Desire-Magloire Bourneville could hardly have predicted how the disorder that he discovered and described in the late 1800’s would shape the field of neuroscience two centuries later. Studying the brain of an unfortunate 15 year old girl who had died from status epilepticus, he noted sclerotic potato-like lesions (Figure 1A), and coined the term tuberous sclerosis. Since his astute discovery, our understanding of this disorder, now called tuberous sclerosis complex (TSC), has increased exponentially, even leading to novel therapeutic trials to help afflicted individuals. Here I present a brief history of the remarkable progress made in the understanding of this disease, how it has led to major areas of study in neuroscience, and some of the basic science work we are doing to further our knowledge, and ultimately improve the health of these unfortunate patients.

TSC is an autosomal dominant, tumor suppressor disorder. Although many organ systems may be affected, the brain, skin, kidney and heart bear the brunt of this debilitating disease. Patients are predisposed to the development of tumors, usually benign, in many organs. Brain lesions are characterized by cortical and cerebellar tubers, subependymal nodules, and a variety of other less common structural abnormalities. Substantial morbidity and mortality result from epilepsy, developmental and behavioral disability, and autism. Two genes causing TSC have been identified. TSC1, encoding hamartin, was discovered in 1997. TSC2, encoding tuberin, was isolated 5 years earlier. About two thirds of patients represent new dominant mutations in a family, and one third have inherited the defective allele from a parent. Hamartin and tuberin are 130 kDa and 200 kDa proteins respectively. It was unclear how mutations in these proteins (TSC1 and TSC2) affected the nervous system.

Modification of the nervous system is required for memories of places and events to be formed and stored. Whereas short-term memory (memories lasting for minutes to hours) involves the phosphorylation of existing proteins, long-term memory (memories lasting days to weeks, and sometimes a lifetime) requires gene expression and protein synthesis, and is accompanied by growth processes such as increased synaptic numbers, button size, and number of dendritic branch points. The mechanism(s) by which learning leads to alterations in gene expression and protein synthesis, as well as the identification of the genes and proteins whose expressions are altered, remains an intense area of research. A number of studies have shown that neurotrophic factors, including brain derived neurotrophic factor (BDNF), nerve growth factor (NGF), and insulin like growth factor-1 (IGF-1), participate in memory formation. Binding of these neurotrophic factors to their receptors activates three key intracellular signaling cascades: MAPK/ERK, PLC and PI3K. Work performed in our laboratory has delineated a role for each of these cascades in spatial memory storage.

Recently, the tuberous sclerosis protein complex (a protein complex consisting of TSC1 (hamartin) and TSC2 (tuberin)) has been shown to be a key signaling component of the PI3K and MAPK cascades. The TSC1-TSC2 complex integrates intracellular signals initiated by growth factors and nutrients (e.g., glucose, amino acids), making it an important regulator of growth processes. When activated (in low nutrient or growth factor conditions), the TSC1-TSC2 complex reduces the activity of mammalian target of rapamycin (mTOR), a protein kinase that normally stimulates protein translation, thereby reducing protein synthesis and growth. Upon binding of neurotrophic factors to their cellular receptors, PI3K is activated leading to the phosphorylation of TSC2 (Ser939, Ser1130, and Thr1462) and disruption of the TSC1-TSC2 complex. This results in the activation of mTOR (Figure 1). Activated mTOR phosphorylates two key regulators of translation, ribosomal S6 kinase (S6K) and elf-4E-binding protein 1 (4EBP1). Thus, growth factor binding decreases TSC inhibition of mTOR, allowing for the enhanced protein synthesis required for growth. In addition to its phosphorylation of TSC2, PI3K (via AKT) has...
Brain Awareness Month and other UTHSC-Houston Neuroscience Successes

From the director, John H. Byrne, Ph.D.

