Unrevealing the Mysteries of Neurodegenerative Diseases

By Claudio Soto, Ph.D.

Abstract: Neurodegenerative diseases are fearsome illnesses, because they affect the most precious qualities of human beings. Research over the past 10 years has provided evidence for a common mechanism of neurodegeneration in which the critical event is the misfolding, aggregation and accumulation in the brain of otherwise normal proteins. Each neurodegenerative disease is associated with abnormalities in the folding of a different protein, but the molecular pathway leading to misfolding and aggregation and the mechanism by which this process might lead to neuronal damage seem similar. These findings provide hope for a common therapeutic strategy to treat these devastating illnesses.

Neurodegenerative diseases (NDs) are some of the most debilitating disorders, which include common illnesses such as Alzheimer’s (AD) and Parkinson’s (PD), and other rarer as Huntington’s disease (HD), spinocerebellar ataxia (SCA), prion diseases (also called transmissible spongiform encephalopathies or TSEs), and amyotrophic lateral sclerosis (ALS). In spite of the important differences in clinical manifestation, neurodegenerative disorders share some common features such as their appearance late in life, the progressive and chronic nature of the disease, the extensive neuronal loss and synaptic abnormalities and the presence of cerebral deposits of misfolded protein aggregates. These deposits are a typical disease signature and although in each dis-

The UTHealth-Memorial Hermann Memory Disorders and Dementia Clinic

By Paul Schulz, Ph.D.

Abstract: The dementias have a devastating effect on people’s ability to think, interact socially, and experience normal emotions. They cause untold suffering for patients and their loved ones. Our group is studying diseases that dramatically increase the risk of contracting dementia in order to gain insight into the cellular processes underlying these disorders. The long-term goals are to develop tests that diagnose these disorders before symptoms develop and to test treatments in presymptomatic individuals that may prevent the development of these diseases.

The Challenge

The Alzheimer’s Association estimates that 5.3 million Americans have Alzheimer’s disease (AD) and projects a 74% increase in Texas over the next 15 years. AD is the seventh leading cause of death in the U.S., with annual costs in excess of $170 billion. 60,000 Americans are diagnosed with Parkinson’s disease (PD) each year, which is associated with another form of dementia. More than 35,000 Houstonians and their families suffer from the devastating effects of AD, vascular dementia (VaD), and PD dementia.

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As the fall semester begins and the long days of summer draw to an end, we reflect on the past academic year and gear up for another exciting year filled with new ventures and collaborations.

Over eight months ago, Congresswoman Gabrielle Giffords came to Houston to receive treatment and rehabilitation after a mass shooting in Tuscan left her severely injured. This horrific incident heightened public interest in neurotrauma and rehabilitation and facilitated media attention towards brain awareness. As the public searched for answers, the national spotlight was directed at two prominent leaders at the NRC who are leading Giffords’ road to recovery, Dr. Dong Kim and Dr. Gerard Francisco. Dr. Kim serves on the NRC Executive Committee and is the Director of the Mischer Neuroscience Institute at Memorial Hermann and Chair of the Department of Neurosurgery at UTHealth. Dr. Francisco is a member of the NRC and is Chief Medical Officer at TIRR Memorial Hermann Hospital and Chair of the Department of Physical Medicine & Rehabilitation at UTHealth. Both Drs. Francisco and Kim have been an integral part of the continued success of the NRC. This spring, Dr. Gerard Francisco will lead the NRC Annual Public Forum in conjunction with Brain Awareness Week 2012. The topic this year, “Rehabilitation,” will promote efforts in public awareness regarding rehabilitation following brain and spinal cord injury and stroke. Please check the NRC website in the next few months for more information regarding this event.

