



TSC ALERT

Edited by Vicky H Whittemore, PhD

August 2005

Welcome to the August 2005 edition of *TSC Alert* – an online research newsletter for individuals interested in Tuberous Sclerosis Complex (TSC) research and clinical care. This online newsletter contains information of interest to the TSC research and health care community. Please forward this newsletter to colleagues who are interested in TSC. To be added/deleted to/from the mailing list for *TSC Alert* and/or to submit information for the September 2005 *TSC Alert* contact: vwhittemore@tsalliance.org

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GRANT ANNOUNCEMENTS

TUBEROUS SCLEROSIS ALLIANCE REQUEST FOR APPLICATIONS

Deadline for submission of Letter of Intent: September 1, 2005

The TS Alliance is currently accepting Letters of Intent (LOI) for its TSC Research Program. The LOIs will be reviewed, and selected applicants will be invited to submit grant applications. The following grants are available from the TS Alliance:

- Predoctoral Awards - \$50,000 per year for up to 3 years
- Clinical and Postdoctoral Fellowship Awards - \$50,000 per year for up to 3 years
- Junior Investigator Awards - \$50,000 per year for up to 3 years
- Senior Investigator Awards - \$50,000 per year for up to 3 years
- Pilot Clinical Trial Awards - \$30,000 for one year awards
- Clinical Trial Planning Awards - \$30,000 for one year awards
- Conference Grants - \$50,000 maximum for one year awards

Deadlines for TS Alliance Research Grants Program:

Submission of Letter of Intent: September 1, 2005
Submission of Invited Applications: November 1, 2005
Grant Review: December 2005 – February 2006
Notice of Grant Awards: June 2006
Earliest Grant Start Date: July 1, 2006

For the complete Request for Proposals (RFPs) and LOI application forms:
<http://www.tsalliance.org>

Questions? Contact Dr. Vicky Whittemore at: vwhittemore@tsalliance.org

NIH RELEASES TUBEROUS SCLEROSIS COMPLEX PROGRAM ANNOUNCEMENT

The TS Alliance is pleased to announce the release of the National Institutes of Health (NIH) Program Announcement with set-aside funds (PAS) entitled "Understanding and Treating Tuberous Sclerosis Complex." This is a joint Program Announcement with NIH and the TS Alliance. The participating organizations intend to commit a total of approximately \$2 million to this PAS in addition to funds available for applications sent in response to this initiative that score within the pay lines of the participating NIH Institutes (NINDS, NIDDK, NIMH, NIAMS and NCI). For more information and the complete text of the Program Announcement see:
<http://grants.nih.gov/grants/guide/pa-files/PAS-05-085.html>

PARENTS AGAINST CHILDHOOD EPILEPSY, INC. (PACE)

Deadline: September 15, 2005

PACE will consider grant applications for innovative research to encourage investigation into the causes and cures of seizure disorders in children. The primary areas of research they are interested in stimulating are:

- Innovative pediatric models of epilepsy
- Electrophysiologic recording on live human tissue from epilepsy surgery
- Evaluation of neocortical epilepsies
- The role of immune or inflammatory mediators in epilepsy
- Neuro immunological effects of inflammatory molecules with the emphasis on dietary pathogens
- Other innovative proposals that fall outside the above areas that address pediatric epilepsy will be considered, including quality of life.

Send for the two page screening application and file the application by September 15, 2005

For more information: www.paceusa.org

E-mail: pacenyemail@aol.com

Phone: 212-665-PACE (7223)

FAX: 212-327-3075

ROBERT S. MORISON FELLOWSHIP FOR ACADEMIC CLINICIAN SCIENTISTS IN EPILEPSY

Deadline: September 1, 2005

The American Epilepsy Society (AES) is proud to announce its partnership with The Grass Foundation to offer the Robert S. Morison Fellowship for the training of academic clinician scientists in epilepsy. This two year post-doctoral fellowship will be awarded to a promising young investigator possessing an MD degree who intends to continue training in basic science in an epilepsy research laboratory. The fellowship was created in honor of the contributions of Dr. Morison, one of the founding Trustees of The Grass Foundation. Albert and Ellen Grass started The Grass Foundation in the 1950's and have made many contributions to the scientific and social aspects of epilepsy. The Fellowship will be \$40,000 per year for two years for salary with