Brain Awareness Month In Houston in 2008

Brain Awareness Week was extended to Brain Awareness Month with a proclamation by Houston mayor Bill White. The annual Public Forum was held early in Brain Awareness Month on March 1, and this year’s subject was “Stem Cells: Their Potential for Neurologic Disease”. The Forum was moderated by James Grotta, M.D., Chairman of the Department of Neurology of the UT Medical School, and panelists included James Baumgartner, M.D. of Memorial Hermann Hospital who works with epilepsy and other neurological disorders in children, Sean Savitz, M.D. of the UT Medical School Department of Neurology who works with stroke, Paul Simmons, Ph.D. of the UT Brown Institute for Molecular Medicine who works with stem cell therapies, and Henry Strobel, Ph.D. of the UT Medical School Department of Biochemistry and Molecular Biology who works with monitoring the brain’s response to physical injury or treatment for neurological disorders. The discussion was lively, and the enthusiastic lay audience from the community was joined by many members affiliated with institutions within the Texas Medical Center. Discussions between audience members and the panelists continued for almost an hour after the official close of the Public Forum, and attendees were treated to brain-related demonstrations given by faculty from the Departments of Neurobiology and Anatomy and Neurology. A number of Advocacy Groups handed out information and gave some demonstrations. These included the Alzheimer’s Association of Houston and Southeast Texas, Parkinson Foundation of Harris County, UT Physicians, Mission Connect of the Texas Institute for Rehabilitation and Research, and a Rehabilitation Team from the Texas Woman's University.

During Brain Awareness Week (March 9-15), several local bookstores featured displays on brain related issues, and on March 22, in conjunction with the Houston Independent School District Spring Break, Brain Night for Kids was held at the McGovern Museum of Health and Medical Sciences. This event featured 12 interactive booths, including two new ones on Comparative Brain Anatomy of primates, canids, felids, birds, amphibians, reptiles and fish, and one demonstrating brain anatomy using complex human brain models. All booths were run by faculty, postdoctoral fellows, and graduate students from the UTHSC-Houston and Texas Woman's University, and the event was its usual outstanding success with more than 300 children and their families coming to the museum during this two-hour time period. Photos of the enthusiastic children and their families can be seen in the Spotlight section on page 7.

UTHSC-Houston Neuroscience News

The Dan L. Duncan Children’s Neurodevelopmental Clinic opened this spring as part of the UTHSC-Houston Children’s Learning Institute. The clinic is funded through a $10 million dollar donation from the Duncan family of Houston, and is named for the patriarch of the family. The clinic is to help in the diagnosis and treatment of children with autism, head injuries, learning disorders, and many other neurological disorders affecting children. The clinic is directed by NRC member Linda Ewing-Cobbs and the medical director is NRC member W. Daniel Williamson. The Duncan family has a personal interest in this as one of their children was helped at the Children’s Learning Institute, and they wanted less fortunate families to have the same resources available to them that they did. The Children’s Learning Institute is under the Direction of NRC member Susan Landry.

On another note, the Department of Defense awarded $33.6 million dollars to the Mission Connect Mild TBI Translational Research Consortium, which includes research teams from the UTHSC-Houston, UT Medical Branch at Galveston, Baylor College of Medicine, Rice University, and the Transitional Learning Center in Galveston. NRC member Alex Valadka is the principal investigator for UTHSC-Houston, and other NRC faculty members included on the grant are Ponnada Narayana, Paul Swank, Raymond Grill, Pramod Dash, and Andrew Papanicoulou. There are approximately 1.5 million people per year that suffer a traumatic brain injury (TBI), including a concussion. Although many of these are considered mild injuries, they often lead to long-term or permanent impairments that can be overlooked. The increase in TBI is especially noticeable in war veterans, making the effort to intervene early even more timely. This research initiative is focused on the early diagnosis and development of innovative therapies for TBI, including imaging for diagnosing and tracking treatment. Patients being treated at Memorial Hermann (UTHSC-Houston), Ben Taub Hospital and the Michael E. DeBakey VA Medical Center will be recruited for clinical trials. UTHSC-Houston is at the forefront of this both exciting and urgently needed research. ✨
news&information

Honors

Pedro Mancias, M.D., Associate Professor of Neurology and Pediatrics, received the 2008 Leonard Tow Humanism in Medicine Award, sponsored by the Arnold P. Gold Foundation.