The NRC houses an extensive collaboration of neurotrauma research and rehabilitative medicine with an integrated focus on the anatomical, biochemical, molecular and behavioral aspects of traumatic injury of the nervous system, with the ultimate goal of improved therapies. Every fall, the NRC hosts a seminar course which integrates bench, translational and clinical research to examine the Neurobiology of Disease. Continuing to promote interest and education surrounding neurotrauma and rehabilitation, the topic this year is “Stem Cells and Regenerative Medicine”. This course will address the emerging role of stem cells and other regenerative strategies as potential, novel treatments for acute neurological disorders and neurodegenerative diseases. The audience for this course is as diverse as the methods used to study various diseases and consists of undergraduate, graduate and medical students, residents, faculty members and clinicians. This course is led by Dr. Sean Savitz, Associate Professor in the Department of Neurology and a Bentsen Investigator at the Bentsen Stroke Center at the Brown Foundation Institute of Molecular Medicine, UTHealth. His pioneering research investigating stem cell-based therapy for stroke has contributed greatly to the discipline of regenerative medicine. In addition to Dr. Savitz, lecturers for this course include leaders within this field from the UTHealth community. The Methodist Hospital, Baylor College of Medicine, as well as a special guest lecture by Dr. Randolph Nudo from the University of Kansas Medical Center on November 30, 2011. For more information regarding this seminar series, please check the NRC website.

In addition to our efforts to promote brain awareness and neuroscience education, the NRC is pleased to announce the Distinguished Lecturer of 2012, Dr. Roger Tsien. Dr. Tsien is a Professor of Pharmacology and Chemistry & Biochemistry at the University of California San Diego and was awarded the Nobel Prize in Chemistry in 2008 for his discovery and development of the green fluorescent protein (GFP) with two other scientists, Dr. Martin Chalfie of Columbia University and Dr. Osamu Shimomura of Boston University Medical School and Marine Biological Laboratory. The lecture is scheduled for February 8, 2012 at the UTHealth Medical School.

Finally, and with a heavy heart, we regret to inform of the passing of Mr. Wayne Hightower. The initial support of Mr. Hightower in 1992 and the continued support by the Hightower family have been essential to the lasting success of the NRC. For that, the impact that Mr. Hightower and his family have had on the Houston community is vast and immeasurable.

Please be sure to check out our “Upcoming Events” in this Newsletter. If you are planning to attend the 2011 Annual Meeting of the Society for Neuroscience in Washington, DC, please be sure to stop by NRC members presentations. We look forward to seeing you at one of our many upcoming events, either in Houston or in Washington, DC. 🌃
ease the main protein component is different, they have similar morphological, structural and staining characteristics (Fig. 1).

![Figure 1. Accumulation of Misfolded Protein Aggregates are a common feature of Neurodegenerative Diseases. Compelling evidence suggest that a common cause of NDs may be the misfolding of a protein to form toxic oligomeric structures that over time accumulate in large protein fibrillar deposits in the brain.](image)

Protein aggregates at the root of neurodegenerative diseases

Each neurodegenerative disease is associated with the accumulation of a different protein. In AD there are two types of protein deposits. Amyloid plaques accumulate outside the cells and around the cerebral vessel walls and their main component is a 40-42 residues peptide, termed amyloid-β-protein (Aβ). Neurofibrillary tangles are located in the cytoplasm of degenerating neurons and are composed of aggregates of hyperphosphorylated tau protein. Lewy bodies are aggregates observed in the cytoplasm of neurons of the substantia nigra in brains from people affected by PD. The major constituents of these aggregates are fragments of a protein named α-synuclein. Intranuclear deposits of a polyglutamine-rich version of huntingtin protein are a typical feature of brains from HD patients. ALS patients exhibit aggregates, mainly composed of superoxide dismutase, in cell bodies and axons of motor neurons. Finally, the brains of humans and animals affected by diverse forms of TSEs are characterized by accumulation of protease-resistant aggregates of the prion protein (PrP).

Compelling evidence coming from biochemical, genetic and neuropathological studies suggest a key role of protein misfolding and aggregation in the pathology of NDs. For example, the presence of abnormal aggregates usually occurs in the brain regions most damaged by each disease. Mutations in the gene encoding for the misfolded protein produce inherited forms of the disease, which usually have an earlier onset and more severe phenotype than the sporadic forms. Transgenic animals expressing the human mutant gene for the misfolded protein develop some of the typical neuropathological and clinical characteristics of the human disease. Misfolded protein aggregates produced in vitro are toxic; inducing neuronal apoptosis. Finally, in TSEs, which is the only neurodegenerative disease that can be transmitted by infection, the infectious material is composed exclusively of the misfolded prion protein that has the surprising ability to propagate the disease in a similar way as a living microorganism. Indeed, injection of highly purified misfolded PrP induces the disease in wild type animals.

