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Dear Friends,

Some 50 million people in this country—one in five—suffer from brain disorders, including degenerative disorders like Alzheimer’s disease, cerebrovascular disease such as stroke or vascular dementia but also schizophrenia, bipolar disorder and depression.

Scientists have learned more about the brain in the last 10 years than in all previous centuries because of the accelerating pace of research in neurological and behavioral sciences and the development of new research techniques. Yet despite all of our advances, the brain remains the least understood, most complex part of the human body. At ZNI, we are working to change that.

At ZNI we are exploring emerging technologies, innovative imaging capabilities like functional MRI which allows scientists to make microscopic blood flow movies and map the activity of human brains in action. We are looking to diagram brain function in the same detailed way that we map cities, investigating how the billions of neurons in the brain work together. We are improving our existing collaborations and forging innovative relationships with colleagues in divisions, departments and institutes across USC as well as private foundations and industry partners. And so much more.

It is my pleasure to share with you in this report the successes we have achieved over the past year at ZNI. In spite of difficult economic times and budget challenges, we were fortunate to maintain our momentum and successfully meet our goals. By being early adopters of new USC system rollouts, our administrative support team generated further organizational efficiencies. We said goodbye to some old friends and welcomed new faculty. Our scientists have been working hard to submit and secure a record number of proposals while publishing papers in leading scientific journals.

In the coming year we face challenges with funding models, changes that hold promise for even greater efficiencies and progress. We look forward to embarking upon a campaign initiative with a goal to arrest and reverse the effects of Alzheimer’s disease and other neurodegenerative conditions while at the same time, strengthening and securing the Institute’s future for many years to come. We have much work ahead of us but some of the most promising minds in the country to help. We welcome your thoughts and participation.

All the best,

“Today, our scientists are mapping the human brain to unlock the answers to Alzheimer’s… Now is the time to reach a level of research and development not seen since the height of the Space Race.”

—President Barack Obama, 2013 State of the Union
Established in 2003 with the support of the W.M. Keck Foundation and a generous gift from Mr Selim Zilkha, the Zilkha Neurogenetic Institute is an integral part of a broader Keck School of Medicine and USC neuroscience initiative promoting collaboration between researchers from diverse disciplines across campuses and the world. Scientists at the ZNI are breaking boundaries to embrace methods and techniques from other fields of study, identifying new approaches to examine nervous system function so we may all better understand the underlying causes of neurological and psychiatric disorders.

Multidisciplinary by nature, neuroscience at ZNI integrates traditional scientific approaches—including anatomy, physiology and biochemistry—with molecular biology, genomics, biomedical engineering, vascular biology, and translational neuroscience, applying cutting-edge molecular neuroimaging techniques and genetic approaches to understand the functions of nervous system in health and disease. The goals are significant: exploring new ways to identify those at risk, promoting preventive measures, developing innovative therapies and ultimately discovering and translating cures from bench to bedside, for a spectrum of devastating brain disorders from Alzheimer’s disease to schizophrenia.

Join us as we advance the research and therapeutics for brain disease.
ZNI Faculty

Back (L to R): Alexandre Bonnin, Ansgar Siemer, Ralf Langen, Janos Peti-Peterdi, Brian Henderson, Berislav Zlokovic, James Knowles, Greg Field, Derek Sieburth, Alapakkam Sampath, Marcelo Coba

Front (L to R): Kai Wang, Tobias Ulmer, Jeannie Chen, Michele Pato, Karen Chang, Huizhong Tao, Robert Chow, Carlos Pato

Not Present: Daniel Campbell, David Conti, Pat Levitt, Le Ma, Terrence Town, Li Zhang

Photo Credit: Steve Cohn
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<th>Name</th>
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<tr>
<td>Alexandre Bonnin PhD</td>
<td>Assistant Professor Cell &amp; Neurobiology</td>
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<td>Daniel B. Campbell PhD</td>
<td>Assistant Professor Psychiatry &amp; the Behavioral Sciences</td>
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<td>Karen Chang PhD</td>
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<td>Jeannie Chen PhD</td>
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<td>Robert Chow MD PhD</td>
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<td>Marcelo Coba PhD</td>
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<td>David V. Conti PhD</td>
<td>Associate Professor Preventive Medicine</td>
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<td>Greg Field PhD</td>
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<td>James A. Knowles MD PhD</td>
<td>Professor Psychiatry &amp; the Behavioral Sciences</td>
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<td>Ralf Langen PhD</td>
<td>Professor Biochemistry &amp; Molecular Biology</td>
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<td>Carlos Pato MD PhD</td>
<td>Professor and Chair Psychiatry &amp; the Behavioral Sciences</td>
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<tr>
<td>Berislav V. Zlokovic</td>
<td>Director, ZNI Professor and Chair, Physiology &amp; Biophysics</td>
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Clinician Scientist Incubator
William Mack MD
Assistant Professor
Neurological Surgery

Gabriel Zada MD
Assistant Professor
Neurological Surgery

Research Faculty
Zemin Deng PhD
Assistant Professor of Research
Psychiatry & the Behavioral Sciences

Oleg Evgrafov PhD
Assistant Professor of Research
Psychiatry & the Behavioral Sciences

Photo Credit: Steve Cohn
Research at the Zilkha Neurogenetic Institute is broad-based. Scientists at the 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 current topics of study with related 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.

Dr Karen Chang's lab is trying to determine the role nebula plays in ameliorating axonal transport defects associated with Alzheimer's disease; relatedly her group is trying to identify the genotype to phenotype correlations in Down syndrome. Dr Jeannie Chen is studying how Annexin A5 modifies disease progression in a mouse model for Alzheimer's disease.

Dr Berislav Zlokovic’s Center for Degeneration and Regeneration is working on the cellular and molecular mechanisms in blood vessels and the neurovascular unit causing blood-brain barrier disruption which leads to neuronal dysfunction and degenerative changes using models of AD and pericyte-deficient rodents as well as analysis of human brain. His discoveries have contributed to the development of clinical trials based on amyloid-beta clearance in AD patients, and a new therapeutic approach for stroke based on activated protein C mutant circuits.
Psychiatric Genetics

The Center for Genomic Psychiatry investigates the role genes play in disorders of the mind. Dr Marcelo Coba is seeking to understand how modulation of signaling molecules is involved in psychiatric disorders, synaptic function and cognition. Dr Dan Campbell is deploying a Genome Wide Association Study to chart a functional analysis of autism. Dr Alex Bonnin has discovered a crucial role the placenta may play in the developing fetal brain, specifically looking at tryptophan metabolism modulation by maternal infections in pregnancy and separately, the effects of maternal antidepressant treatment on fetal brain development. This research uncovers new pathways for the developmental origins of mental disorders.

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. Dr James Knowles searches for the genetic factors that have an etiological role in psychiatric illness; he recently discovered two loci for panic disorder, but he has also found specific chromosomes linked to obsessive-compulsive disorder (OCD).

Genomics

Dr Kai Wang is working on creating an automated pipeline for whole exome/genome sequencing analysis on Mendelian diseases. His lab also investigates DNA methylation in the malignant transformation of meningiomas. Dr David 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. 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.

Circuits

The aim of Dr Robert Chow’s laboratory is to advance our understanding of how hormone and neuronal secretion is controlled in normal and pathological states. The research in Dr Le Ma’s laboratory attempts to understand the general principles underlying neurite growth, guidance and branching, three key steps in establishing synaptic connection during development. The Derek Sieburth lab combines behavioral, genetic, RNA interference, and live imaging techniques to dissect synaptic function at a systems and molecular level in the C. elegans model. Dr Li Zhang’s research is focused on understanding the structure and function of neural circuits so as to decipher the brain, which includes four aspects: 1) how neural circuits assemble and operate, 2) how circuit structure determines behavioral function, 3) how circuit functions are modulated, as well as 4) how circuit disorders lead to brain disorders. Dr Huizhong Tao’s work also explores establishment and development of functional visual circuits (please see Vision/Eye on the next page).
Vascular

Dr William Mack deploys an experimental strategy to determine the effects of air pollution on acute stroke, which is a leading cause of death and disability worldwide. He is further investigating innovative treatment platforms for rapid delivery of neuroprotective agents to otherwise inaccessible cortical territories in the setting of acute stroke. The broad interest of the Janos Peti-Peterdi lab is renal (patho)physiology, specifically the intrarenal mechanisms involved in the control of blood pressure and body fluid balance under normal and disease conditions (hypertension, diabetes). 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 (AD) and more recently amyotrophic lateral sclerosis (ALS), as foundations for development of new therapies for AD and related neurodegenerative disorders as well as stroke.

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. The goal of the Alapakkam Sampath lab is to correlate the physiological properties of the retina with changes in visually guided behavior. This work will provide insights into how the retina shapes signals that are functionally relevant for vision. 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 how functional visual circuits are established during development. She is currently examining how neural activity of various patterns leads to modulations of synaptic connections and shapes the formation of visual circuits.

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 that great minds come together, exploring new ways to enhance our understanding so we may improve the outlook for future patient care.
Listed below are the notable accomplishments from the previous year.