Pedro Ruiz, M.D., Professor and interim Chair of the Department of Psychiatry and Behavioral Sciences, was the keynote speaker at the First International Symposium on Addiction Medicine. In addition, he was appointed to the Senior Advisory Editorial Board of FOCUS: The Journal of Lifelong Learning in Psychiatry of the American Psychiatric Association.

UTHSC-Houston recently honored some of the health science center’s outstanding young researchers, including NRC faculty members Raymond Grill, Ph.D. for his work on “Acute and Chronic Models of Spinal Cord Injury”, and M. Sriram Iyengar, Ph.D. for his work on “Computational Technologies for Algorithmic Medicine”.

Awards

Jason L. Anthony, U.S. Dept. Education, Efficacy of Earobics Step 1 in English Language Learners and Low SES Minority Children.


Michael Beierlein, American Heart Association Award for beginning Grant-in-Aid, Properties and Functional Consequences of Transmitter Release from Neocortical Astrocytes.

John H. Byrne, National Institute of Health, Analysis of the Neural Control of Behavior.

Staley A. Brod, National Multiple Sclerosis Society, Clinical Conversion of Female Monozygotic Twins Discordant for CIS/MS.


Valentin Dragoi, University of California at San Francisco, Network Mechanisms of Visual Behavior.

Michael J. Gambello, NIH, Mouse Models of the Neuropathology of Tuberous Sclerosis Complex.

Raymond J. Grill, Paralyzed Veterans of America, Inflammation in Chronic Spinal Cord Injury.

James C. Grotta, NIH, funding for 26th Princeton Conference on Cerebrovascular Disease.

M. Sriram Iyengar, Microsoft Research, Structured Multi-Modal Clinical Guidelines on Cell Phones.

Elizabeth B. Jones, NIH, Neurological Emergencies Treatment Trials Southeast Texas Clinical Site Hub.

Giridhar P. Kalamangalam, American Epilepsy Society, Oxygen-Enhanced FMRI in Refractory Nonlesional Focal Epilepsy.

Susan Landry, Texas Education Agency, Texas Early Education Model (TEEM).

Scott Lane, NIH, Neural Correlates of Alcohol Effects on Aggression.

Katherine A. Loveland, University of Houston, Somatosensory, Motor and Auditory Function in Individuals with Autism Spectrum Disorder.

David W. Marshak, Society for Neuroscience, Houston Area Chapter SN BAW Support.

Stephen L. Mills, NIH, Connectivity Patterns of Retinal Bipolar Cells.

F. Gerard Moeller, The University of Texas Medical Branch at Galveston, Clinical Neurobiology of Serotonin and Addiction.

Ponnada A. Narayana, 1) Teva Neuroscience Inc., Effective Communication between Neuroradiologists and Multiple Sclerosis Physicians; 2) NIH/NIBIB, Automated MR Image Analysis in MS: Identification of a Surrogate Marker in Multiple Sclerosis; 3) Department of Defense, Mission Connect Mild TBI Translational Research Consortium.

Hope Northrup, 1) Texas Department of State Health Services, Comprehensive Metropolitan and Outreach Genetic Services; 2) Tuberous Sclerosis Alliance, Tuberous Sclerosis Complex Natural History Database Project.

Gary C. Rosenfeld, NIDDK, Short-Term Research Training for Medical Students.

Sean I. Savitz, Howard Hughes Medical Institute, Physician-Scientist Early Career Award.

Angela L. Stotts, Health Resources & Services Administration, Reducing Environmental Tobacco Smoke in NICU Infants’ Homes.

Alex Valadka, DoD TIRR Mission Connect, Post-traumatic Stress Disorder and Traumatic Brain Injury Research Program.

Steven Wang, Matilda Ziegler Foundation for the Blind, Inc., Using Math5 Locus to Study the Mechanism of Retinal Stem Cell Formation.

Jerry S. Wolinsky, Clayton Foundation for Research, Viral Mimicry and Multiple Sclerosis.