The pathways of brain degeneration

Selective neuronal loss, synaptic alterations and neuroinflammation (in the form of reactive astrogliosis and activated microglia) are typical features of NDs. The region of the brain most affected differs among diseases and determines the distinct clinical symptoms of each. Although, it was widely thought that neuronal apoptosis was the most important problem in neurodegeneration, recent evidence from different diseases, suggest that extensive neuronal death may not be the initial cause of the disease. Indeed, clinical symptoms have been clearly described before significant neuronal loss and a better temporal and topographic correlation is found with synaptic dysfunction.

Although protein misfolding and aggregation is undoubtedly associated with neurodegeneration and disease, the mechanism by which misfolded aggregates produce synaptic dysfunction and neuronal damage is unknown. Loss of normal protein function through misfolding is one possible mechanism underlying aberrant protein aggregation and subsequent neurodegeneration. Although this idea is appealing, there is no experimental support for this hypothesis; indeed, the generation of knock out animals for the respective proteins does not lead to
Akhtar Alam, UTHealth Department of Psychiatry and Behavioral Sciences, and Myriam Fornage, UTHealth Institute of Molecular Medicine, as part of a collaboration with Nasiya Ahmed, Joan Engebretson and Nahid Rianon, received an award from the Albert and Ethel Herzstein Charitable Foundation. This award is given to integrate geriatrics studies across all the schools of UTHealth, increase collaboration and cooperation between school faculties, instill geriatrics studies into student curriculum, and foster future geriatrics practitioners.

Andrew Bean, Department of Neurobiology and Anatomy, UTHealth, was nominated by GSBS students and presented with the 2011 John P. McGovern Award for Outstanding Teacher at the Commencement ceremony on May 7th.

Michael Beierlein, UTHealth Department of Neurobiology and Anatomy, received a Research Grant from the Epilepsy Foundation.

James Grotta, Professor and Chair of the Department of Neurology, UTHealth, was presented with the President’s Scholar Awards in Research and Teaching by Dr. Giuseppe Colasurdo, President ad interim and Dean.

Susan Landry, Founder and Director of the Children’s Learning Institute (CLI) received the Distinguished Professional Woman Award by The Committee on the Status of Women (CSW, UTHealth), as well as the Golden Oak Award from the Parish School of Houston.

Pedro Mancias, UTHealth Department of Pediatrics, received the 2010 Herbert L. and Margaret W. DuPont Master Clinical Teaching Award.

Roberta B. Ness, Dean of School of Public Health, UTHealth, has been appointed by President Barack Obama to the Board of Directors of the Mickey Leland National Urban Air Toxics Research Center (NUATRC).

Priyanka Parekh, UTHealth medical student received the Alpha Omega Alpha Carolyn L. Kuckein Student Research Fellowship to perform research in the laboratory of Edgar T. Walters in the Department of Integrative Biology and Pharmacology.

NRC Member Recipients of the 2010-2011 Dean’s Teaching Excellence Awards

Biochemistry & Molecular Biology
Vasanthi Jayaraman, Ph.D.
Henry W. Strobel, Ph.D.

Neurobiology and Anatomy
Leonard J. Cleary, Ph.D.
Terry Crow, Ph.D.
Daniel J. Felleman, Ph.D.
Carla S. Rogers, Ph.D.
Han Zhang, M.D.

Neurology
Andrew D. Barreto, M.D.
Suur Biliciler, M.D.
Nicole R. Gonzales, M.D.
Nneka Ijeji Jones, M.D.
Raymond A. Martin, M.D.
Mya C. Schiess, M.D.

Ophthalmology & Visual Science
Judianne Kellaway, M.D.
Stephen L. Mills, Ph.D.
John O’Brien, Ph.D.

Pediatrics
Ian J. Butler, M.D.
Michael J. Gambello, M.D., Ph.D.
Pedro Mancias, M.D.

