted by David Warren and a group of highly enthusiastic volunteers. USC had 20 undergraduate and graduate students who assisted with preparing, planning and executing new hands-on demonstrations including: sheep brain dissections for students to learn brain anatomy; the staining of sheep brain sections to learn about microscopic brain structures; and a rope neuron model where participants acted through the essential steps of an action potential (in which the electrical membrane potential of a cell rapidly rises and falls, following a consistent trajectory). The USC demonstrations were a huge success with the participants truly engaged in learning! USC volunteers Anita Ramanathan, Priya Rangan and Elisabeth Gilmore were part of a professional panel who fielded questions from high school participants on topics about graduate school, working in a lab, and future opportunities for employment when graduating with a science degree. Drs. Kassandra Kisler, Hong Wei Dong and Nicholas Foster sat on a professional panel for the parents, addressing their questions and concerns, with the latter two also acting as judges for the Jeopardy quiz rounds.

At the end of the day, the top three finalists were: Arjun Srivata (first place), Shriraj Susarla (second place) and David Hsiou (third place).

ZNI is proud to be a part of the Los Angeles/Irvine Brain Bee competition, which fosters interest in the brain and neuroscience research. The Brain Bee will be hosted by ZNI in early 2016. Thanks to all who volunteered!

The top three finalists from left to right: David Hsiou (third place), Arjun Srivata (first place), and Shriraj Susarla (second place).
Music to Remember - LA Opera/Alzheimer's Association

A joint program offered by LA Opera, the Alzheimer’s Association, California Southland Chapter, the Zilkha Neurogenetic Institute (ZNI), and Alzheimer Disease Research Center (ADRC) at the Keck School of Medicine of USC

Whether it is a couple’s favorite melody (“our song”), an aria from a famous opera, a lullaby, a hymn or a holiday carol, music evokes memories. Music stirs the soul, but also involves the brain, in ways neuroscientists are still exploring: Listening to music involves the auditory pathways, auditory cortex and sensory association cortex. Registering emotion likely involves the amygdala. Memory is accessed via the hippocampus. The connections among these regions help guide and process a complicated set of actions within the brain.

For the second year, the Zilkha Neurogenetic Institute continued a unique partnership with the Alzheimer’s Association, California Southland Chapter and LA Opera, to bring music—and perhaps memories—to people who need it most, those experience various stages of dementia. A pilot program brought young singers from LA Opera to perform for residents (and workers) in long-term care and assisted living facilities throughout Los Angeles.

This program was made possible by research funds from the ZNI, as well as the generosity of Alzheimer’s Association, California Southland Chapter and LA Opera. As an added benefit, the performers went caroling on the Health Science Campus, surprising workers and visitors at the Keck School of Medicine of USC. We received such positive feedback from the community that we will continue this program again in 2016.
ZNI Administration

The Zilkha Neurogenetic Institute has an experienced administrative staff led by David Warren, senior director of operations, finance and administration. The 300 staff, faculty and students who work at ZNI are supported by a facilities manager Rusty King, human resources manager Barbara Lockely, two full-time contracts & grants coordinators Gabriela Torres and Muoi Thang, purchasing agent Leslie Ortiz, budget/business technician Marlen Turcios, program manager Emily Chu, who joined us in late 2015 replacing Julie Carl, executive assistant Monica Castro and two lab aides, Benilda Ramos and Manuela Osorio, who provide glassware and autoclave services.

The institute acts as a hub for the neuroscience community across campuses, offering a weekly seminar series, hosting neuroscience graduate courses, journal clubs, special lectures, as well as grand rounds for the departments of Psychiatry, Neurology and Neurosurgery. At ZNI, science comes first and everything else is built around supporting the best research being conducted today.

<table>
<thead>
<tr>
<th>FY15 Operating Budget</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Program Funds (Endowment)</strong></td>
</tr>
<tr>
<td>$ 2,431,040</td>
</tr>
<tr>
<td><strong>Departmental Funds (KSOM-Provided)</strong></td>
</tr>
<tr>
<td>Administrative</td>
</tr>
<tr>
<td>Facilities</td>
</tr>
<tr>
<td>Deans Development Funds</td>
</tr>
<tr>
<td><strong>Philanthropy</strong></td>
</tr>
<tr>
<td>Unrestricted Gifts</td>
</tr>
<tr>
<td>Restricted Gifts</td>
</tr>
</tbody>
</table>
ZNI Development

The Zilkha Neurogenetic Institute is an integral part of a broader USC neuroscience initiative that is exploring new ways to examine nervous system function in order to better understand the underlying causes of neurological and psychiatric disorders. At our world-class center for research excellence, USC faculty, fellows and graduate students are reaching across boundaries to embrace methods and techniques from other fields of study to discover innovative cures and treatment for neurogenetic diseases such as Alzheimer’s, Parkinson’s, Stroke, Multiple Sclerosis, Kidney Disease and many other devastating illnesses.

There are many ways that you can help. Under the Keck Medicine Initiative, the Zilkha Neurogenetic Institute fundraising priorities include:

- Support of world-class core research faculty and facilities with state-of-the-art equipment and laboratories
- Seed funding to allow ZNI investigators to pursue innovative research, leading to further external sponsored project support
- Graduate and postdoctoral fellowships to assist in the recruitment of clinical and research leaders of the highest distinction who share our vision of excellence and innovation

Gifts and grants help us meet our nation’s growing demand to improve the quality of life for individuals and society by promoting health, preventing and curing disease and advancing medical research. By applying emerging technologies and forging new partnerships and collaborations, ZNI investigators will continue to lead Keck Medicine of USC into the forefront of medical research and treatment. We hope you will join us in contributing to the future of transformative medicine and patient care.

Christopher Sickels serves as the Senior Director of Development for Brain Sciences and the Zilkha Neurogenetic Institute at the Keck School of Medicine of USC. Please contact him at christopher.sickels@med.usc.edu or call (626) 710-3266 if you would like more information about ZNI funding opportunities.