2007-2008 Dean’s Teaching Excellence NRC Awardees

Han Zhang, M.D., Senior Lecturer in the Department of Neurobiology and Anatomy, received the John Freeman Faculty Teaching Award. This is the second time he has received this award, an award which is determined by the senior class in the Medical School.

Jaroslaw Aronowski, Ph.D. Neurology

Parveen Athar, M.D. Neurology

Michael R. Blackburn, Ph.D. Biochemistry and Molecular Biology

Eugene Boisabuin, M.D. Internal Medicine

Ian J. Butler, M.D., Pediatrics

Philip B. Carpenter, Ph.D. Biochemistry and Molecular Biology

Louvenia Carter-Dawson, Ph.D. Ophthalmology and Visual Science

Chitra Chandrasekhar, M.B. B.S. Diagnostic and Interventional Imaging

John W. Crommett, M.D. Neurosurgery

Terry Crow, Ph.D. Neurobiology and Anatomy

Elizabeth H. David, M.D. Psychiatry and Behavioral Sciences

Daniel J. Felleman, Ph.D. Neurobiology and Anatomy

Gerard E. Francisco, M.D. Physical Medicine and Rehabilitation

Carin A. Hagberg, M.D. Anesthesiology

Judiianne Kellaway, M.D. Ophthalmology and Visual Science

James J. Knierim, Ph.D. Neurobiology & Anatomy

Pedro Mancias, M.D. Pediatrics

Nidal Moukaddam, M.D. Psychiatry and Behavioral Sciences

Hope Northrup, M.D. Pediatrics

John O’Brien, Ph.D. Ophthalmology and Visual Science

Sonja L. Randle, M.D. Psychiatry and Behavioral Sciences

Donna T. Rocha, M.D. Psychiatry and Behavioral Sciences

Dawnelle J. Schatte, M.D. Psychiatry and Behavioral Sciences

Mya C. Schiess, M.D. Neurology

Nurun N. Shah, M.D. Psychiatry and Behavioral Sciences

Clark W. Sitton, M.D. Diagnostic and Interventional Imaging

Alicia B. Vittone, M.D. Psychiatry and Behavioral Sciences

Edgar T. Walters, Ph.D. Integrative Biology and Pharmacology

Han Zhang, Ph.D. Neurobiology and Anatomy
either gene could cause a similar disease until yeast two-hybrid experiments, and co-immunoprecipitation studies confirmed that the two proteins interact in a complex. This biochemical association explained how loss of either could lead to TSC.

Comprehensive genotype/phenotype studies done by Hope Northrup's laboratory here at UT and in David Kwiatkowski's laboratory at Harvard University have demonstrated that the majority of mutations in the TSC1 and TSC2 genes in patients with TSC are loss of function mutations. This has led to the hypothesis that TSC is indeed a tumor suppressor disorder. In other words, the normal function of the TSC genes is to control cell growth. In the disease state, there is uncontrolled cell growth leading to tumors in a variety of organs.

Elegant genetic studies in Drosophila put the TSC1-TSC2 complex on the cellular map. The TSC1-TSC2 complex inhibits an evolutionarily conserved pathway called the growth signaling/mTOR pathway (Figure 1B). The mTOR pathway, dubbed so because the TOR protein is the target of a fungal metabolite called rapamycin (hence mammalian Target of Rapamycin = mTOR), regulates translation, cell growth and proliferation in response to growth factor signaling, nutrients, and oxygen tension. The TOR protein exists in two mTOR complexes, mTORC1 and mTORC2. It is mTORC1 that is rapamycin sensitive. In an unstimulated state, the TSC complex suppresses mTOR through its GTPase activity of a Ras-like protein called RHEB. Stimulation of the pathway leads to Akt-mediated TSC1-TSC2 dissociation and increased mTOR activity, with subsequent increased translation, proliferation and cell growth. The giant cells seen in the brain lesions of TSC patients are a direct result of uninhibited mTOR stimulation. It was soon realized that the inhibition of the mTORC1 pathway by rapamycin might rescue the inhibition lost in patients with TSC. Studies in traditional knockout mice showed promising regression of renal tumors, leading to human clinical trials that have been quite encouraging. There have also been a few promising trials in the treatment of some of the brain lesions of TSC, though much more research is needed. Luckily for patients in the Houston area, we have a comprehensive TSC Clinic that was started by Hope Northrup in collaboration with UT and Memorial Hermann Hospital. Some of these patients are receiving rapamycin.