an additional \$10,000 (maximum) per year to be used for institutional fringe benefits plus \$1,000 for the fellow to travel to the AES Annual Meeting to present his/her results. The award will be announced and presented during the AES Annual Meeting. The next available fellowship will be funded July 1, 2006 through June 30, 2008. The application deadline will be September 1, 2005 and notification will be made by December 10, 2005. Physicians interested in being considered for a Robert S. Morison Fellowship should apply for either a Postdoctoral Fellowship or a Research and Training Fellowship for Clinicians administered by the Epilepsy Foundation. For application information go to <http://www.epilepsyfoundation.org/research/grants.cfm>
**Please note in the application the desire to be considered for a Morison Fellowship.
The Morison Fellowship will be selected by the AES/Epilepsy Foundation Clinical Grant Selection Committee from among qualified applicants for the Postdoctoral Fellowships and Research and Training Fellowships. Applicants for this fellowship can at the same time be considered for a fellowship in the category under which he/she applied.

NEW EARLY CAREER PHYSICIAN SCIENTIST AWARD PROGRAM

Deadline: September 15, 2005

The American Epilepsy Society (AES) and the Milken Family Foundation announce a new funding mechanism for physician scientists who are embarking on academic careers and wish to develop outstanding epilepsy research programs. Funded by the Milken Family Foundation and administered by AES, this new program seeks to encourage the development of new therapies for epilepsy by providing research training for physicians early in their academic career.

Applications must be received by September 15, 2005. Awardees will be announced and funding will be distributed at the AES Annual Meeting in December 2005 in Washington, DC.

Funding Available: Awards will be made in the amount of \$50,000. Competitive renewals for a second year of funding will be considered.

For more information: <http://www.aesnet.org>

AMERICAN SKIN ASSOCIATION

Deadline: October 3, 2005

The following grants are available from the American Skin Association:

- Research Scholar Award - \$50,000
- Research Grants – supports research on five (5) skin disorders: skin cancer, melanoma, vitiligo/pigment cell biology, childhood skin diseases/disfigurement, and autoimmune/inflammatory skin diseases: \$15,000
- Health Services/Quality of Life/Outcome Studies - \$15,000
- Medical Student Grants – targeting melanoma/skin cancer - \$7,000

For more information, contact the American Skin Association at:

346 Park Ave South, 4th Fl.

New York, NY 10010

Phone: (212)889-4858 or 1-800-499 SKIN (7546)

FAX: (212)889-4959

E-mail: info@americanskin.org

Web site: www.americanskin.org

NIDDK AND NCI CAREER DEVELOPMENT PROGRAM UROLOGIC SURGEONS (NOT-DK-05-015)

National Institute of Diabetes and Digestive and Kidney Diseases

National Cancer Institute

<http://grants.nih.gov/grants/guide/notice-files/NOT-DK-05-015.html>

BASIC AND PRECLINICAL RESEARCH ON COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM) (PA-05-141)

National Center for Complementary and Alternative Medicine
National Cancer Institute
Office of Dietary Supplements
Application Receipt Date(s): Multiple dates, see announcement.
<http://grants.nih.gov/grants/guide/pa-files/PA-05-141.html>

BIOBEHAVIORAL METHODS TO IMPROVE OUTCOMES RESEARCH (PA-05-142)

National Institute of Nursing Research
National Cancer Institute
National Institute on Deafness and Other Communication Disorders
National Institute of Diabetes and Digestive and Kidney Diseases
National Institute of General Medical Sciences
Office of Behavioral and Social Science Research
Application Receipt Date(s): Multiple dates, see announcement.
<http://grants.nih.gov/grants/guide/pa-files/PA-05-142.html>

MENTORED PATIENT-ORIENTED RESEARCH CAREER DEVELOPMENT AWARD (K23) (PA-05-143)

National Institute on Aging
National Center for Complementary and Alternative Medicine
National Cancer Institute
National Center for Research Resources
National Eye Institute
National Heart, Lung, and Blood Institute
National Institute on Alcohol Abuse and Alcoholism
National Institute of Allergy and Infectious Diseases
National Institute of Arthritis and Musculoskeletal and Skin Diseases
National Institute of Biomedical Imaging and Engineering
National Institute of Child Health and Human Development
National Institute on Drug Abuse
National Institute on Deafness and Other Communication Disorders
National Institute of Dental and Craniofacial Research
National Institute of Diabetes and Digestive and Kidney Diseases
National Institute of Environmental Health Sciences
National Institute of General Medical Sciences
National Institute of Mental Health
National Institute of Neurological Disorders and Stroke
National Institute of Nursing Research
Office of Dietary Supplements
Application Receipt Date(s): Multiple dates, see announcement.
<http://grants.nih.gov/grants/guide/pa-files/PA-05-143.html>