Alexandre Bonnin

The Bonnin lab made significant progress in understanding how infection during pregnancy (in mice) alters fetal brain neurochemistry. They are currently investigating the physiological and molecular pathways linking the effect of maternal infection on placental physiology and fetal brain development. For this project, Dr Bonnin was awarded an Idea Development Award by the DoD. In parallel, the Bonnin Lab pursued investigations on the effect of antidepressant drug exposure during pregnancy on fetal brain development and the consequences on long-term brain function. These projects aim at understanding the mechanisms of the developmental origins of adult mental diseases.

Daniel Campbell

The Campbell lab reported the first evidence for contributions of non-coding RNAs to autism risk. They continue to focus on understanding the biological impact and the diagnostic potential of non-coding RNAs in autism.

Karen Chang

The Chang lab discovered that a protein overexpressed in Down syndrome and mutated in autism is required for reliable communication between neurons. They are continuing to investigate the function of this protein in order to understand common mechanisms underlying both disorders. In collaboration with Dr. Min atUNIST, Korea, the Chang Lab found that Down syndrome and Fragile X syndrome share common disturbances in the molecular events that regulate the development of dendritic spines.

Jeannie Chen

The Chen lab has made the following scientific advances: (1) The discovery that persistent G-protein signaling causes endoplasmic reticulum stress and photoreceptor cell death (2) The creation of a novel mouse model for age-related macular degeneration.
Robert Chow

The Chow lab made the following exciting discoveries: (1) ruthenium bipyridine complexes injected into the eyes of confirmed-blind Royal College of Surgeon (RCS) rats exhibit visually stimulated electrical activity in the superior colliculus. This may pave the way to a new generation of treatments of blind patients, as well as prosthetic devices, based on light signaling. (2) We have created a novel genetically encoded ratiometric calcium indicator that facilitates quantitative calcium measurements in vitro and in vivo.

Marcelo Coba

The Coba lab helped to define the role of the schizophrenia susceptibility gene TNIK in synaptic signaling and cognitive function. They continue their systems biology studies on synaptic signaling alterations in neurodevelopmental disorders.

Greg Field

The Field lab focused on understanding how the retina, the neural tissue at the back of the eye, transforms visual images into a set of electrical impulses that are sent to the brain. In particular, they have been studying how different types of neurons in the retina transmit different signals to the brain, such as signals containing information about color, motion, or contrast. These neurons are called retinal ganglion cells (RGCs). They have been focusing this year on how the encoding and transmission of these signals by RGCs depends on light level, such as the low light levels encountered during night versus the high light levels encountered during day. They have found that changes in light level have different effects on different RGC types. This discovery has major implications for the development of retinal prosthetics and for our understanding of how the brain processes signals from the retina. They have also been investigating how the function of RGCs is altered in diseases like retinitis pigmentosa and glaucoma. They are discovering that some RGC types are effected earlier than others. This is a significant insight for developing diagnostics and therapies to treat these neural degenerative diseases as early as possible.
James Knowles

The Knowles lab completed data generation for the BrainSpan project and the results are available for the entire scientific community online (www.BrainSpan.org). We were one of the first to demonstrate the feasibility of using RNA-Seq to determine the full complement of genes expressed in a single-cell. We have sequenced ~100 whole genomes of individuals with various psychiatric disorders, and the sequencing of ~700 more are in progress in collaboration with the Broad Institute in Boston. The Knowles Lab received a grant from NHGRI to support continued development and distribution of RseqFlow, and software package to analyze RNA-Seq data. As part of this grant, we have joined the iSeqTools network and are now part of the NHGRI Sequencing Network (formally known as the Human Genome Project).

Ralf Langen

During the past year, the Langen lab further developed electron paramagnetic resonance-based approaches that can be used to visualize the structures of misfolded proteins which are thought to cause Alzheimer’s disease, Parkinson’s disease, Huntington’s disease and type-2 diabetes. It is the ultimate goal of these structural studies to find ways to prevent the misfolding and, thereby, treat the aforementioned diseases. One interesting candidate for these studies are cyclotide-based inhibitors of misfolding that we have developed during the past year in collaboration with the Camarero group.

Pat Levitt

Previous work from the Levitt lab demonstrated that polymorphisms in Met increase the risk for developing Autism Spectrum disorder; furthermore, these polymorphisms are enriched in those individuals with a co-occurring gastrointestinal conditions. Research findings over the past year, further characterized the gastrointestinal dysfunction in ASD and found that functional constipation is the most common type of gastrointestinal condition. Contrary to popular belief, medications and diet are not associated with gastrointestinal dysfunction in individuals with ASD.

Le Ma

The Ma lab has developed a new computer vision method to analyze microtubule dynamics in live cells. They used this method to study microtubule regulation in the growth cones and link it to the CNP signaling in sensory axon development. Using single cell labeling, they have discovered a novel role of Slit/Robo signaling in regulating dendritic development in cerebellar Purkinje cells. Finally, they have completed successful collaborations with scientists to study Slit/Robo signaling in different areas of animal development.

Scientific Advancements
Carlos and Michele Pato

The Pato lab is completing the creation of one of the largest partnerships with patients suffering with schizophrenia and bipolar disorders, and patients with no evidence of psychosis in the Genomic Psychiatry Cohort. This Cohort now numbers over 30,000 individuals world-wide. One of the first initiatives will be the whole genome sequencing of between 2,000 and 3,000 individuals in an attempt to discover new genomic variants. The first phase will be completed with over 1,000 individuals January of 2013. Further, we have genotyped on the 2.5 million illumina snp platform over 10,000 participants, including over 4,000 African-American, and 5,000 Latino members of the cohort.

Janos Peti-Peterdi

The Peti-Peterdi lab continued to study the function of physiologically important renal anatomical structures, the glomerular filtration barrier, the juxtaglomerular apparatus (JGA) and the distal nephron-collecting duct (CD). Over the last year we have identified novel players and molecular mechanisms in these kidney regions that help maintain body fluid and electrolyte homeostasis and control blood pressure. These include the localization and functional characterization of the novel succinate receptor GPR91 both in the JGA and CD and its role in the control of renin synthesis and release, the rate-limiting step in the activation of the renin-angiotensin system. A new direction of research aims to identify novel mechanisms of kidney tissue repair after injury and regeneration by intrinsic renal progenitor cells. This project is based on an innovative technology, our capability to track the fate (proliferation, migration) of specific renal cell lineages in novel transgenic mouse models in vivo in the intact kidney using serial multiphoton fluorescence imaging. The first report on this groundbreaking new technology was accepted for publication in Nature Medicine, the top basic medical research journal.

Alapakkam Sampath

The Sampath lab remains highly interested in understanding how signal transduction and transmission in the outer retina shapes our visual experience. We have shown that the photoreceptor G-protein is interchangeable between rods and cones, and also that the proper wiring of the retinal circuitry is a requirement for optimal signal transfer to control behavior. We have also developed more sophisticated behavioral tests to quantify behavioral threshold in mice.
Derek Sieburth

The Sieburth lab is interested in how signals from the environment can impact behavioral programs by influencing how neurons communicate with each other in the brain. This year the lab discovered that neuropeptides are capable of activating neurons that control a rhythmic behavior by rhythmically opening specific calcium channels at synapses. The lab also discovered that the neurotransmitter acetylcholine can act as a modulator of neuronal function by activating its receptor at sites far away from synapses. Finally, the lab identified a novel molecular link between stress and synaptic transmission in which the activation of a cellular stress response pathway inhibits the function of neurons by blocking synaptic vesicle release.

Huizhong (Whit) Tao

The Tao lab made three important discoveries. First, in the mouse visual cortex they found that orientation selectivity of excitatory neurons is sharpened when the stimulus contrast is increased, as reflected by a reduction of tuning width. Contrary to a conventional idea of contrast-invariance, the data suggest that the quality of cortical processing is improved with increasing stimulus strength. Second, with intracellular voltage-clamp recordings, they found that while orientation tuning of excitatory input to layer 4 neurons is not changed with increasing stimulus contrast, the tuning of inhibitory input becomes broadened. In addition, the strength of both excitation and inhibition increases with increasing contrast. With neuron modeling, they demonstrated that the broadening of inhibitory tuning is critical for the sharpening of orientation selectivity of output response. Third, using in vivo two-photon imaging guided targeted recording from genetically labeled inhibitory neurons, they found that parvalbumin-positive inhibitory neurons exhibit a very different contrast-dependent change from excitatory neurons: their orientation selectivity becomes broadened as contrast increases. This change results in a broadening of summed inhibitory input to excitatory neurons. Together, their results indicate a critical inhibitory synaptic mechanism for maintaining sharp visual perception across a wide range of stimulus strength.

Terrence Town

The Town lab joined ZNI on May 1, 2013. The Town lab’s focus is to develop 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, my 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. Dr. Town’s lab is continuing to pursue this line of research in hopes of developing a next-generation drug for Alzheimer’s disease. Earlier this year, the Town 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, they 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.
Tobias Ulmer

The Ulmer lab examined the initial event in the misfolding of the prevalent neuronal protein α-Synuclein by molecular dynamics simulations. A mechanism for forming amyloid fibrils was identified. This aids the understanding of the molecular chain of events that underlie Parkinson disease. In addition, we characterized the regulatory domain of the human brain enzyme carnitine palmitoyltransferase 1. This enzyme controls feeding behavior in mammals.