The mTOR pathway had been studied extensively by cancer biologists, primarily due to its crucial role in cell growth and proliferation. The discovery that the TSC genes are a crucial component of this pathway, in part, paved the way for neuroscientists to enter the evolving story. Currently, multiple studies are investigating the role of the TSC1-TSC2 complex in the regulation of neuronal growth, axon guidance, synapse function and dendritic networks in various animal model systems. Active research is underway in Pramod Dash's laboratory here at UT in collaboration with us to analyze the involvement of the TSC complex in learning and memory. Indeed, we have come a long way from the initial observation by Bourneville.

Our laboratory has concentrated on understanding the in vivo etiology of the brain lesions of TSC using the mouse as a model system. The brain pathology of TSC suggests that it is a developmental disorder of neuronal migration. Tuberous lesions have been detected in utero as early as 20 weeks of gestation. Brain lesions demonstrate many features of neuronal migration disorders such as abnormal cortical gyri and other heterotopias surrounded by normal cortex. Traditional heterozygous knockout mouse models have developed the renal lesions of TSC, but minimal brain pathology. Homozygous knockouts of either gene are embryonic lethal. Given the apparent global importance of both Tsc1 and Tsc2 in development, selective ablation of either gene is needed to model and study brain disease. Selective gene ablation is most commonly performed using the Cre-loxP system. Conditional null mice contain a genomic copy of the gene of interest flanked by loxP sites. When mated to a Cre transgenic mouse, the floxed gene will only be deleted in cells expressing Cre recombinase enzyme. The expression of Cre is dependent upon the tissue or temporal specific promoter driving its expression. Hence a mosaic mouse can be created and the effect of gene deletion can be studied in a temporal

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and/or site-specific manner.

Because TSC is a developmental tumor suppressor disorder, a current hypothesis of TSC neuropathogenesis is that loss of function of the TSC complex in a subset of neural progenitors predisposes to perturbations in neuronal proliferation, differentiation and migration, leading to cortical dysplasias and other lesions of TSC. This hypothesis remains largely untested. Our hypothesis is that loss of either TSC1 or TSC2 in radial glial neuroprogenitors might be an important site of TSC neuropathology. We have begun to address this hypothesis by generating a conditional allele of Tsc2 in the mouse. Using this mouse and an hGFAP-Cre mouse that expresses Cre recombinase in radial glial cells, we have created a Tsc2flox/ko;hGFAP-Cre mouse to model the neuropathology of TSC. This mouse has one null allele of Tsc2 (the ko allele), similar to human patients. The floxed allele behaves as a wildtype. When the floxed allele is exposed to Cre recombinase, it will be converted to a null (ko) allele. In our Tsc2flox/ko;hGFAP-Cre mice, Cre will only be expressed in radial glia. Hence complete loss of function of the TSC complex will only occur in these neuroprogenitor cells. In essence the Tsc2flox/ko;hGFAP-Cre mouse is a mosaic animal in which all cells of the animal are Tsc2+/-, and all cells derived from radial glia are Tsc2 -/-.