DEVELOPING CENTERS FOR INNOVATION IN SERVICES AND INTERVENTION RESEARCH (DCISIR) (PAR-05-144)

National Institute of Mental Health
National Institute on Alcohol Abuse and Alcoholism
Application Receipt Date(s): November 1, 2005; June 1, 2006, 2007, 2008
<http://grants.nih.gov/grants/guide/pa-files/PAR-05-144.html>

NEW TSC PUBLICATIONS

Basso AD, Mirza A, Liu G, Long BJ, Bishop WR, Kirschmeier P (2005) The FTI SCH66336 (Lonafarnib) inhibits Rheb farnesylation and mTOR signaling: Role in FTI enhancement of taxane and tamoxifen anti-tumor activity. *J Biol Chem* 2005 Jul 8 [Epub ahead of print]

Byfield MP, Murray JT, Backer JM (2005) hVps34 is a Nutrient-regulated lipid kinase required for activation of p70 S6-kinase. *J Biol Chem* 2005 Jul 27 [Epub ahead of print]

Camoretti-Mercado B, Solway J (2005) Transforming Growth Factor-beta1 and Disorders of the Lung. *Cell Biochem Biophys* 43(1):131-48

Cepeda C, Andre VM, Vinters HV, Levine MS, Mathern GW (2005) Are cytomegalic neurons and balloon cells generators of epileptic activity in pediatric cortical dysplasia? *Epilepsia* 46 Suppl 5:82-8

Cohen MM, Pollock-Barziv S, Johnson S (2005) The emerging clinical picture of lymphangioliomyomatosis. *Thorax* 2005 Jul 29 [Epub ahead of print]

Feng Z, Zhang H, Levine AJ, Jin S (2005) The coordinate regulation of the p53 and mTOR pathways in cells. *Proc Natl Acad Sci U S A* 2005 Jun 7 102(23):8204-9 Epub 2005 May 31

Gan B, Melkounian ZK, Wu X, Guan KL, Guan JL (2005) Identification of FIP200 interaction with the TSC1-TSC2 complex and its role in regulation of cell size control. *J Cell Biol* 2005 Jul 25 [Epub ahead of print]

Goh S, Kwiatkowski DJ, Dorer DJ, Thiele EA (2005) Infantile spasms and intellectual outcomes in children with tuberous sclerosis complex. *Neurology* 65(2):235-8

Hahn-Windgass A, Nogueira V, Chen CC, Skeen JE, Sonenberg N, Hay N (2005) Akt activates mTOR by regulating cellular ATP and AMPK activity. *J Biol Chem* 2005 Jul 15 [Epub ahead of print]

Hedhli N, Pelat M, Depre C (2005) Protein turnover in cardiac cell growth and survival. *Cardiovasc Res* [Epub ahead of print]

Hengstschlager M, Rosner M, Fountoulakis M, Lubec G (2005) The cellular response to ectopic overexpression of the tuberous sclerosis genes, TSC1 and TSC2: a proteomic approach. *Int J Oncol* 27(3):831-8

Kanda S, Miyata Y, Mochizuki Y, Matsuyama T, Kanetake H (2005) Angiotensin 1 is mitogenic for cultured endothelial cells. *Cancer Res* 65(15):6820-7

Lambrecht V, Van Goethem JW, Ozsarlak O, Maes M, Parizel PM (2005) Tuberous sclerosis and subependymal giant cell astrocytoma. *JBR-BTR*. 88(3):144-5

Law BK (2005) Rapamycin: An anti-cancer immunosuppressant? *Crit Rev Oncol Hematol* 2005 Jul 20 [Epub ahead of print]

