Mary Hayley and Selim Zilkha receive the Jerome H. Stone Philanthropy Award for Alzheimer’s Research at AAIC 2014 Copenhagen

At the most recent Alzheimer’s Association International Conference this past July in Copenhagen, Denmark, Selim Zilkha and Mary Hayley were honored with the Jerome H. Stone Philanthropy Award for Alzheimer’s Research. This award, named after Jerome Stone, the primary founder of the Alzheimer’s Association, serves to recognize and celebrate philanthropic individuals who actively support Alzheimer’s research efforts and causes. Mr. Zilkha and Ms. Hayley were lauded for their tireless generosity toward Alzheimer’s research, in particular for establishing the Zilkha Neurogenetic Institute (ZNI) as well as their continued support of ZNI researchers. “Through their efforts, Selim and Mary have made an extraordinary impact on the advancement of Alzheimer’s research,” said Harry Johns, President and CEO of the Alzheimer’s Association.

Dr. Berislav Zlokovic, director of ZNI and holder of the Mary Hayley and Selim Zilkha Endowed Chair in Alzheimer’s Research, was on hand in Copenhagen to receive the award on behalf of the recipients.

The Alzheimer’s Association International Conference (AAIC) is the world’s largest gathering of leading researchers from around the world focused on Alzheimer’s and other dementias. AAIC serves as a catalyst for generating new knowledge about dementia and fostering a vital, collegial research community. Scientists leading the advancement of research gather to report and discuss the most current data on the cause, diagnosis, treatment and prevention of Alzheimer’s disease and related disorders. In addition, the AAIC hosted health leaders from G7 governments to continue discussing the “Global Action Against Dementia Legacy Events” stemming from the first-ever G8 (now G7) dementia summit organized by U.K. Prime Minister David Cameron in December 2013.

The Alzheimer’s Association has awarded over $315 million in grants for research relating to Alzheimer’s Disease and related disorders with 350 active investigations ongoing across 22 countries. AAIC 2015 will be held in Washington, DC.

Patch Clamp Workshop at ZNI led by Dr. Robert Chow

Dr. Robert Chow, associate professor at ZNI and the Department of Physiology & Biophysics, recently held a series of workshops at ZNI exploring the patch clamp technique, bringing together interested graduate students, postdoctoral fellows, research associates and investigators through hands-on trainings and lectures. A total of six events were open to interested parties and included a wide range of participants from biomedical and electrical engineering laboratories across the Keck School of Medicine as well as scientists from the broader USC research community.

Electrophysiology, which is the study of electrical properties (or more precisely the flow of ions in biological matter), is a critical component of many experiments conducted at ZNI. The patch clamp technique is a refinement of the voltage clamp first designed in the 1970s. The current variation allows...
What is a Neurogenetic Institute?

If you ask a neuroscientist, neurologist, psychiatrist or neurosurgeon to define neurogenetics, you will probably receive different answers. What they would likely agree upon is that neurogenetics is a subfield of neurosciences that studies the impact and associations of different genes and their variants on diseases of the nervous system, as well as how the disease-associated gene variants influence the structure and function of the brain. Because studies of neurogenetics pertain to genes that in aggregate determine our individuality, scientific research on the biology of genes associated with disorders is needed to yield further knowledge. One of the problems that the field has begun to realize in recent years is that the vast majority of gene variants identified by the genome-wide association studies as linked to different brain disorders have no established biological relevance to disease or clinical utility for prognosis or treatment. Identifying causative mutations have had much less success and remain a major challenge in the field. Ideally, we hope that with the better understanding of biology, identification of causative mutations, and better knowledge of the cellular and molecular mechanisms underlying the affected gene functions, we will be able in the not so distant future to develop pharmacological, cell therapy and/or gene therapy approaches to control onset and/or halt the progression of devastating brain disorders, from autism to schizophrenia to Alzheimer’s disease.

The National Institute of Neurological Disorders and Stroke estimates that 20% of the United States population—about 50 million people—suffer from at least one of more than 600 clinically defined brain diseases. Some of these disorders have been linked to genetic factors, while for most the etiologies and whether or not they are genetically influenced remains unknown. Indeed, advances in next generation DNA sequencing, state-of-the-art neuroimaging and use of pluripotent stem cell technologies has rejuvenated the field of neurogenetics today more than ever before.

At the Zilkha Neurogenetic Institute, physician-scientists from the departments of Psychiatry, Neurology and Neurosurgery work side-by-side with faculty in basic science departments like Cell & Neurobiology, Physiology & Biosphysics and Biochemistry & Molecular Biology to collaborate on a number of projects, as they attempt to understand how normal brain functions and how genes that are associated with disease affect the underlying biology mechanisms. Additionally, gene-environment interactions likely contribute in a major way to the underlying changes in brain during development, adulthood and aging. And the same may hold for systemic changes in the body that can influence brain disorders, such as for example, well-established vascular contributions to dementia.

Importantly, advances in the field of neurogenetics always lead to a series of new questions about brain disorders, function and biology that researchers at ZNI continue to explore.


Cross-Disorder Group of the Psychiatric Genomics Consortium [includes C Pato and M Pato] “Genetic relationship between five psychiatric disorders estimated from genome-wide SNPs.” Nature Genetics 45(9):984-94 2013. The research findings show that genetic correlation is high between schizophrenia and bipolar disorder; moderate between schizophrenia and major depressive disorder, bipolar disorder and major depressive disorder, and ADHD and major depressive disorder; low between schizophrenia and ASD; and non-significant for other pairs of disorders as well as between psychiatric disorders and the negative control of Crohn’s disease.