In this manner we can bypass the embryonic lethality caused by homozygous deletion of either gene in all cells. The phenotype of these Tsc2flox/ko;hGFAP-Cre mice is quite striking. Their growth slows from postnatal day 5 leading to runted, rather sick animals at weaning (Figure 2A) that die between 3 and 4 weeks of age from seizures. They exhibit marked postnatal megalencephaly (Figure 2C), cortical thickening, hydrocephalus (Figure 2E), lamination defects, giant cells (Figure 2G) and hippocampal heterotopias. These are all features of the human disease. We are currently trying to understand the cause of the megalencephaly and apparent migration defects through developmental analyses. Preliminary data demonstrate abnormalities in cortical lamination markers and an apparent increase in the basal progenitor cell population. Cell counts however have shown that the total number of cells in the cortex remains the same, but the proportion of different layer specific cells vary. This suggests that the TSC complex is crucial for neuronal differentiation. The megalencephaly is likely due in part to the increase in cell size, however we have noted a marked increase in the extracellular matrix of mutant mice. Further characterization of this model will provide new insights into the neurodevelopmental functions of the TSC complex as well as the TOR pathway. We have begun to try to rescue the defects in the Tsc2flox/ko;hGFAP-Cre mice by treating them with rapamycin. In addition we hypothesize that treating mice in utero might significantly reduce the adult neuropathology. While treating the unborn child with rapamycin is far off, it is exciting to think that tuber burden could be kept to a minimum in unborn children with TSC.

The TSC story is quite remarkable, starting with the initial description of this disorder, to the discovery of the genes, some of their functions, and therapeutic interventions. But many more chapters need to be written. Our work will help to understand the in vivo neurodevelopmental functions of the TSC complex, as well as unravel new pathways that may be targets for disease. There is clearly much more hope for patients today than for those unfortunate ones initially described by Bourneville.

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**About the author**

Michael J. Gambello, M.D., Ph.D., is an assistant professor of pediatrics in the division of medical genetics at the University of Texas Houston Medical School. He earned his bachelor’s degree in chemistry from the Massachusetts Institute of Technology. He received his M.D. and Ph.D. in microbiology and immunology at the University of Rochester School of Medicine and Dentistry. Pediatric residency training was done at St. Louis Children’s Hospital/Washington University. He completed his fellowship in Medical Genetics at the NIH/NHGRI, and did postdoctoral training in mouse genetics at UCSF. He joined the UT faculty in October 2001. Dr. Gambello is a diplomate of the American Board of Pediatrics and the American Board of Medical Genetics.
been shown to directly phosphorylate mTOR (Ser2448). It is thought that this phosphorylation may serve to relieve an intrinsic inhibition, allowing growth factors to activate mTOR independent of TSC1-TSC2 regulation. As long-term memory requires de novo protein synthesis, we questioned if memory formation depends on the function of mTOR.

To test this possibility, we examined the influence of post-training manipulation of the TSC-mTOR cascade on performance in the Morris water maze task. The hidden platform version of the Morris water maze task assesses learning and memory by requiring that the animal learn the spatial relationship between a set of fixed extra-maze cues and a submerged escape platform. With repeated training, animals are capable of finding the platform with decreased latency and will spend more time searching the area in which the platform is located. Memory is assessed by removing the escape platform from the maze (probe trial) and measuring the latency to cross the previous location of the hidden platform, the number of platform crossing, as well as the time spent searching in each quadrant. Our results using intra-hippocampal administration of rapamycin, a selective inhibitor of mTOR, demonstrated that this drug effectively reduces hippocampal S6K phosphorylation. When infused into the hippocampus of animals immediately following training, rapamycin caused an impairment in spatial memory as indicated by poor performance in a probe trial given 48hr post-training. The memory-impairing influence of post-training infused rapamycin was observed following both massed (single-session training) and spaced (multi-day training) paradigms. As the infusions were performed after behavioral training, rapamycin likely interfered with memory formation rather than affecting learning or motivation. These results suggest that the TSC-mTOR cascade is required for long-term memory, and may provide one mechanism by which growth factors contribute to memory formation.