- Ma L, Teruya-Feldstein J, Behrendt N, Chen Z, Noda T, Hino O, Cordon-Cardo C, Pandolfi PP (2005) Genetic analysis of Pten and Tsc2 functional interactions in the mouse reveals asymmetrical haploinsufficiency in tumor suppression. *Genes Dev* 2005 Jul 18 [Epub ahead of print]
- Majores M, Blumcke I, Urbach H, Meroni A, Hans V, Holthausen H, Elger CE, Schramm J, Galli C, Spreadfico R, Wiestler OD, Becker AJ (2005) Distinct allelic variants of TSC1 and TSC2 in epilepsy-associated cortical malformations without balloon cells. *J Neuropathol Exp Neurol* 64(7):629-37
- Manning BD, Logsdon MN, Lipovsky AI, Abbott D, Kwiatkowski DJ, Cantley LC (2005) Feedback inhibition of Akt signaling limits the growth of tumors lacking Tsc2. *Genes Dev* 2005 Jul 18 [Epub ahead of print]
- McClung AA, Blumberg MA, Huttenbach Y, Colome-Grimmer MI, Raimer SS (2005) Development of collagenomas during pregnancy. *J Am Acad Dermatol* 53(2 Suppl 1):S150-3
- Milunsky A, Shim SH, Ito M, Jaekle RK, Bassett LL, Brumund MR, Milunsky JM (2005) Precise prenatal diagnosis of tuberous sclerosis by sequencing the TSC2 gene. *Prenat Diagn* 2005 Jul 20;25(7):582-585 [Epub ahead of print]
- Patel U, Simpson E, Kingswood JC, Saggarr-Malik AK (2005) Tuberose sclerosis complex: analysis of growth rates aids differentiation of renal cell carcinoma from atypical or minimal-fat-containing angiomyolipoma. *Clin Radiol* 60(6):665-73
- Schaffer JV, Gohara MA, McNiff JM, Aasi SZ, Dvoretzky I (2005) Multiple facial angiofibromas: a cutaneous manifestation of Birt-Hogg-Dube syndrome. *J Am Acad Dermatol* 53(2 Suppl 1):S108-11
- Siemes H, Brandl U, Helmstadter C, Kurlemann G, Rating D, Salke-Kellermann RA, Stephani U, Uberall M, Wiemer-Kruel A, Bergmann L (2005) [Optimizing epilepsy therapy in children and adolescents with lamotrigine.] *Klin Padiatr* 217(4):222-9 [Article in German]
- Takahashi K, Nakagawa M, Young SG, Yamanaka S (2005) Differential membrane localization of ERas and Rheb, two ras-related proteins involved in the PI3 kinase / mTOR pathway. *J Biol Chem* 2005 Jul 26 [Epub ahead of print]
- Teleman AA, Chen YW, Cohen SM (2005) *Drosophila* Melted Modulates FOXO and TOR Activity. *Dev Cell* 9(2):271-81
- Wenaden AE, Copley SJ (2005) Unilateral lymphangiomyomatosis. *J Thorac Imaging* 20(3):226-8
- Wu EH, Wong YH (2005) Activation of delta-, kappa-, and mu-opioid receptors induces phosphorylation of tuberin in transfected HEK 293 cells and native cells. *Biochem Biophys Res Commun* 334(3):838-44
- Zikou A, Ioannidou MC, Tzoufi M, Astrakas L, Argyropoulou MI (2005) Magnetization transfer ratio measurements of the brain in children with tuberous sclerosis complex. *Pediatr Radiol* 2005 Jul 29 [Epub ahead of print]

CONFERENCES

August 28 – September 1, 2005

26th International Epilepsy Congress

Le Palais des Congres de Paris

Paris, France

<http://www.epilepsycongress.org>

September 11-14, 2005

The Second International Conference on Birth Defects and Disabilities in the Developing World

Jiuhua Spa and Resort, Beijing, China

www.chinamed.com.cn/birthdefects

September 26-27, 2005

Access to Quality Testing for Rare Diseases: A National Conference

Doubletree Executive Meeting Center and Hotel

Rockville, MD

<http://rarediseases.info.nih.gov/QTRD/>

September 29-30, 2005

Personalized Management of Neurological Diseases: A Multidisciplinary Conference

Marriott Hotel, Crystal City, VA

<http://www.aacc.org/meetings/neuro/>

October 7-12, 2005

4th World Congress of Cellular and Molecular Biology

Poitiers, France

<http://www.cmbworldcongress2005.com>

October 14-18, 2005

World Congress on Psychiatric Genetics XIII: Advancing on the Pathway to Discovery