Psychiatry & Behavioral Sciences
Jeffrey V. Bar, M.D.
Prashant Gajwani, M.B., B.S.
Iram Kazimi, M.D.
Svetlana Malkina, M.D.
Cheryl L. Person, M.D.
Dawnelle J. Schatte
Nurun N. Shah, M.B., B.S.
Alan C. Swann, M.D.
Adel A. Wassef, M.B., B.Ch
Susan Landry, UTHealth Department of Pediatrics and Director of the CLI, and the CLI was awarded a four-year grant from the U.S. Department of Education’s Institute of Education Sciences.

David Marshak, UTHealth Department of Neurobiology and Anatomy, became a Fellow of the Association for Research in Vision and Ophthalmology, and his grant from the National Eye Institute “Structure and Function of Primate Retinal Neurons” was renewed.

Flavia Nelson, UTHealth Department of Neurology, received K-23 award to develop and apply a multimodal MRI approach to the evaluation of cognitive impairment in patients with multiple sclerosis.

Sean Savitz, UTHealth Department of Neurology, received an R-01 for the study of autologous bone marrow cells for stroke.

Publications


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clinical disease. The most widely accepted theory of brain degeneration proposes that misfolding and aggregation results in the acquisition of neurotoxic activity by the misfolded protein.

Several mechanisms have been proposed for the neurotoxic activity of misfolded aggregates, and it is likely that different pathways operate simultaneously, depending on the size and structure of the aggregates (e.g. small soluble oligomers or large deposited fibrils) and whether the proteins accumulate intra- or extra-cellularly. Extracellular aggregates might activate a signal transduction pathway leading to apoptosis by interacting with specific cellular receptors. Intracellular aggregates might damage cells by recruiting factors essential for cell viability. Another well-supported mechanism is membrane disruption and depolarization mediated by pore formation, resulting in alteration of ion homeostasis and disregulation of cellular signal transduction. Extensive data has also accumulated to support the idea that misfolded proteins induce endoplasmic reticulum stress, altering the entire machinery for protein synthesis and folding. Finally, protein aggregates could induce oxidative stress by producing free radical species, resulting in protein and lipid oxidation, elevation of intracellular calcium and mitochondrial dysfunction.

Advances on therapy for neurodegenerative diseases

Despite dramatic progress in understanding the pathogenesis of NDs, none of these disorders can yet be successfully treated. If protein misfolding and aggregation is a central event in the pathogenesis of NDs, a therapy directed to the cause of the illness should aim to correct protein misfolding. Several approaches have been proposed to target the process of protein misfolding and aggregation: 1) decrease of the expression of the protein implicated in misfolding and aggregation; 2) stabilization of the native protein conformation; 3) inhibition and reversal of protein conformational changes and aggregation; 4) increase the biological clearance of the misfolded protein.

Among the possible targets to treat protein misfolding in NDs, the inhibition and reversal of structural changes involved in the formation of misfolded aggregates is possibly the one most frequently attempted. Many small chemical compounds have been reported to prevent protein misfolding and aggregation, which have been identified either serendipitously, from high-throughput screening, or because epidemiological studies have suggested they may be active. These compounds result in a net reduction of misfolded aggregates, but achieve this goal acting through diverse mechanisms. The usefulness of these molecules is compromised by their lack of specificity, and their unclear mechanism of action in most of the cases. In addition, many of them are highly toxic making it difficult to use them in humans. A more rational approach employed by several groups to make inhibitors of protein misfolding and aggregation is the design of specific peptide ligands based on the well-known self recognition ability of the protein and the incorporation of chemical groups that disrupt misfolding.

Perhaps the most promising strategy to remove misfolded proteins is the immunization approach, first described for AD, and later expanded to all NDs. Aggregates of synthetic Aβ protein were used as antigens to induce the immune system to produce antibodies to clear them. Immunization can reduce amyloid load, cerebral damage and behavioral impairments in transgenic animal models of AD. However, a clinical trial to evaluate the efficacy of the immunization strategy in humans affected by AD was stopped owing to several cases of meningoencephalitis. Little is known about the reason for this side-effect, but future research should bring both more knowledge about this problem and also should result in new strategies to minimize brain inflammation after vaccination.