Gray et al. [includes H.W. Dong] “Cortical and Striatal Pathogenic Synergy and Non-cell-autonomous Aggregate Suppression in HD Mice.” Nature Medicine 20(5):536-41, 2014. This study reveals novel insights into Huntington’s disease (HD) by identifying the underlying interactions of cortical and striatal mutant huntingtin (mHTT) in HD pathogenesis, suggesting that optimal HD therapeutics may require targeting mHTT in both cortical and striatal neurons.

Recent neurogenetic publications by ZNI researchers
Kai Wang is an investigator who uses mathematical and statistical tools in search of disease-related genes. His team interrogates the human genome—all of our DNA and its downstream products—to isolate aberrant sequences that increase risk. These researchers develop and apply highly sophisticated, novel statistical tools to increase our understanding of the human genome in both health and disease.

DNA provides the basic blueprint for human and other life forms. While the human genome contains over 3 billion DNA bases, only a fraction is transcribed into RNA and then translated into proteins and other molecules essential to life. Mutations in the DNA sequence, aberrations in transcriptional control, and other changes can lead to disease. With the development of high-throughput DNA and RNA sequencing technologies, genome (DNA) and transcriptome (RNA) data are being generated at an unprecedented rate. However, the computational and statistical approaches (bioinformatics) for handling these data lags behind, creating a gap between the massive amount of information being generated and the ability to fully exploit biological contents of these data. The Wang lab aims to reduce this gap and facilitate in-depth understanding of these data sets.

Wang and his lab are applying their bioinformatics tools to a variety of brain diseases.

Collaborating with multiple researchers, Wang and his group are developing innovative gene-finding approaches for rare or undiagnosed diseases. A significant number of Mendelian diseases (disorders stemming from single gene mutations such as Huntington’s disease or cystic fibrosis), especially those involving neuronal phenotypes, remain undiagnosed or misdiagnosed. Accurate genetic diagnosis may potentially benefit disease management or treatment. One bioinformatics method to aid in genetic diagnosis, called Phenolyzer, is an approach to prioritize candidate genes by user-supplied phenotype (observed disease characteristics) terms. Most tools available today are restricted to specific phenotypic vocabularies or ontologies in their approach. Wang’s method allows users to use free text to describe disease characteristics. By employing user-supplied terms, researchers should be able to identify a broader array of unique disease-causing genes.

In addition, in collaboration with neurosurgeons and fellow ZNI researchers William Mack and Gabriel Zada, the Wang group is studying a large clinical collection of tumors and blood from patients with meningiomas, a diverse set of tumors that arise from the membranous layers surrounding the brain and spinal cord. Although meningiomas typically are benign tumors that can often easily be cured by surgery, roughly 3% can become malignant and invasive. Even after surgical removal, malignancies recur in 50-80% of cases, with a median survival time of 1.5 years. Dr. Wang has applied his tool set to understand why some meningiomas become killers while others do not, with the aim of implementing advanced strategies for patient treatment.

Psychiatric disorders such as schizophrenia and bipolar disorder are another set of brain diseases in which genetics play an important role. Approximately 2-3% of the world’s population suffers from these two disorders. Drs. Carlos and Michele Pato and Dr. James Knowles, at the Center for Genomic Psychiatry at ZNI conduct basic wet-lab bench research on brain cells as well as population studies of affected individuals and controls. Over 30,000 individuals are enrolled in genetic studies in which DNA and RNA sequences of affected and unaffected subjects are compared in search of differences that may increase or decrease disease risk. Neuronal cell lines were being made from selected groups of patients to better characterize genetic materials from these patients. Dr. Wang and others are applying bioinformatics tools in this endeavor, studying how mutations in DNA affect transcription and translation of gene products and how they may relate to the disease.

In summary, new bioinformatics tools and approaches deployed by Dr. Wang play a critical role in all of these studies, helping researchers identify and apply targeted treatments to a wide range of brain disorders.
Dr. Berislav Zlokovic, director of ZNI, was one of five KSOM researchers named by Thomson Reuters as having “The World’s Most Influential Scientific Minds” for 2014.

The New York City-based multinational media and information firm assessed papers indexed between 2002 and 2012 in 21 fields of study. It tracked authors who published numerous articles ranking among the top 1 percent that are the most cited in their fields in the year of publication. The documents represent research that the scientific community has judged to be the most significant and useful.

The compilation is meant to attest to the power and scope of citations in determining influential research across disciplines.

Dr. Zlokovic is among only 80 researchers worldwide in the area of neuroscience & behavior featured in the rankings.


Patch Clamp Workshop at ZNI led by Dr. Robert Chow

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for more refined, high-resolution recording of single and multiple ion channels in cells. The technique can be applied to a wide variety of cells, but is especially useful in the study of excitable cells such as neurons, cardiomyocytes (cardiac muscle cells), other muscle fibers and pancreatic beta cells.

A commercially available patch clamp costs approximately $20,000, an expense prohibitive to many researchers. However, Dr. Chow informed participants that the Patch Clamp setup is fairly standardized and with the right know-how, one can build a set-up for just a few hundred dollars. Dr. Chow himself is a self-taught patch clamp enthusiast and designed the workshops to assist other researchers and students still learning about the Patch Clamp technique.

Dr. Chow plans on offering these workshops as part of a course through the neuroscience graduate program in the future. Depending on interest, he is hoping to combine the patch clamp course with a course on microscopy as well.

The focus of the Chow laboratory is the control of cellular electrical activity and secretion in health and disease. Areas of study include retinal prosthesis, amyloid diseases such as Alzheimer’s and Parkinson’s, and glucose-responsive insulin-secreting cells from human stem cells. For more information about Dr. Chow and his research, please visit http://www-hsc.usc.edu/~rchow/Home.html.

Researchers build their own patch clamps at one of the hands-on workshops led by Dr Robert Chow at ZNI

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