The Westin Copley Place, Boston, MA

<http://www.ispg.net>

October 17-19, 2005

Genomes, Medicine and the Environment

Presented by the J. Craig Venter Institute

Hilton Head Marriott Beach and Golf Resort

Hilton Head, SC

For program and registration information, go to

<http://www.venterininstitute.org/gvac/programandspeakers.php>

For general information on conference registration, exhibiting and sponsorship opportunities

contact Kris Robinson at krobinson@venterscience.org or (301)-529-5581

October 18-23, 2005

American Academy of Child and Adolescent Psychiatry & Canadian Academy of Child and Adolescent Psychiatry: Joint Annual Meeting

Sheraton Centre Toronto

Toronto, Canada

<http://www.aacap.org>

October 25-29, 2005

American Society of Human Genetics

Salt Lake City, UT

<http://genetics.faseb.org/genetics/ashg/menu-annmeet.shtml>

**Visit the TS Alliance exhibit booth at ASHG meeting, and attend the symposium on Friday, October 28, 2005 that includes TSC!

November 12-16, 2005

Society for Neuroscience

Washington, DC Convention Center

Washington, DC

<http://web.sfn.org/am2005>

**Visit the TS Alliance exhibit booth at the SFN meeting!

December 2-6, 2005

American Epilepsy Society & American Clinical Neurophysiology Society

Washington, DC Convention Center

Washington, DC

For more information: <http://www.aesnet.org>

****Come to the TSC SIG at this year's meeting on Saturday, December 3, 2006, and visit the TS Alliance exhibit!**

May 3-5, 2006

TSC International Research Conference 2006

Spandau, Ev. Johannesstift

Hotel "Christophorus Haus"

Berlin, Germany

<http://www.tsc2006.org>

March 31 – April 2, 2006

LAM Foundation 2006 Research Conference

Hilton Netherlands Cincinnati Hotel

Cincinnati, OH

<http://lam.uc.edu>

July 2-6, 2006

7th European Congress of Epileptology

Helsinki Fair Centre, Helsinki, Finland

<http://www.epilepsyhelsinki2006.org>

SAVE THE DATE!

July 14-16, 2006

National TSC Conference

Organized by the Tuberous Sclerosis Alliance

[Indian Lakes Resort](http://www.tsalliance.org)

Chicago, Illinois

<http://www.tsalliance.org>

October 30 – November 2, 2006

World Congress on Autism

Cape Town, South Africa

Call for Papers closes 30th September 2005

Early Bird Registration Closes June 30th 2006

Please visit www.autismcongress.com

March 2007

NINDS Epilepsy Conference

Follow-up to 2000 Conference "Curing Epilepsy: Focus on the Future"

<http://www.ninds.nih.gov>

NEWS

REQUEST FOR INFORMATION ON THE PLAN TO RECOGNIZE MULTIPLE PRINCIPAL INVESTIGATORS ON NIH GRANTS (NOT-OD-05-055)

Response Date: September 16, 2005

Issued by the National Institutes of Health, Office of the Director, Office of Extramural Research
The NIH is seeking input and advice from the scientific community on various concepts associated with permitting more than one Principal Investigator to be associated with an NIH funded grant, contract, or cooperative agreement. This Request for Information (RFI) is being issued at the same time as a companion RFI from the Office of Science and Technology Policy (OSTP), as described below. The RFI issued by the OSTP asks for input from the broader scientific community about the overall concept of permitting multiple PIs on applications and awards for federal research support. This RFI, issued by the NIH, asks for input on policies and issues of special interest to the health-related research community.

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-055.html>

SCIENTISTS UNCOVER NEW CLUES ABOUT BRAIN FUNCTION IN HUMAN BEHAVIOR

Researchers at the National Institute of Mental Health (NIMH), part of the National Institutes of Health, have discovered a genetically controlled brain mechanism responsible for social behavior in humans - one of the most important but least understood aspects of human nature.

The study compared the brains of healthy volunteers to those with a genetic abnormality, Williams Syndrome, a rare disorder that causes unique changes in social behavior. This comparison enabled the researchers to both define a brain circuit for social function in the healthy human brain, and identify the specific way in which it was affected by genetic changes in Williams Syndrome.

"Social interactions are central to human experience and well-being, and are adversely affected in psychiatric illness. This may be the first study to identify functional disturbances in a brain pathway associated with abnormal social behavior caused by a genetic disorder," said NIMH Director Thomas R. Insel, M.D.