Our research strategy

Over the past sixteen years, My laboratory has been investigating the molecular basis of NDs associated with misfolded proteins, mainly focusing in AD and in prion disorders. Our earlier studies were pioneering by proposing that amyloid formation in AD is triggered by conformational changes in the normal Aβ protein. We also identified some of the factors that may induce the Aβ misfolding and provided strong evidences that at least some of them (for example apolipoprotein E, RAGE receptor) might play a critical role in vivo. In the last twelve years, our lab has been working on strategies for altering protein misfolding and aggregation in order to learn more about the molecular mechanism of this process and to generate novel approaches for therapy and diagnosis. The work has been built around

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two important discoveries that represents novel platform technologies: β-sheet breakers peptides for preventing and correcting protein misfolding and aggregation (therapeutic use) and the concept of cyclic amplification of protein misfolding for detecting the early pathogenic event in these diseases (diagnostic use).

Based on the knowledge of the structural determinants for protein misfolding, we have developed the concept of β-sheet breaker peptides for the treatment of protein misfolding diseases. β-sheet breaker peptides are short synthetic peptides homologous to the fragment of the protein undergoing misfolding, and engineered to contain residues that specifically block and reverse the conformational changes. β-sheet breakers have been created to correct the misfolding of the amyloid-β protein and the prion protein. The compounds have been demonstrated to be active in several in vitro and cellular models as well as in transgenic animal models for AD and in scrapie models of prion diseases. We have also characterized and improved the pharmacological properties of these compounds to make them suitable for in vivo use in CNS diseases. The prototype β-sheet breaker reached human clinical trials and was tested in AD patients.

Cyclic amplification of protein misfolding (PMCA) is considered a major breakthrough in science and technology because it recreates (mimics) in vitro the pathological process associated with these diseases in a rapid and efficient way. The PMCA technology has been applied to convert large amounts of the normal prion protein into the abnormal form by incubating it with minute amounts of misfolded infectious prion protein. The system consists of multiple cycles of accelerated prion replication to cause an exponential increase in the conversion. These findings mark the first time in which the folding and biochemical properties of a protein have been cyclically amplified in a manner conceptually analogous to the amplification of DNA by PCR. PMCA has contributed enormously to our understanding of the underlying biology of prions, as well as assisting in the identification of other factors that may be implicated in prion protein conversion, and finally, to foster discovery of novel drugs for prion disease treatment. In addition, PMCA has enormous potential in allowing current diagnostic tools to detect TSEs during the pre-symptomatic period and perhaps in living individuals, because it can multiply the number of prions facilitating their detection. Indeed, PMCA enables a more than 3 billion-fold increase in sensitivity for PrP detection and the possibility to detect as little as a single molecule of the misfolded protein. This level of sensitivity allowed us to detect for the first time prions in the blood and urine of sick as well as pre-symptomatic animals. These findings have had a major beneficial impact in various fields including the diagnosis of prion disease, blood bank safety, meat industry, etc. In addition, using the PMCA technology we have been able to generate infectious prion protein in vitro by propagating the protein misfolding process. This experiment is widely considered by most scientists in the field as the final and definitive proof for the controversial prion hypothesis and as such is a major breakthrough in science. More recently we have adapted the PMCA technology to amplify the process of Aβ misfolding and aggregation implicated in AD and used the technology to detect misfolded Aβ oligomers in the cerebrospinal fluid of patients. This finding may enable the development of a much needed early and sensitive biochemical diagnosis for AD. This achievement would be a major breakthrough in the field, since it will enable us to identify people early in the disease and treat them before irreversible brain damage occurs.

Our research has also focused on understanding the mechanism by which misfolded proteins induce cell death and tissue damage. We demonstrated that misfolded proteins induce neuronal apoptosis through endoplasmic reticulum (ER) stress. Interestingly, the initial response to ER-stress is a defense mechanism, termed unfolded protein response, characterized by the up-regulation of several ER chaperones. Strikingly, activation of this defense mechanism can be induced by life-style changes, such as exercise, leading to a substantial delay of the disease onset and decrease on the severity of the clinical symptoms. Our work to understand the pathways by which ER stress leads to neurodegeneration enabled us to identify novel targets for therapeutic intervention, some of which may even permit treatment at the late stages of the disease.

A recent area of research in the lab has focused on determining whether other diseases associated with protein misfolding, such as AD and type 2 diabetes, can be also transmissible in a manner similar to prion diseases. In a series of studies, we have uncovered evidence indicating that under experimental conditions various other diseases associated to...
protein misfolding have the potential to propagate in a prion-like manner. These studies may substantially change our view of the origin of some of the most devastating human diseases.