Kai Wang

The Wang lab has established two automated workflows for the analysis of whole genome/exome sequencing data and RNA-Seq data. The first workflow is SeqMule, which takes raw FASTQ files from sequencers, and process it with dozens of software tools, and generated VCF files with called mutations. The second workflow is RSeqMule, which takes raw FASTQ files from sequencers, and process it with alignment and transcript quantification methods, and generate detailed expression report for every gene or transcript.

Li Zhang

The Zhang lab starts to produce results from the exploring of the auditory processing at the different stages along the auditory ascending pathway, including cochlea, cochlear nuclears, inferior colliculus and the auditory cortex. Using auditory system as a model, they try to establish the whole logics governing the sensory information processing from periphery to central, as well as its regulation.

Berislav Zlokovic

The Zlokovic lab developed a new compound that was shown to inhibit the Receptor for Advanced Glycation Endproducts (RAGE) in mice. RAGE is a molecular factor that causes the type of inflammation and vascular problems of the brain and propagation of amyloid-beta toxin seen in people with Alzheimer’s disease. Dr. Zlokovic and his team reported the results of a study investigating why a gene called ApoE4 makes people more likely to develop Alzheimer’s disease. They found that the gene’s presence makes it more probably that toxic substances will leak from blood vessels into the brain, damaging neurons and reducing blood flow. Preclinical studies contributing to understanding of the role of a chronic blood-brain barrier disruption in the pathogenesis of neurodegenerative disorders including loss of pericytes in Alzheimer’s disease and ALS were conducted. Additionally, Phase 1 study with 3k3A-apc for stroke patients was successfully completed as were the preclinical studies contributing to development Phase 2 studies with 3k3Apc for stroke patients. Also, the Zlokovic lab saw the development of a new lipoprotein receptor-mediated peripheral sink therapy for Alzheimer’s disease based on amyloid-beta clearance.
Collaborations
Alexandre Bonnin

Gerard Karsenty of Columbia University; collaborating on a study related to the role of a bone-derived molecule in fetal brain development.

George Anderson of Yale University; collaborating on work related to fetal, placental and maternal measures of biogenic amines.

Robert Schwarcz of Uni. of Maryland; collaborating on work related to fetal, placental and maternal measures of specific biogenic amines.

Brett Lund of USC, Dept. of Neurology; investigating the effect of maternal infection on fetal cytokine levels.

James Knowles of Zilkha Neurogenetic Institute; working on single-cell transcriptome analysis of human placental cell types.

Skyla Herod of Azusa Pacific College; studying placental and fetal brain development in serotonin transporter knockout mouse model.

Jerold Chun of The Scripps Institute; collaborating on a project related to the role of lipids in fetal brain development.

Daniel Campbell

James Knowles of Zilkha Neurogenetic Institute; studying gene expression changes caused by non-coding RNAs.

Kai Wang of Zilkha Neurogenetic Institute; studying gene expression changes caused by non-coding RNAs.

Gerry Coetzee of USC, Dept. of Urology; collaborating on strategies for following up genome wide association study hits in autism.


Kevin V. Morris of The Scripps Institute; studying the molecular mechanisms of non-coding RNAs.

Judy Van de Water of UC Davis; collaborating on 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.

Jeannie Chen

Amy Lee of USC, Dept. of Biochemistry and Molecular Biology; investigating the role of endoplasmic reticulum stress in certain blinding disorders.

Ralf Langen of Zilkha Neurogenetic Institute; investigating amyloid structures in eyes affected with macular degeneration and exploring therapeutic agents to dissolve these structures.

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 the 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

Ralf Langen of Zilkha Neurogenetic Institute; 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. They are working together on a pilot grant funding from USC’s NIH-funded Alzheimer’s Disease Research Center and the Clinical and Translation Science Institute, and they intend to apply for R01 funding based on the data collected in the next year.

Janos Peti-Peterdi of Zilkha Neurogenetic Institute; collaborating on a project about the molecular control of renin secretion, which leverages Dr. Chow’s expertise in synaptic protein biology and Dr. Peti-Peterdi’s expertise in renin biology.

Derek Sieburth of Zilkha Neurogenetic Institute; mentoring members of Dr. Sieburth’s lab in fluorescence imaging and patch clamp electrophysiology for studies of C elegans neurotransmission.

Jeannie Chen of Zilkha Neurogenetic Institute; Dr. Chen’s lab is testing the Chow lab’s new genetically encoded ratiometric calcium indicator in retina, and Dr. Chow’s lab is performing experiments testing the indicator in cells in culture, as well as in retinal slices.

James Knowles of Zilkha Neurogenetic Institute; collaborating to study transcriptome variability among ostensibly identical and non-identical cells, in order to validate the newest generation of RNA-Seq platforms. They 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, Dept. of Ophthalmology; collaborating on the Biomimetic Microelectronic Engineering Systems Engineering Research Center on two projects: 1) Retinal Prosthesis, and 2) Cellular Prosthesis.

Koping Kirk Shung of USC, Viterbi School of Engineering; working 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

Marco Bortolato of Kansas University; collaborating on the role of NMDAR signaling in the pathophysiologica processes underlying impulsive aggression and related neurodevelopmental disorders (autism-spectrum disorder, ADHD, Tourette syndrome).

James Knowles of Zilkha Neurogenetic Institute; studying the role of synaptic signaling complexes in Obsessive compulsive disorder.

Stephanie Dulawa of University of Chicago; studying the role of synaptic signaling complexes in Obsessive compulsive disorder.

Thomas O’Dell of UCLA; collaborating on the role of TNiK and Dlgap1 protein complexes in synaptic plasticity and learning and memory.

Chao Zhang of USC; investigating the chemical genomics approaches to the study of protein kinase signaling.

Ted Abel of University of Pennsylvania; studying the role of Shank3 and AKAP signaling mechanisms associated to neurological disease.
David Conti

Graham Casey and Fred Schumacher of USC Dept. of Preventative Medicine; investigating the role of genetic variants in colon cancer risk using genetic association studies and functional assays.

Fred Gilliland and Jim Gauderman of USC Dept. 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 Zilkha Neurogenetic Institute; examining genetic sequence data to identify variants involved in schizophrenia.

Wendy Cozen of USC Dept. of Preventative Medicine; through genetic association studies they are investigating the role genes play in multiple myeloma and Hodgkin’s lymphoma.

Neal Benowitz of UCSF, 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 Dept. 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 Sergey Nuzhdin of USC Dept. 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, Dept. 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, Dept. of Neurology; investigating the impact of genetics in Multiple Sclerosis using a Hispanic population sampled in Los Angeles and novel statistical methods.
Collaborations

**Greg Field**

*Alexander Sher of UC Santa Cruz; collaborating on the development of advanced, large-scale neuronal recording technologies.*

*Edward Callaway of the Salk Institute and Nicholas Brecha of UCLA; working to use engineered viruses to inactivate neurons in the retina to reveal their function.*

*E.J. Chichilnisky of Stanford University; investigating the effects of glaucoma on retinal ganglion cell physiology.*

*Jeannie Chen of Zilkha Neurogenetic Institute and Norberto Grzywacz of USC; investigating the effects of retinitis pigmentosa on retinal ganglion cell physiology.*

**James Knowles**

*Carlos and Michele Pato, Robert Chow, Derek Sieburth, Kai Wang, Li Zhang, Marcelo Coba, David Conti, Chris Haiman, William Mack, Alexandre Bonnin, and Pat Levitt of Zilkha Neurogenetic Institute; collaborating on various projects.*

*Oleg Evgrafov, Zemin Deng, Ting Chen, Ewa Deelman, Ann Chervenak, Peter Laird, Ben Berman, Jonathan Buckley, Graham Casey, Colin Dias, Mike Kahn, Carl Kesselman, Helena Mederios, Pragna Patel, Jerold Shinbane, Melissa Wilson and Emily Liman of USC; collaborating on various projects.*

*Myrna Weissman and Abby Fyer of Columbia University, Steve Hamilton of UCSF, and Mark Logue of Boston University; studying panic disorder.*

*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 the NIH, Carol Matthews of UCSF, Stephanie Dulawa of University of Chicago, and Evelyn Stewart of University of British Columbia; studying Obsessive-Compulsive Disorder (OCD).*

*Doug Levinson of Stanford University, Myrna Weissman of Columbia University, James Potash and Bill Coryell of University of Iowa, Bill Schetfner of Rush University, Bill Lawson of Howard University, Peter Holmans of Cardiff University, Ray DePaulo of Johns Hopkins University, and Doug Blackwood and Mohammad Ayub of University of Edinburgh; working on Early-Onset Major Depression.*

*Ayman Fanous of the Washington DC, Veterans Administration and Doug Blackwood and Mohammad Ayub of University of Edinburgh; studying Schizophrenia.*

*Ed Lein and Michael Hawrylycz of Allen Institute for Brain Science, Nenad Sestan and Mark Gerstein of Yale University, and Joel Kleinman, Danny Weinberg, Tom Hyde and Richard Straub of the NIMH and the Lieber Brain Institute; collaborating on BrainSpan.*
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 Zilkha Neurogenetic Institute; combining NMR and EPR-based approaches to determine structures of amyloidogenic proteins involved in neurodegeneration.

Martin Kast of USC, Dept. of Molecular Microbiology & Immunology; investigating membrane-bound annexin A2 complexes as receptors for HPV entry.