Over the past several years, studies in humans and rodents have indicated that modest increases in glucose levels can improve memory. How glucose modulated memory, however, was not clear. Recently, it has been shown that a kinase upstream of mTOR, AMP-activated protein kinase (AMPK), is a cellular energy sensor. AMPK is activated when AMP concentrations rise, resulting in the direct phosphorylation of TSC2 (Thr1227 and Ser1345). However, unlike the phosphorylation caused by PI3K/AKT, the phosphorylation of TSC2 by AMPK makes the TSC1-TSC2 complex a stronger inhibitor of mTOR activity. Thus, in conditions where AMP levels are high, phosphorylation of TSC2 by AMPK may serve as a means of reducing mTOR activity and protein synthesis (Figure 2). In contrast, in high energy conditions (e.g. elevated glucose concentrations), AMPK is inhibited resulting in decreased TSC inhibition of mTOR and enhanced protein synthesis. Based on these observations, we hypothesized that the memory-enhancing effect of glucose is due, at least in part, to elevated mTOR activity.

To test the above hypothesis, we first tested if glucose activates the TSC-mTOR pathway in rodent hippocampus. Animals were infused with glucose into one hippocampus while being simultaneously infused with vehicle into the contralateral hippocampus. Use of the contralateral hippocampus as a control, allows for intra-animal comparison to test the efficacy of an agent. Comparison of AMPK, 4EBP1, and S6K phosphorylation revealed that glucose, by inactivating AMPK, resulted in enhanced mTOR activity. In contrast, the AMPK activator AICAR (5-aminoimidazole-4-carboxyamide) suppressed mTOR activity. Consistent with these results, we found that intra-hippocampal infusion of glucose enhanced, while AICAR impaired, long-term spatial memory. This memory-enhancing effect of intra-hippocampal glucose infusion could be blocked by co-administration of rapamycin. The involvement of the TSC-mTOR pathway for glucose utilization and memory formation may have clinical implications. Tuberous sclerosis (TS), an autosomal dominant disorder occurring in about 1 in 6,000 – 10,000 births, is caused by mutations of TSC1 or TSC2 and is characterized by the development of tumor-like growths, named hamartomas in the kidneys, heart, skin, and brain. These mutations are associated with overactive mTOR and sustained phosphorylation of S6K and 4EBP1. Approximately 31% of TS patients have an estimated IQ < 21 with only 55% having an IQ >70, with deficiencies most frequently observed in the areas of executive control and memory. Although numerous pathological changes are observed in these patients that can contribute to cognitive dysfunction, our results suggest that some of the behavioral and memory problems seen in patients carrying mutations in either tsc1 or tsc2 genes may be due to an inability to properly regulate the protein synthesis required for long-term plasticity.

About The author

Dr. Pramod Dash received his master’s in Physics from the Indian Institute of Technology in Physics in 1979 and his Ph.D. in Biological Sciences from Carnegie-Mellon University in Pittsburgh in 1986. Following a postdoctoral fellowship under Eric Kandel at Columbia University in New York, he joined the faculty in the Department of Neurobiology and Anatomy at the University of Texas-Houston Medical School in 1990. He is presently a full professor in the Departments of Neurobiology and Anatomy and Neurosurgery, and is the Director of Head Injury Research of the TIRR/Mission Connect Consortium. Anthony Moore received his Bachelor of Science from Texas A&M University in Biochemistry in 1989, and holds the position of Research Coordinator for Dr. Dash.
Brain Night for Kids was held at the McGovern Museum of Health and Medical Sciences on March 20, 2008. UT-Houston faculty, postdocs and graduate students presented interactive demonstrations on aspects of the brain, and children and their families enthusiastically joined in.

Public Forum

The Public Forum on “Stem Cells: Their Potential for Neurologic Disease” was held on March 1, 2008. Dr. James Grotta (standing left) was the moderator and Dr. John Byrne (standing right) introduced the Forum. Questions from the audience were lively!

Annual Poster Session

The Annual Poster Session was held December 1, 2007. Graduate students Diego Gutnisky and Jing Zhao tied for first place and shared the Dee S. and Patricia Osborne Endowed Scholarship in the Neurosciences, while postdoctoral fellows Yoganarasimha Doreswamy and Francesco Savelli tied for first place for the NRC prize.
15th Annual Neuroscience Poster Session

Hosted by the NRC

Saturday, December 6, 2008

UTHSC-Houston
MSB Leather Lounge
6431 Fannin St.
10:00 AM to 12:00 noon