Recently, we have become interested in the identification of non-disease-associated proteins that undergo misfolding and aggregation as part of normal biological function. We identified a bacterial protein that normally polymerizes as an amyloid-like aggregate which participates in modulating the biological activity of the protein. Strikingly, the changes in folding and oligomerization of the protein can self-propagate in the bacterial ecosystem, providing evidence for this protein to be the first prokaryotic prion. The idea that many proteins adopt multiple conformations to exert different functions, and that this biological information can be propagated between different individuals, may revolutionize our understanding of biology. 

About the Author

Dr. Claudio Soto received his Ph.D. in Biochemistry and Molecular Biology from the University of Chile in 1993 and was a postdoctoral fellow at the Catholic University of Chile and at the New York University School of Medicine, where he became an Assistant Professor in 1995. Between 1999 and 2003, Dr. Soto was Senior Scientist, Chairman of the Department of Molecular Neurobiology and Senior Executive Scientific Advisor for Neurobiology at Serono International in Switzerland. Between 2003 and 2008, he served as Director of the George and Cynthia Mitchell Center for Neurodegenerative Diseases and Professor on the Departments of Neurology, Neuroscience & Cell Biology and Biochemistry & Molecular Biology at the University of Texas Medical Branch in Galveston. He is currently a Professor of Neurology and Director of George and Cynthia Mitchell Center for Alzheimer’s disease and related Brain Disorders at the University of Texas Medical School in Houston. Currently he is also the Founder, Vice-President and Chief Scientific Officer of AMPRION Inc.

There are several major barriers to treating these disorders. First, the cellular inclusions that define each of the major forms of dementia have been known for some years. In the case of AD, the characteristic amyloid depositions have been known for decades. And yet, it has been very difficult to translate the direct study of them into our being able to definitively diagnose these disorders when patients present with symptoms. We especially cannot diagnose them before symptoms develop, and hence before brain damage occurs. Thus, it is difficult to tell patients the disorder from which they suffer with any certainty and then to give disease-specific treatments. Moreover, when performing clinical studies, it is difficult to include only persons with one disease: we may inadvertently include patients with different neurodegenerative disorders.

Second, because we cannot diagnose these disorders before symptoms develop and before significant brain damage occurs, we have great difficulty testing medications to delay or prevent them. Who do we test if we cannot definitively determine who will develop a particular disorder? We would especially not want to give experimental medications with potential side effects to persons who are not going to develop the disease. But how do we exclude them?

Finally, it has been observed that medications may have different effects at different points in the disease. Non-steroidal anti-inflammatory (NSAID) drugs, for example, appear to dramatically reduce the probably of developing AD if given earlier in life for one or more years. And yet, multiple trials have shown that NSAIDs do not alter the course of AD once it is diagnosed. This has led to the hypothesis that treatments given after these diseases are fully developed may be too late to stop them as the molecular cascade of events producing them may have been inexorably set in motion.

There is a critical need, then, to be able to diagnose these disorders, especially before symptoms develop and brain tissue and function are lost, and to test treatments to delay or prevent them as millions of people worldwide are affected by them.

A New Approach to Dementia

Researchers and clinicians at UTHealth and Memorial Hermann-Texas Medical Center (MH-
Currently amenable to treatment, such as a family history of dementia, increasing age, a subtype of cholesterol carrying proteins (ApoE4), and several genetic mutations in the genes for amyloid precursor protein and presenilin. Nonetheless, studying these factors may also generate important information that will help in developing treatments.

In addition to identifying and treating dementia risk factors, we are taking a novel approach to developing new diagnostic tests and treatments. We are following patients who have several risk factors for dementia since they have, unfortunately, a high probability of developing it. Our goal is to discover biomarker changes in these patients that can be used to develop definitive diagnostic tests that will work years prior to disease symptoms and before brain damage occurs. The biomarkers we are investigating include ones in spinal fluid and brain structure (MRI), fiber pathway integrity (DTI), and function (PET and magnetoencephalography).