Jonah Chan of UCSF; 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, Dept. 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

Pat Levitt
Shri Narayanan of USC, Viterbi School of Engineering; developing a program in children with autism to test methods for extracting social and communication data from high resolution videos. They also are testing wireless methods for monitoring autonomic states in children with autism.

Michele Kipke of Children’s Hospital Los Angeles; studying a population of children with autism and gastrointestinal disorders for unique genetic and other biomarkers that help define this subpopulation.

Takahiro Ohyama of Zilkha Neurogenetic Institute; studying the impact of Met receptor tyrosine kinase signaling on inner ear development. They have created a unique mouse model in which the Met gene is deleted specifically from the developing tissues of the inner ear to examine this.

Evon Lee and BethAnn McLaughlin of Vanderbilt University; through a collaborative grant from NICHD, they are working on a project to characterize children with autism and co-occurring gastrointestinal disorders.

Randy Blakely of Vanderbilt University; through a NIHM Conte Center project, they are studying the role of maternal and paternal serotonin on fetal brain development.

Dan Geschwind of UCLA; studying the interaction between autism and language disorder genes at the experimental level, including MET, CNTNAP2, PLAUR and FOXP2. The studies examine how the master regulator FOXP2 controls the expression of the other autism risk studies.

Kai Wang of Zilkha Neurogenetic Institute; using bioinformatics and statistical genetics approaches to examine gene networks that are implicated in autism and co-morbid medical conditions.

Mariaintina Gotsos of USC, School of Cinematic Arts; working on using interactive technologies for communicating policy issues regarding brain and child development to the public and policy makers. This project is being done in collaboration with the Center for the Developing Child at Harvard.

Nathan Fox of University of Maryland; collaborating on an NIH-funded project to study the development of social behavior in human infants and in mouse models in which genes underlying social behavior are deleted.
Le Ma

Oscar Marin of Instituto de Neurociencias de Alicante & Universidad Miguel Hernandez; researching the role of Slit/Robo signaling in neurogenesis.

David Ginty of HHMI/Johns Hopkins University; studying the regulation of Slit signaling by dystroglycan.

Xin Sun of University of Wisconsin, Madison; investigating Slit/Robo signaling in foregut development.

Li Zhang of Zilkha Neurogenetic Institute; studying the guidance and targeting of spiral ganglion neurons during ear development.

Alain Chedotal of Universite Pierre et Marie Curie-Paris 6; investigating the role of Slit/Robo signaling in postnatal brain development.

Joshua Sanes of Harvard University; investigating the genetic interaction between Slit/Robo and protocadherin in dendrite self-avoidance.

William Mack

Kai Wang of Zilkha Neurogenetic Institute; collaborating on studies characterizing genetic and epigenetic signatures of Meningiomas.

James Knowles of Zilkha Neurogenetic Institute; 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 Zilkha Neurogenetic Institute; collaborating on a large study designed to evaluate cellular heterogeneity of temporal and cerebellar cells using patchclamp and RNA-Seq of single cells.

Photo Credit: Steve Cohn
Collaborations

Carlos and Michele Pato

*Steve McCarroll of Harvard and The BROAD Institute;* collaborating on extensive sequencing and genotypic projects.

*Michael Boehnke of University of Michigan;* working on the BRIDGES project on sequencing in Bipolar Disorder.

*Mark Rapaport of Emory University;* working on immune activated states in psychosis.

*Laura Bierut of Washington University;* studying substance Use and abuse in the Genomic Psychiatry Cohort.

*Pamela Sklar of Mt. Sinai;* creating a cohort of 30,000 individuals at USC for genomic studies and using next generation sequencing in multiple large scale population studies.

*Oleg Egrafov of Zilkha Neurogenetic Institute;* studying olfactory neurons in psychiatric patients.

*Carl Kesselman of USC, Viterbi School of Engineering;* developing the informatics infrastructure for the Partners in Health and Discovery.

*Kai Wang of Zilkha Neurogenetic Institute;* using bioinformatics and statistical genetics approaches to examine gene networks that are implicated in a variety of conditions.

*James Knowles of Zilkha Neurogenetic Institute;* using next generation sequencing in multiple large scale population studies.

*David Conti of Zilkha Neurogenetic Institute;* using next generation sequencing in multiple large scale population studies.

*Susan Roseof USC, Office for Human Research Protections;* developing the ethical profile for the Partners in Health and Discovery.

*Jordan Smoller of Harvard University, Peter Buckley of Medical College of Georgia, Dolores Malaspina of New York University, Evelyn Bromet of SUNY Stonybrook, and Maria Helena Azevedo of University of Coimbra Portugal;* collaborating on an NIH-funded project creating a cohort of 30,000 individuals at USC for genomic studies and using next generation sequencing in multiple large scale population studies.
Janos Peti-Peterdi

Michael Caplan of Yale University and Jennifer Pluznick of Johns Hopkins University; collaborating on the role of olfactory receptors in the kidney.

Andrew McMahon of USC; using optogenetic tools in the living mouse kidney in vivo, and analysis of the molecular fingerprint of macula densa cells, a chief renal cell type.

Genevieve Nguyen of College de France; studying the role of the prorenin receptor in macula densa cells.

Jan Danser of Erasmus University; studying the role of the prorenin receptor in macula densa cells.

Dominique Eladari and Regine Cambrey of INSERM; working on characterizing 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 endothelial glycocalyx.

Thomas Benzing of University of Cologne; collaborating on calcium imaging of podocytes in vivo.

Akira Nishiyama of Kagawa University; studying the glomerular filtration of angiotensinogen.

Joris Robben of University of Nijmegen; investigating the role of the novel metabolic receptor GPR91 in distal ion transport.

Attila Szabo and Agnes Prokai of Semmelweis University; studying multiphoton imaging of the effects of calcineurin inhibitors in the kidney.

Laura Perin of Childrens 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 renin-angiotensin system.

Rudy Ortiz of UCMerced; 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.

Alapakkam Sampath

Carter Cornwall of Boston University; working to establish the role of electrical conductances in photoreceptors for setting the sensitivity following bright light exposure.

Kirill Martemyanov of Scripps Florida; studying the role of the proteins RGS7 and RGS11 in signal transduction in ON bipolar cells. Current work is now focusing on determining the concentration dependence on this effect using conditional knockouts, as well as behavioral testing to determine how visual performance is affected.

Nikolai Artemyev of University of Iowa; identifying a novel role for the G protein transducin in the synaptic release machinery at the rod synapse that controls visual sensitivity.

Collaborations
Derek Sieburth
James Knowles of Zilkha Neurogenetic Institute; are sequencing entire genomes of the nematode C. elegans to identify mutations that cause defects in synaptic transmission.

Robert Chow of Zilkha Neurogenetic Institute; 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 Zilkha Neurogenetic Institute; studying the structure and dynamic of toxic huntingtin fibrils.

Kausik Si of Stowers Institute for Medical Research; studying the structure of the functional amyloid Orb2 responsible for long-term memory.

Huizhong (Whit) Tao
Josh Z. Huang of Cold Spring Harbor; researching functional properties of inhibitory neurons.

Gage Crump of USC, Dept.of Cell and Neurobiology; studying a generation of inhibitory neurons specific zebrafish reporter line.

Li Zhang of Zilkha Neurogenetic Institute; studying common inhibitory mechanisms underlying visual and auditory cortical processing.
Collaborations

Terrence Town

Erol Fikrig of Yale University; collaborating on how to interrogate neuro-immune mechanisms of West Nile encephalitis.

Richard A. Flavell of Yale University; collaborating on developing mouse models with human immune systems as a critical tool to examine stem cell graft tolerance vs. rejection.

Pasko Rakic of Yale University; working with Dr. Rakic, whose wide-reaching expertise in neurobiology has been invaluable for understanding cellular biological aspects of the Town lab’s rodent models of neurodegenerative disease.

Eliezer Masliah of UCSD; collaborating on developing and characterizing rodent models of Alzheimer’s disease.

Caleb ‘Tuck’ Finch of USC; working together to understand different forms of neuroinflammation.

Helena Chui of USC, Dept. of Neurology; working to validate observations that Dr. Town has made in mouse models using human Alzheimer patient samples.

Berislav Zlokovic of Zilkha Neurogenetic Institute; collaborating on a project together to extend his findings with the blood-brain-barrier into a novel Alzheimer transgenic rat model.

Tobias Ulmer

Mark Ginsberg of UCSD; collaborating on the integrin receptor cell biology.

Stanley Opella of UCSD; collaborating on the integrin receptor membrane immersion.

Kai Wang

William Mack and Gabriel Zada of Zilkha Neurogenetic Institute and USC, Dept. of Neurosurgery; working to perform integrative analysis on DNA methylation, DNA copy number change and whole-genome gene expression in malignant and benign meningiomas.

Wange Lu of USC, Broad CIRM Center; researching the functional impact of NRXN1 and NLGN4 deletions in neurodevelopment, using neural stem cell models and next-generation sequencing techniques.

Gary Chen of USC Dept. of Preventive Medicine; working to develop a copy number alteration calling algorithm for tumor samples, as well as a copy number variation calling algorithm for next-generation DNA/RNA sequencing data.