The researchers found a delicate network by which these three regions modulate amygdala activity. In Williams Syndrome, this fragile system was significantly abnormal, particularly the orbitofrontal cortex. This area did not activate for either task and was not functionally linked to the amygdala, as it was in healthy controls. Instead, the scientists observed increased activity and linkage in the medial region, which is consistent with the high level of empathy exhibited by people with Williams Syndrome.

"We had previously seen that the orbitofrontal cortex is structurally abnormal in Williams Syndrome, but we didn't know what role it played functionally in the disorder; it is now clear that this area can play a major role in producing social behavioral abnormalities," said Berman. "The over-activity of the medial-prefrontal cortex may be compensatory, but the result is still an abnormal fear response. The medial-prefrontal cortex still works and in fact it is working over-time because it may be the only thing that still regulates the amygdala in Williams Syndrome."

For more information, please visit <http://www.nih.gov/news/pr/jul2005/nimh-10.htm>

NEW WEB SERVICE HELPS MEDICARE BENEFICIARIES WITH LIMITED MEANS GET MORE HEALTH CARE ASSISTANCE; INCLUDES ASSISTANCE WITH ENROLLING IN EXTRA HELP FOR THE MEDICARE DRUG BENEFIT AND STATE MEDICAID BENEFITS AND OTHER ASSISTANCE PROGRAMS

A new web-based service will help Medicare beneficiaries of limited income and resources gain access to the extra help available to them through the Medicare Modernization Act of 2003. The service, which will also help them enroll in other health care and prescription drug assistance programs, was developed by the Administration on Aging (AoA) with the assistance of the Centers for Medicare & Medicaid Services (CMS) and the National Council on the Aging (NCOA).

"This new resource helps bring together many assistance programs available to seniors who need the most help - and that includes the comprehensive extra help with drug costs that will soon be available for up to one third of Medicare beneficiaries through the new Medicare drug benefit," said Mark B. McClellan, M.D., Ph.D., administrator of the Centers for Medicare & Medicaid Services. "Through this partnership, we have taken another important step forward in our goal of providing better healthcare and more help to America's seniors."

The new service is a special version of BenefitsCheckUpRx updated for the extra help with Medicare drug coverage. It is available at <http://www.BenefitsCheckUp.org/rx>. BenefitsCheckUpRx will help older adults and the advocates who work with them take advantage of the Medicare low-income subsidy, the comprehensive extra help that covers 95 percent of drug costs on average for people with Medicare who have limited means.

Applications are available now and altogether, about one in three Medicare beneficiaries are eligible for the extra help. The new service screens beneficiaries for eligibility and then provides a quick link to applying online for the extra help through the Social Security Administration's Web site. At the same time, it helps seniors and those who work with them apply for other needs-based government programs including the Medicare Savings Programs and other federal, state and private programs that can save seniors money.

For more information, visit <http://www.cms.hhs.gov/media/press/release.asp?Counter=1502>

BRAIN SIZE MAY DEPEND UPON HOW NEURAL CELLS ARE CLEAVED Howard Hughes Medical Institute (HHMI) researcher Li-Huei Tsai, Ph.D. from Harvard Medical School, has discovered a novel way in which the brain size of developing mammals may be regulated. They have identified a signaling pathway that controls the orientation in which dividing neural progenitor cells are cleaved during development. The researchers speculate that this type of regulatory decision point may play a powerful role in determining the ultimate size of the mammalian brain. This research was published in the July 15, 2005, issue of Cell. For the full story, go to <http://www.hhmi.org//news/tsai3.html>

SYNAPSES MAY FIRE NEUROTRANSMITTERS LIKE A SHOTGUN HHMI researchers have developed a "nano-map," which shows the tiny spines and valleys of the synapse resolved at nanometer scale. The map is already changing scientists' views of the synaptic landscape.

The researchers' in silico modeling indicates that the synapse may behave more like a shotgun than a rifle when it comes to firing the neurotransmitters involved in neuronal communication. Their studies are challenging the textbook notion of how synapses release neurotransmitters.