Finally, our clinic is collaborating with the George P. and Cynthia W. Mitchell Center for Research in Alzheimer’s Disease and Related Brain Disorders where laboratory investigators are taking findings from the human studies and are using animal models to investigate how risk factors increase the probability of developing these diseases, to iden-...
in the Spotlight

Brain Night at Health Museum
March 17, 2011

Spring Public Forum
Topic: Bipolar Disorder and Depression
February 12, 2011

Distinguished Lecturer
Daniel R. Weinberger, M.D.
May 19, 2011
Upcoming events

Neurobiology of Disease: Stem Cells and Regenerative Medicine Course: Wednesdays from Noon to 1:00 pm, from August 31, 2011 to December 14, 2011. Course Director, Dr. Sean Savitz, Department of Neurology. This course will address the emerging role of stem cells and other regenerative strategies as potential, novel investigational treatments for acute neurological disorders and neurodegenerative diseases. Lecturers will be given from faculty members at UTHealth and Methodist Hospital with a special guest lecturer, Dr. Randolph Nudo, Ph.D., Director, Landon Center on Aging, University of Kansas Medical Center, on November 30th. Course Contact: Sean.I.Savitz@uth.tmc.edu. Held at the UTHealth Medical School at Houston, Room 7.037.

NRC Poster Session: Saturday, December 3, 2011, 10:00 am to Noon. Held in the Leather Lounge of the UTHealth Medical School at Houston. Sign-up on the NRC website.

The NRC sponsors a number of activities in association with “Brain Awareness Week” which is part of an international campaign created by The Dana Alliance for Brain Initiatives to promote the public and personal benefits of brain research.

Public Forum: Saturday, January 21, 2012, 10:30 am to Noon. This year’s topic will be “Rehabilitation” and will be moderated by Dr. Gerard Francisco, Chair of the Department of Physical Medicine and Rehabilitation. Held at the UTHealth Medical School Building, Room 3.001.

Brain Night: Thursday, March 15, 2012, 6:00-8:00 pm. As a major event associated with National Brain Awareness Week, Brain Night is packed with activity booths aimed to educate children and families about how the brain works and to spark an interest in neuroscience at an early age. Held at The Health Museum, Houston, Texas.

Neurofax: A schedule of neuroscience-related events provided by the NRC available online and by e-mail. This schedule lists events such as seminars, grand rounds, research colloquia, symposia, and local or national conferences that are sponsored by UTHealth, the Texas Medical Center, or Houston area universities and research institutions (including Baylor College of Medicine, Rice University and the University of Houston). To post your event or subscribe to Neurofax, please email: nba-nrc@uth.tmc.edu.

ADRC will be part of the nationwide ADRC network such that Houston-based research will be shared nationally and will be informed by insights gained at other ADRCs around the country.

It is a very exciting and rewarding time to be studying dementia at UTHealth and MH-TMC as we are poised to make significant clinical and basic science advances in the diagnosis and treatment of these devastating disorders.

About the Author
Dr. Paul Schulz went to Boston University for their six year combined BS-MD Degree Program and stayed for an Internship in Internal Medicine. He came to Houston for a Neurology Residency and then a Fellowship in Cellular Neurophysiology at Baylor College of Medicine. He was a faculty member at BCM until moving to UTHealth and Memorial Hermann one year ago. He is an Associate Professor and the Vice Chair for Quality in the Department of Neurology and directs the Memory Disorders and Dementia Clinic.

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tify biomarker changes in animals that can be tested in humans, and to test for medications that are effective against these diseases. Later, medications that are efficacious in animals will be translated back to the Clinic where human trials will test treatments to delay or prevent these disorders.

The UTHealth/MH-TMC Alzheimer's Disease Research Center
Collaborations between the Brain Health and Wellness Clinic, the Mitchell Center, and other Medical Center investigators will form the basis for a 2013 proposal to the National Institutes of Health (NIH) to establish an Alzheimer’s Disease Research Center (ADRC) here in Houston. The ADRC will deliver outstanding patient care and community education in Houston, while conducting cutting-edge research. The ADRC will support clinical and basic research into disease mechanisms and new diagnostic tests and treatments for dementia. The Houston ADRC will be part of the nationwide ADRC network such that Houston-based research will be shared nationally and will be informed by insights gained at other ADRCs around the country.

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