Yufeng Shen of Columbia University; developing novel next-generation sequencing techniques to examine V(D)J recombination of the immune repertoire in human peripheral blood.
Li Zhang

Pin Wang of USC, Dept. of Engineering; investigating engineering of viral vector for controlling the activity status of brain.

Jonah Chan of UCSF; studying myelination of cortical inhibitory neurons during development.

Huizhong Tao of Zilkha Neurogenetic Institute; investigating imaging processing in the visual cortex.

Le Ma of Zilkha Neurogenetic Institute; studying the role of axonal guidance molecules in the formation of the spatial and functional organization of the cochlear.

Berislav V. Zlokovic of Zilkha Neurogenetic Institute; investigating the impact of brain vascular defects on the functional cortical circuitry.

Berislav Zlokovic

Arthur Toga of USC, Institute for Neuroimaging and Informatics; Paul Thompson of USC, Depts. Neurology, Psychiatry, Behavioral Sciences and Engineering; Scott Fraser of USC, Depts. 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 Disease Research and Clinical Center and the Pharmacology program of USC NIH Alzheimer’s Disease Research Center; Terrence Town of Zilkha Neurogenetic Institute; Hong-Wei Dong of Zilkha Neurogenetic Institute and Institute of Neuroimaging and Informatics; 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; These investigators are currently developing USC Interdisciplinary Program in Research and Treatment of Alzheimer’s disease with a goal to position USC as a world leader in studying the role blood-brain barrier and vascular damage in human and animal brain in relation to neuronal dysfunction, cognitive decline, neuronal degeneration and neuronal loss using state-of-the art human brain neuroimaging, mapping brain structure and function, mathematical, computer science and software engineering to generate human and mouse brain atlases, and imaging the molecular signals, cell motions, and tissue morphogenesis using advanced imaging technologies that can be used in developing experimental therapeutics for Alzheimer’s disease and studying the effects of drugs on mental processes and behavior.

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. Just renewed their former Javits grant.

John Griffin of Scripps Institute; working on manufacturing and testing new APC variants for stroke.

William Mack of Zilkha Neurogenetic Institute; 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 constants in neurologically normal and MS patients and patients at risk for Alzheimer’s disease.

Collin 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. Biological Sciences and Biomedical Engineering and Andy McMahon of USC, Broad CIRM Center; working on the installation of serial two-photon tomography, cutting-edge equipment that allows for fully automated brain imaging

Scott Fraser of USC, 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 Zilkha Neurogenetic Institute; 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 trial with 3K3A-APC, as well as on brain organoids.
Collaborations

Berislav Zlokovic, cont’d

*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 in 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 Zilkha Neurogenetic Institute;* studying pericytes in the rat model of Alzheimer’s disease

*Dean Pinchas Cohen of USC, Davis School of Gerontology;* initiated discussions on MSD biomarkers of vascular injury, angiogenesis, immune response and inflammation in patients at risk for Alzheimer’s disease and individuals with mild cognitive impairment and Alzheimer’s disease.

*Pat Lyden of Cedars Sinai;* working on Phase 2 clinical trial for stroke with 3K3A-APC.

*Ron Peterson of Mayo Clinic;* initiated discussions on collaboration on biomarkers for Alzheimer’s disease.

*Gujon Bu of Mayo Clinic Florida;* collaborating on lipoprotein receptor-mediated clearance of amyloid-beta across the blood-brain barrier.

*Peter Carmeliet of Vesalius Research Center (VIB) of KU Leuven;* studying the role of glucose metabolism in brain endothelium during stroke.

*Caleb Finch of USC;* examining the blood-brain barrier permeability in 5FAD mice on different apoE genotypes.

*Leslie Weiner and Wendy Gilmore of USC;* studying the 3k3apc treatment for multiple sclerosis.

*David Baron and Daniel Holschneider of USC;* initiated discussions on 3k3apc treatment for repetitive traumatic brain injury.
New 600 MHz Solid-State NMR Spectrometer Installed at ZNI

After waiting for over one year, Dr. Ansgar Siemer recently accepted delivery of a 600 MHz Agilent solid-state nuclear magnetic resonance (NMR) spectrometer. Ordered in FY12 and custom-built, the one-ton device is the only solid-state NMR spectrometer at USC and the most modern and powerful instrument of its kind in LA County. This instrument adds tremendously to the capabilities to Dr. Siemer’s research group and the Protein Structure Center at ZNI as a whole.

A solid-state NMR spectrometer is an emerging technology to study non-soluble matter with atomic resolution that is very difficult to investigate with any other method. Important samples in a biomedical context are membrane proteins or amyloid fibrils which is the focus of the Siemer lab. NMR spectroscopy is a radio wave spectroscopy that requires a very strong magnetic field which is produced by a superconducting magnet shown in the picture. Inside this, the magnetic field samples can be excited with radio frequency pulses and consequently send radio frequencies back to the spectrometer. From this process we can learn not only about the atomic structure but also about the dynamics of the sample. The results from these solid-state NMR experiments are very complementary to data obtained from the labs of Dr. Tobias Ulmer (who uses a liquid-state NMR) and Dr. Ralf Langen (accessing electron paramagnetic resonance) in the Protein Structure Center of the ZNI.

The Siemer lab is using this spectrometer to investigate both amyloid fibrils that are known to cause neurodegenerative diseases such as Alzheimer’s and Huntington’s Disease and different amyloid fibrils that were found to cause no harm but are functional. One of the most important goals of the lab is to understand what distinguishes pathological and functional amyloid fibrils. Understanding the difference between these types of amyloid could lead to the development of new therapeutics and will deepen our understanding of the role of amyloid in biology.

The Siemer lab will be making this new technology accessible to other researchers at USC that are interested in getting structural data from systems that are difficult to be studied with any other method.
In March 2013 Terrence Town PhD, previously at Yale University and most recently Cedars-Sinai Medical Center, joined ZNI as Dr Zlokovic’s first faculty recruit. Dr Town's primary focus is to develop and mechanistically interrogate neurogenetic models of disease, with a specific interest in the immune system and inflammation as related to Alzheimer Disease (AD). He is considered an intellectual leader in the fields of neuroimmunology and neuro-inflammation, and has published over 100 papers, with nearly 20 years of experience in the fields of basic and translational immunology, neurobiology, and inflammation. Dr Town currently holds one R01, one R21, a grant from the California Institute for Regenerative Medicine, and awards from the Alzheimer’s Association of America and the American Federation of Aging Research. The recruitment of Dr Town as a transformative faculty was greatly assisted by the generous support of Mr Selim Zilkha, USC Provost Elizabeth Garrett and Dean Carmen Puliafito.

In early 2013, after having been instrumental in the formation of the Zilkha Neurogenetic Institute for 10 years, former Dean of the Keck School of Medicine of USC and renowned epidemiologist Brian Henderson MD officially relocated his research operations from ZNI to the Norris Comprehensive Cancer Center (NCC). Joining Dr Henderson at NCC is Christopher Haiman DSc, who conducts genome wide association studies of breast and prostate cancer in African American women and men respectively. This was a long-planned move of their operations to the more-fitting home of NCC and comes at a time when ZNI, under the leadership of Dr Zlokovic, has begun to re-focus, on the core mission of the Institute: investigating the biology and genetics of Alzheimer’s and other neurogenetic diseases.

In June 2013, Pat Levitt PhD, Provost Professor and former Director of ZNI, began the process of relocating his research laboratory to the Saban Research Institute at Children’s Hospital Los Angeles (CHLA). CHLA will provide Dr Levitt more opportunities to expand his successful program, investigating the development of brain architecture that controls learning, emotional and social behavior, especially Autism Spectrum disorder, through research in animals and children.

In October 2012, ZNI welcomed a second physician-scientist from the department of Neurosurgery to our Clinician-Scientist Incubator Lab. Gabriel Zada MD who is an expert in neurosurgery, traumatic brain injury and brain tumors will develop his research program at ZNI. The next fiscal year will present new opportunities for additional faculty recruitment with the department of Otolaryngology. Neuroscientists who are examining noise-induced hearing loss, physical and physiological basis of sensory transduction in the inner ear, and the molecular mechanisms of inner ear development fit well with ZNI’s basic science program. Additionally, we anticipate strong partnerships in the areas of neuroimaging with Arthur Toga PhD and Paul Thompson PhD of the Institute for Neuroimaging and Informatics at USC, specifically using mouse brain to provide accurate and reliable knowledge of the nervous system’s basic wiring diagram at the structural level.
Outside of this reporting period (in the summer of 2013), Hong-Wei Dong MD PhD, will move his lab from UCLA to ZNI, as part of a larger recruitment of Dr Toga’s group. Dr Dong, who will have a joint appointment in Neurology, has an R01 which aims to create a three-dimensional, Google Earth-like, digital Connectome atlas of the C57Black/6J mouse brain to provide accurate and reliable knowledge of the nervous system’s basic wiring diagram at the structural level.