This research by Terrence J. Sejnowski, Ph.D. from The Salk Institute for Biological Studies, was published in the July 15, 2005, issue of Science. For the full story, go to <http://www.hhmi.org/news/sejnowski3.html>

RESEARCHERS IDENTIFY GENE'S ROLE IN SUPPRESSING LONGEVITY HHMI researchers led by Frederick W. Alt, Ph.D. from Children's Hospital Boston, have determined that a gene present in mouse cells limits the number of times that a cell can divide. The gene is involved in senescence, a process that is thought to ensure that aging cells do not pass on harmful mutations. The researchers said the gene, known as SIRT1, suppresses longevity, and may play a role in regulating the aging process. This research was published in the July 19, 2005, issue of Cell Metabolism. For the full story, go to <http://www.hhmi.org/news/alt7.html>

CONTROLLING THE SYNAPSE - 49 PROTEINS AT A TIME In the exquisitely regulated networks of the brain, hundreds of channels, receptors, and other specialized proteins work together to control communication at the synapses, or junctions between neurons. Working with mice, Robert Darnell, M.D., Ph.D. of The Rockefeller University, and his collaborators have found that a single molecule, known as Nova, helps control the production of a large, closely related set of these specialized proteins. This research was published in the July 24, 2005 issue of Nature Genetics. For the complete story, go to <http://www.hhmi.org/news/darnell2.html>

TOPIRAMATE (TOPAMAX) FIRST-LINE MONOTHERAPY FOR SEIZURES IN PATIENTS AGED 10 YEARS AND OLDER On June 29, the FDA approved a new indication for topiramate (Topamax tablets, capsules, and sprinkle capsules, made by Ortho-McNeil Pharmaceutical, Inc.), allowing its use as initial monotherapy for partial onset or primary generalized tonic-clonic seizures in patients aged 10 years and older. The approval was based on results of a double-blind clinical efficacy trial in 470 patients randomized to titrate up to 50 or 400 mg per day of topiramate. Approximately 58% of patients achieved the maximal dose (mean dose, 275 mg/day). All patients had experienced one or two documented seizures for a three-month pretrial period.

Comparison of Kaplan-Meier survival curves of time to first seizure favored the 400-mg per day group vs the 50-mg per day group ($P = .0002$). Adverse events more commonly reported in adults administered 400 vs 50 mg per day of topiramate included paresthesias, weight loss, somnolence, anorexia, dizziness, and difficulty with memory. Weight loss, upper respiratory tract infection, paresthesias, anorexia, diarrhea, and mood problems were more commonly reported in children aged 10 to 16 years.

Topiramate was previously approved as adjunctive therapy for this indication in patients aged two years and older, for the treatment of seizures associated with Lennox-Gastaut syndrome in patients aged two years and older, and for migraine prophylaxis in adults.

NEW WARNINGS ADDED TO TOPIRAMATE LABELING Ortho-McNeil has revised the prescribing information of its anti-epileptic drug topiramate (Topamax) to include updated information about oligohydrosis and hyperthermia, according to a notice from the U.S. Food and Drug Administration (FDA) MedWatch safety information and adverse event reporting system. Although oligohydrosis and hyperthermia are potentially serious, they may be preventable by prompt recognition of symptoms and appropriate treatment.

According to a letter from Ortho-McNeil to healthcare professionals, most of the reports have involved children. High temperatures and vigorous physical activity contributed to these cases, and children should be observed carefully in these settings. The letter adds that adequate hydration before and during exercise and exposure to warm temperatures is recommended.

The rate of reported potential cases of oligohidrosis is approximately 35 per 1,000,000 patients treated, and the rate for patients treated for oligohidrosis is 1.6 per 1,000,000, as of February 2002.

The letter to healthcare professionals and the revised labeling are available on the FDA Web site at <http://www.fda.gov/medwatch/SAFETY/2003/safety03.htm#topama>.

EMPLOYMENT OPPORTUNITIES

POSITIONS AVAILABLE AT NHLBI The National Heart, Lung, and Blood Institute (NHLBI) at the National Institutes of Health (NIH) is seeking exceptional candidates for the positions of Deputy Director and Special Assistant for Clinical Research to the Director. CV, bibliography, and two letters of recommendation must be received by September 1, 2005. For further information, contact Mr. Rubenstein by e-mail: Rubinstb@nhlbi.nih.gov or telephone: (301)496-2411.

TSC INFORMATION

For information about TSC, visit the TS Alliance Web site at: <http://www.tsalliance.org> or contact the TS Alliance at info@tsalliance.org or by telephone: 1-800-225-6872 or 301-562-9890.