Also in the summer of 2013, ZNI will welcome three investigators formerly associated with the House Research Institute. Rick Friedman MD PhD, who will hold a joint appointment in Otolaryngology, will move his lab to ZNI. He has an R01 which studies noise-induced hearing loss using high-resolution mapping strategies to comprehensively define loci that contribute to strain variation in phenotypes. Takahiro Ohyama PhD and Radha Kalluri PhD will also relocate their laboratories from House Research Institute to ZNI. Both will hold joint appointments in Otolaryngology. Dr Ohyama has an R01 that just started this year and Dr Kalluri has an R03 that that runs for three more years. A major goal of research in the Ohyama lab is to understand the molecular mechanisms of inner ear development at to explore the possibility of regenerating sensory cells to treat balance and hearing disorders. Dr Kalluri’s research focuses on understanding the physical and physiological basis of sensory transduction in the inner ear.

We will expand on the work of these individuals in the next annual report but in the meanwhile we wish our departing investigators continued success as we eagerly welcome these new faculty to ZNI.
Over the course of the year, many of ZNI’s faculty members have received individual accolades for their research achievements and activities. Some of these awards and activities from FY13 are noted below.

**Alexandre Bonnin**

Dr. 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 to several national and international symposia (including those held in France, Italy, Australia). Dr. Bonnin is also a member of the USC Institutional Biosafety Committee.

**Daniel Campbell**

Dr. Campbell was featured in both the 24th Annual Dr. Richard N. Boylan Memorial Lecture in Riverside, CA and the International Meeting For Autism Research in San Sebastian, Spain.

**Jeannie Chen**

Dr. Chen was a reviewer for the NIH BVS study section. She was also a part of the Scientific Advisory Board of the Karl Kirchgessner Foundation.

**Robert Chow**

Dr. Chow served as a mentor for the following programs: CIRM summer internship, CIRM Bridges Internship, Bridging the Gaps: Bench to Beside Summer Research Program, Engineering Research Center, and Engineering Health Academy. Additionally, Dr. Chow has the following two new patients: USC File No. 13-170: “Medical Imaging Apparatus and Method for Determining Cancer Invasiveness” and USC File No. 13-394: “Photoactivated Molecules for Light-Induced Depolarization of Retinal Ganglion Cells and Other Targeted Cell Types: Molecular Structure, Mechanism and Method for Targeted Delivery, Activation & Inactivation”.

Faculty Activities
**Ralf Langen**

Dr. Langen served as editor for the Journal of Biological Chemistry and reviewer for NIH study sections.

**William Mack**

Dr. Mack was elected to the Society of Neurointerventional Surgeons Board of Directors and was appointed an Associate Scientific Advisor for the journal Science Translational Medicine.

**Janos Peti-Peterdi**

Dr. Peti-Peterdi served as the director of the USC Multiphoton Microscopy Core. He also established the institutional research base for a new kidney research center and applied for NIH funding for the center (P30 USC O’Brien Kidney Research Center).

**Alapakkam Sampath**

Dr. Sampath participated in Bridging the Gaps: Bench-to-Bedside Summer Research Program. Additionally, he was the Associate Co-Director of the Neurosciences Graduate Program and directed an NRSA Grant Writing Workshop for students to write F31 Individual Training Grants from the NIH.

**Ansgar Siemer**

Dr. Siemer served on USC’s PIBBS (Programs in Biomedical and Biological Sciences) admission committee.

**Berislav Zlokovic**

Dr. Zlokovic was named the inaugural Zilkha Senior Scholar at ZNI by Dean Carmen A. Puliafito. The appointment recognizes scholars who have made major contributions to the body of research on brain disease, and Dr. Zlokovic will hold the title for two years.
Since July 2012, **23 ZNI PIs** submitted 74 proposals to federal agencies (primarily NIH but also NSF and DoD) and 38 to private foundations for awards or fellowships. ZNI PIs submit an average of 6-7 proposals per month.

### Total Number of Active Grants for FY13

<table>
<thead>
<tr>
<th>Type</th>
<th>Number</th>
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</thead>
<tbody>
<tr>
<td>Non-Federal Fellowship</td>
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<tr>
<td>Federal Fellowships</td>
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<tr>
<td>Federal Grants</td>
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<tr>
<td>Foundation/Private Grants</td>
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<tr>
<td>Industry Grants</td>
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<tr>
<td><strong>Total</strong></td>
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### 2013 Annually Sponsored Awards

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<tr>
<th>Type</th>
<th>Amount</th>
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<tr>
<td>Federal Awards</td>
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<tr>
<td>Private Foundation Awards</td>
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<tr>
<td>Industry</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>$18,447,570</strong></td>
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As noted in the Faculty News section, in a long-planned move, Brian Henderson MD and Chris Haiman DSc relocated their research operations from ZNI to the Norris Comprehensive Cancer Center early in 2013. As epidemiologists conducting genome wide association studies of breast and prostate cancer, their grants portfolio was administered by ZNI administration while we hosted them at the Institute. When we “correct” the FY12 total grant awards by subtracting the cancer research grants, a new baseline is drawn to concentrate on neuroscientists investigating the biology and genetics of Alzheimer’s and other neurogenetic diseases. Comparing FY13 awards against this adjusted baseline demonstrates a steady funding stream from one year to the next, which is remarkable given the current federal funding climate:

| Sponsored Projects FY12 to FY13 |
|---|---|---|
| $18,337,564 | $18,447,570 |

<table>
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<tr>
<th>Direct Costs</th>
<th>F&amp;A Costs</th>
<th>Total Costs</th>
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<tbody>
<tr>
<td>FY12 Adjusted</td>
<td>$12,721,902</td>
<td>$5,615,662</td>
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<tr>
<td>FY13</td>
<td>$12,613,663</td>
<td>$5,833,907</td>
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Number of Awards by NIH Institute/Center:

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<th>Institute/Center</th>
<th>FY13</th>
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</thead>
<tbody>
<tr>
<td>National Institute on Deafness and Other Communication Disorders (NIDCD)</td>
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</tr>
<tr>
<td>National Cancer Institute (NCI)</td>
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</tr>
<tr>
<td>National Eye Institute (NEI)</td>
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<tr>
<td>National Human Genome Research Institute (NHGRI)</td>
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<tr>
<td>National Heart, Lung, Blood Institute (NHLBI)</td>
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</tr>
<tr>
<td>National Institute on Aging (NIA)</td>
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<tr>
<td>National Institute on Drug Abuse (NIDA)</td>
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<tr>
<td>National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)</td>
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<td><strong>Total Federal</strong></td>
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2013 ZNI Sponsored Projects by Federal Agency
New Faculty Awards & Honors

**Dan Campbell PhD** was awarded in February 2013 a 2-year R21 from the NIMH "Non-Coding RNAs in Autism" and a 4-year R01 from the NIMH for $1.6M "Biology of Non-Coding RNAs Associated with Psychiatric Disorders".

**Karen Chang PhD** was the recipient of a Jerome Lejeune Foundation award in 2013 to study “Systematic Analysis of Genes Contributing to Synaptic defects in Down Syndrome”.

**Robert Chow MD PhD** received in March 2013, a research grant from the NEI BRP for “Experimental and Clinical Investigations of Retinal Stimulation”. Dr Chow is co-I on a $8M U01 with James Knowles (please see below).

In his first year at ZNI, **Greg Field PhD** was awarded a new grant from the Kirchgessner Foundation in March 2013 which followed an award he received in December 2012 from the Whitehall Foundation.

**James Knowles MD PhD** received in September 2012, a multi-PI U01 from NIMH "Evaluation of Cellular Heterogeneity Using Patchclamp and RNA-Seq of Single Cells". Bob Chow is co-I on this $8M award. In the same month, Dr Knowles obtained a grant from the International OCD Foundation to study "Replication of Genome-wide Association Findings of OCD".

**Ralf Langen PhD** was given in 2013 a gift from the Batey Family Foundation to study "Prevention of Misfolding and Membrane Permeabilization in Parkinson’s and Other Neurodegenerative Diseases".

In addition to two awards and a fellowship **William Mack MD** received a year prior, he obtained in April 2013, a pilot grant from the Southern California Environmental Health Sciences Center to study "Airborne Particulate Matter from Vehicular Exhaust in the Setting of Acute Stroke".

**Carlos Pato MD** successfully obtained a supplement to his existing Genomic Psychiatry Cohort expanding the research program for two years. **Michele Pato MD** was the recipient of a subcontract from University of Kansas for "Role of 5-alpha Reductase 2 and Androgens in Tourette Syndrome".

A postdoctoral fellow in **Janos Peti-Peterdi PhD**’s lab, Anne Riquier-Brison, received in March 2013 a two-year fellowship from AHA for "Tracking the Fate and Function of the Renin Cell".

**Derek Sieburth PhD** is co-I on a 5-year award to USC Gerontology, “Oxygen Radical Toxicity and Protein Degradation” that started April 2013. The award provides salary coverage for Dr Sieburth.

**Ansgar Siemer PhD** received in March 2013, a grant from the Whitehall Foundation for three years to study “The Function of Amyloid Proteins in Long-Term Memory”.

**Berislav Zlokovic MD PhD** was given in late 2012 a gift from the Kaplan Family Foundation for research into Amyotrophic lateral sclerosis (ALS), often referred to as Lou Gehrig’s Disease. Also in December 2012, Dr Zlokovic received a grant from the Fidelity Biosciences Research Initiative for research on “Blood-Brain Barrier Pericytes: Safeguards Against Amyloid-beta Brain Degeneration".
<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>
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<td>Brain &amp; Behavior Research Foundation</td>
<td>$30,000</td>
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<td>University of Pennsylvania subK (PNAT NIDA U01)</td>
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<td>Discovery of Genetic Variation Influencing Schizophrenia Using Next Generation DNA Sequencing</td>
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<td>F&amp;A Costs</td>
<td>Total Costs</td>
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<td><strong>$12,613,663</strong></td>
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ZNI holds various academic activities and events in order to provide a greater platform for collaboration as well as opportunities to increase visibility for the greater ZNI community. The ZNI Seminar Series allows ZNI students and faculty to listen and interact with some of the most exciting researchers in the field. ZNI faculty play a key role in inviting guest speakers and introducing them to the ZNI Community.

**ZNI Seminar Series for FY 2013**

**August 2012**

“Targeting ‘Good’ Neuroinflammation in Alzheimer’s Disease” - Terrence Town, Cedars Sinai/UCLA

**September 2012**

“Engineering Pseudo-Axonal Scaffolds for Myelination: Fiber Diameter is Sufficient to Initiate Wrapping” - Jonah Chan, UCSF

“Exploring Visual Cortex with Closed-Loop and Optogenetic Techniques” - Gregory Horwitz, University of Washington
October 2012

“Role of Tryptophan Metabolism by the Serotonin and Kynurenine Pathways in Neurodevelopmental Disorders” - Diane Chugani, Children’s Hospital of Michigan

“The Genetics of Neurodegenerative Diseases: GWAS and Beyond” - Gerard Schellenberg, University of Pennsylvania

November 2012


“Circuit Control of Cortical Development and Plasticity” - Patrick Kanold, University of Maryland, College Park

December 2012

“Regulation of Glutamate Receptor Trafficking by the Ubiquitin Signaling System” - Peter Jou, Tufts University School of Medicine

January 2013

“Cortical Circuit Organization, Interaction and Inhibitory Neuronal Control” - Xiangmin Xu, UC Irvine

“VAAST: A Probabilistic Disease-Gene Finder for Personal Genomes” - Mark Yandell, University of Utah

February 2013

“A Genetic Approach to Vertebrate Physiology” - Gerard Karsenty, Columbia University

March 2013

“Dynamic Properties of Neural Circuits for Vision” - W. Martin Usrey, UC Davis

April 2013

“Information Flow in the Auditory Cortex: Anatomical and Physiological Correlates” - Troy Hackett, Vanderbilt University

“Control of Neuronal Morphogenesis and Circuit Formation in the Drosophila Somatosensory System” - Wesley Grueber, Columbia University

May 2013

“Exploiting Nicotinic Mechanisms to Enhance Auditory Processing” - Raju Metherate, UC Irvine

“You Can Learn a Lot Just By Watching: Uses and Abuses of μMRI and Simultaneous μPET/μMRI” - Russell Jacobs, Caltech

“The iConnectome: A High-Throughput Approach for Characterizing Neuronal Networks in the Mouse Brain” - Hong-Wei Dong, UCLA

June 2013

“Genetic Control of Synaptogenesis by Alternative Pre-mRNA Splicing” - Sika Zheng, UCLA

“Molecular Mechanisms of Long-Term Memory Storage” - Ted Abel, University of Pennsylvania
Following a brief hiatus, Faculty Chalk Talks were reinstated in February 2013. Chalk Talks are opportunities to cultivate a highly participatory and creative scientific culture at ZNI. At each Chalk Talk, a faculty member presents his/her unpublished work to other ZNI faculty members. These informal scientific presentations are meant to invite feedback and help develop aims for grants. Through these regular meetings, Chalk Talks aim to be instrumental in encouraging collaboration as well as maintaining a supportive and collegial environment within ZNI.

**Chalk Talks for FY2013**

<table>
<thead>
<tr>
<th>February 2013</th>
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<tbody>
<tr>
<td>Alexandre Bonnin</td>
<td>Scott Fraser</td>
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<td>Daniel Campbell</td>
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<table>
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<th>April 2013</th>
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<tbody>
<tr>
<td>Jeannie Chen</td>
<td>Le Ma</td>
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<table>
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<tr>
<th>June 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marcelo Coba</td>
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</table>

**Tea Time**

Tea Time meetings are unique weekly opportunities for the laboratories housed at ZNI and the neighboring Broad CIRM Center to meet and mingle while enjoying some afternoon tea/coffee and snacks. ZNI and BCC labs take turns hosting Tea Time. These meetings provide an organic and friendly platform for the undergraduate and graduate students as well as postdoctoral and research scholars working the labs to get to know and interact with one another.
ZNI hosted two USC Irene McCulloch Distinguished Lectures in Neuroscience in FY13, both co-hosted by Provost Elizabeth Garrett.

**September 20, 2012**

**Eric Kandel MD**, Nobel Laureate  
University Professor, Columbia University  
Director, Kavli Institute for Brain Science  
Sr Investigator, Howard Hughes Medical Institute

“Perpetuation of Memory Storage”  
USC Irene McCulloch Distinguished Lecturer in Neuroscience  
co-hosted by USC Provost Elizabeth Garrett

Dr. Eric Kandel giving his talk.  
*Photo Credit: USC Health Sciences PR & Marketing*
March 14, 2013

Stanley Prusiner MD, Nobel Laureate
Director, Institute for Neurodegenerative Diseases
Professor, Department of Neurology, University of California, San Francisco

"A Unifying Role for Prions in Neurodegeneration"
USC Irene McCulloch Distinguished Lecturer in Neuroscience
co-hosted by USC Provost Elizabeth Garrett
In recognition of his leadership, dedication and scientific vision for the Zilkha Neurogenetic Institute, Zach W. Hall PhD is celebrated annually by the ZNI through the Zach Hall Lecture. Dr Hall served as ZNI’s inaugural director as well as Senior Associate Dean for Academic Development at the Keck School of Medicine of USC from 2002-2005. He was instrumental in recruiting faculty to ZNI, fueling momentum for the Institute’s good work that continues to this day.

The 3rd Annual Zach Hall Lecture was held on 27 November 2012. The day started with a presentation by Li Zhang PhD, Associate Professor, Physiology & Biophysics and member of the ZNI, who gave a talk entitled “Functional Micro-Architecture of Cerebral Cortex”. The keynote speaker was Tom Südhof MD, Avram Goldman Professor of Molecular & Cellular Physiology at Stanford University School of Medicine. Dr Südhof spoke about “Molecular Mechanisms of Neurotransmitter Release”. As a special note, ZNI congratulates Dr Südhof for receiving the 2013 Nobel Prize for Physiology or Medicine, as announced this past October.

The lectures were followed by a poster session of scientific presentations showcasing work that is ongoing in dozens of ZNI laboratories. Also celebrated at the event were recipients of the Zach Hall Travel Awards, a fund that helps graduate students attend a conference to share their research by presenting a paper or poster. At the end of the day, a wine-and-cheese social was enjoyed by all participants. The Zach Hall Lecture is a day-long event presenting terrific opportunities for scientists to share with each other the wide range of research projects at the Institute, highlighting advancements and sparking new collaborations. Congratulations to all!
After co-hosting this event with UCLA and Los Angeles City College (LACC) for the prior two years, on 26 January 2013 the Zilkha Neurogenetic Institute welcomed the Brain Bee on the USC Health Sciences Campus for the first time. Organized by Drs Amy Sweetman (LACC) and Jason Chan (ZNI) with significant contributions by Trisha Staab and Alex Vazquez, the day was a great success. Over 47 high school students from 14 LA area high schools competed for the top prizes. These are the largest numbers to-date for the Los Angeles Brain Bee.

The event was enhanced by the assistance of undergraduate and graduate volunteers from USC and UCLA. With their help, in addition to the competition, students participated in a scavenger hunt looking through dozens of poster displays for key facts about neuroscience, research, and career information. Talks were given by physician-scientist William Mack MD, a neurosurgeon, and Dan Campbell PhD, an Assistant Professor in Psychiatry and the Behavioral Sciences, both of whose laboratories are at ZNI. Also during the event students were given guided tours of working research labs in ZNI, normally not open to the public, while parents and other family members were offered campus tours.

When all the results were tallied, the winners were:

1st prize:  Devanshu Singh, Windward School
2nd prize:  Shantanu Srivatsa, Clovis North High School
3rd prize:  Charlotte Starling, Marymount High School

At the end of the day, the ZNI was full of very excited students who actively engaged in learning as well as volunteers with great enthusiasm for science education and outreach. Thank you to one and all!
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

Brent Wilkinson (Daniel Campbell), Neurobiological Impact of Rare Loss-of-function Mutations Associated with Autism

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

Chia-Ling Hsieh (Jeannie Chen), Annexin A5 Protects Heart Function in a Mouse Model for Alzheimer’s Disease

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

Zhu Chen (David Conti), Using Quantile Regression for Pathway Analysis in Genome-wide Studies

Sneha Ravi (Greg Field), Mapping the Complete Neural Output of the Mouse Retina

Xiaoyang Yao (Greg Field), Light Adaptation Across Parallel Pathways in the Mouse Retina

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/Alapakkam Sampath), Single Cell RNA Sequencing
Mark Ambroso (Ralf Langen), Curvature Driven Myelination by Myelin Basic Protein

Alan Okada (Ralf Langen), Understanding and Preventing Misfolding in Neurodegeneration and Diabetes

Hanke Heun-Johnson (Pat Levitt), Gene by Environment Influences on Postnatal Forebrain Development

Feng Wang (Pat Levitt), Mechanism of Synapse Formation in Mouse Cortex

Daniel Gibson (Le Ma), Slit/Robo Signaling in Postnatal Neural Development

Trisha Staab (Derek Sieburth), Regulation of neuronal function by the conserved SKN-1/Nrf stress response pathway in Caenorhabditis elegans

Han Wang (Derek Sieburth), Regulation of Rhythmic Behaviors by Neuropeptide Signaling

Xiaolin Chou (Huizhong Tao), Development of the Thalamocortical Receptive Fields in Mice

Leena Ibrahim Marosh (Huizhong Tao), Using Optogenetics to Dissect the Circuitry in the Primary Visual Cortex

Lingyun Li (Huizhong Tao), Feedforward Inhibitory Circuit Mediates Lateral Refinement of Auditory Cortical Processing

Young Joo Kim (Huizhong Tao/Li Zhang), Molecular Mechanisms for the Development of Auditory Cochlear Innervation Pattern
ZNI Graduate Students

Yatang Li (Huizhong Tao/Li Zhang), Synaptic Mechanisms Underlying Contrast-Dependent Sharpening of Orientation Selectivity in Mouse Visual Cortex

Jennifer Sun (Huizhong Tao/Li Zhang), Synaptic Circuitry Mechanisms Underlying the Functional Development of Auditory Cortex

Shengzhi Wang (Huizhong Tao/Li Zhang), The Functional Role of Slit/Robo Signaling in the Spatial Patterning of Cochlear Innervation

Xiaorui Ray Xiong (Huizhong Tao/Li Zhang), Differential Gain Control and Synaptic Scaling Underlies Binaural Computation

Mu Zhou (Huizhong Tao/Li Zhang), Generation of Intensity Selectivity in the Central Auditory Pathway

Lukas Mesik (Li Zhang/Huizhong Tao), Functional Characterization of Inhibitory Interneurons During Development

Thomas Schmidt (Tobias Ulmer), Dual Effects of Transmembrane Proline Residues on Integrin Activity

Yunfei Guo (Kai Wang), Enlight: A Web-based Tool to Integrate GWAS Results with Biological Annotations & SeqMule: An Automated Pipeline for Whole Genome/Exome Analysis on Mendelian Diseases

Chengliang Dong (Kai Wang), Comparison of Functional Prediction Methods for Non Synonymous SNPs in Exome Sequencing Studies of Human Disease
ZNI Postdoctoral Trainees

Tian Wang (Jeannie Chen), Phototransduction in Dark Adaptation and Retinal Degeneration

Reymundo Dominguez (Robert Chow), Molecular Control of Regulated Excytosis

Nuria Royo Gascon (Robert Chow), Cellular Retinal Prosthesis

Ming Yi Sonya Lin (Robert Chow), Cellular Prosthesis Testbed

Andrew Weitz (Robert Chow), Imaging Platform for Determining Tumor Invasiveness

Jing Li (Marcelo Coba), Synaptic Signaling Networks

Jobin Varkey (Ralf Langen), Mechanisms of Membrane Curvature Induction

Jose Mario Issas (Ralf Langen) Structural Studies of Membrane Curvature Induction and Protein Misfolding

Allison Knoll (Pat Levitt), Neurodevelopmental Mechanisms of Social Behavior

Jasmine Plummer (Pat Levitt), Transcriptonal Reglulation of the MET Tyrosine Kinase Receptor Gene
Zhuhui Xie (Pat Levitt), MET-interactive Protein Network and Their Function during Synaptogenesis

Stephen Tymanskyj (Le Ma), Molecular Mechanisms of Axon Branching in Synaptic Development

Anne Riquier Brison (Janos Peti-Peterdi), The Role of the GPR91/ Succinate Pathway in Renovascular Hypertension

Johan Pahlberg (Alapakkam Sampath), Dark Noise in Rod Photoreceptors and the Control of Visual Sensitivity

Charles Ratliff (Alapakkam Sampath), High Throughput Testing of Behavioral Threshold in Mice

Jason Chan (Derek Sieburth), Dissecting the Mechanisms of How Cholinergic Signaling Regulates Neuronal Function and Animal Behavior in C. elegans

Rachel Service (Ansgar Siemer), Structural Characterization of Functional and Disease-related Amyloid

Kevin Doty (Terrence Town), Using Genome Wide Approaches to Identify and Modulate Beneficial Neuroinflammation in Alzheimer’s Disease

Marie-Victoire Guillot-Sestier (Terrence Town), Implication of the Anti-Inflammatory Cytokine Interleukin-10 in Innate Immune Response to Amyloidogenesis in Alzheimer’s Disease

Rodrigo Lopez Leal (Terrence Town), An iPS Disease-in-a-Dish Model of Familial Alzheimer's & Generation of a conditional rat model for genetic ablation of neural stem cell

Tara Weitz (Terrence Town), TGF-beta Inhibitor Therapy in a Transgenic Rat Model of Alzheimer's Disease

Fan Gao (Kai Wang), Higher-order Chromosomal Structure and Interactions by 4C-Seq Techniques, Epigenetic and Transcriptome Analysis of Meningiomas

JiHong Kim (Kai Wang), Comparative Analysis of Multiple RNA-Seq Quantification Tools & Development of Fully Automated RNA-Seq Analysis Pipelines

Lingling Shi (Kai Wang), Functional Genomics Studies of Autism Candidate Genes in Neural Stem Cells

Kassandra Kisler Elliott (Berislav Zlokovic), The Role of PICALM in Vascular Clearance of Amyloid-beta

Yaoming Wang (Berislav Zlokovic), Regulation of Brain Thrombosis in Stroke Models
ZNI PIs published more than 120 papers in peer-reviewed journals in FY13. Many ZNI scientists have published their findings in high-impact journals, those considered to be highly influential in their fields. In FY13, 14% of all publications by ZNI researchers were in high-impact journals.

FY13 Faculty Publications


Photo Credit: Steve Cohn


Wang H and Sieburth D. PKA Controls Calcium Influx into Motor Neurons during a Rhythmic Behavior. PLoS Genetics 2013 Sep;9(9):e1003831. PMID: 24086161


David Warren is Director of Operations for the Zilkha Neurogenetic Institute, a position he has held since 2006. As the senior administrative officer for ZNI, Mr. Warren manages a team who collectively are responsible for all day-to-day activities at the ZNI, including budget and financial reporting, payroll/personnel, grants management, purchasing, facilities and construction, equipment acquisition, faculty recruitment and programmatic events for over 250 faculty, staff and students.

The team includes Barbara Lockley, Office Manager and Home Department Coordinator, who handles payroll and HR. Barbara is assisted by Marlen Turcios, who handles graduate students, visas and faculty dossiers. Rusty King is the Facilities Manager for our 125,000 sq ft building, supervising all services, construction, remodels and moves as well as specialized equipment. Rusty also oversees the glassware and autoclave services for the Institute. Gabriela Torres manages all pre- and post-award grants management, drafting budgets, submitting proposals and administering nearly 100 sponsored projects at any time. Leslie Ortiz handles most of the purchasing, travel and reimbursements for 25 laboratories. Kianna James is Executive Secretary to Dr Zlokovic.

A special thanks to Julie Carl, Project Specialist and coordinator for ZNI Seminars, Chalk Talks and special events. Julie collected and assembled the content for this annual report, working with David on layout.

**FY13 Operating Budget**

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<th>Income</th>
<th>Forward From FY12</th>
<th>Expenses</th>
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<td><strong>Program Funds (Endowment)</strong></td>
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*includes $976,041 for solid-state NMR encumbered in FY12, expensed in FY13*
As Executive Director of Development at the Keck School of Medicine, **Hazel Breen** leads the Brain Sciences Fundraising Initiative. Under this Initiative, the fundraising priorities for the Zilkha Neurogenetic Institute focus on experimental projects designed to further our understanding of the biology and genetics of Alzheimer’s disease as well as research that employs cutting-edge brain imaging techniques to examine neural and vascular connections from the microscopic to the atomic level. Some opportunities for partnership include:

- Funding to help recruit world-class senior scientists and promising junior faculty members to build the critical mass necessary for meaningful breakthroughs
- Seed funding to allow ZNI investigators to pursue innovative research, leading to further external sponsored project support
- Graduate and postdoctoral fellowships to attract the next generation of exemplary neuroscientists

By applying emerging technologies and forging new partnerships and collaborations, ZNI investigators will continue to advance our research efforts, bringing results from bench to bedside. As we enter into 2014, ZNI is re-energizing our fundraising campaign, with the goal of making significant progress to unravel the mystery of brain ailments from Alzheimer’s Disease to Stroke to Schizophrenia. We hope you will join us as we attempt to arrest and reverse these devastating conditions.

Please contact Hazel Breen hbreen@usc.edu (323) 442-2684 for select research funding and capital naming opportunities.

“We are all touched by Alzheimer’s or dementia. More of us will be affected because we are all living longer. We need more people to get involved. Let’s see what we can do together to “arrest” and “reverse” Alzheimer’s.”

—Selim K. Zilkha