



# TSC ALERT

## April 2007

### Table of Contents

[Clicking on one of the headings takes you directly to that section of TSC Alert]

<b>ABSTRACT SUBMISSION DEADLINES</b> .....	<b>1</b>
<b>FUNDING OPPORTUNITIES</b> .....	<b>1</b>
<b>NEW TSC PUBLICATIONS</b> .....	<b>3</b>
<b>RESEARCH RESOURCES</b> .....	<b>5</b>
<b>CONFERENCES AND SEMINARS</b> .....	<b>6</b>
<b>TSC CLINICAL TRIALS AND STUDIES</b> .....	<b>10</b>
<b>TSC INFORMATION</b> .....	<b>15</b>

## **ABSTRACT SUBMISSION DEADLINES**

**September 23-25, 2007**

**Tuberous Sclerosis Complex: From Genes to New Therapeutics**

International TSC Conference organized by the Tuberous Sclerosis Alliance  
Loews Annapolis Hotel, Annapolis, MD

**Deadline for Submission of Abstracts: July 1, 2007**

Information, Abstract Submission Forms, Registration Forms at: [www.tsalliance.org](http://www.tsalliance.org)

## **FUNDING OPPORTUNITIES**

**Understanding and Treating Tuberous Sclerosis Complex (R01) (PAS-07-190)**

National Institute of Neurological Disorders and Stroke  
National Cancer Institute

National Institute of Arthritis and Musculoskeletal and Skin Diseases  
National Institute of Diabetes and Digestive and Kidney Diseases  
National Institute of Mental Health

Application Receipt/Submission Date(s): Multiple dates, see announcement.

<http://grants.nih.gov/grants/guide/pa-files/PAS-07-190.html>

**Multidisciplinary Clinical Research Centers (P60) (RFA-AR-07-001)**

National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Application Receipt Date(s): June 29, 2007

<http://grants.nih.gov/grants/guide/rfa-files/RFA-AR-07-001.html>

**Genome-Wide Studies in Biorepositories with Electronic Medical Record Data (U01) (RFA-HG-07-005)**

National Human Genome Research Institute  
Application Receipt Date(s): May 17, 2007

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-07-005.html>

**High-Priority Phenotype and Exposure Measures for Cross-Study Analysis in Genome-Wide Association Studies (U01) (RFA-HG-07-006)**

National Human Genome Research Institute  
National Institute of General Medical Sciences  
Application Receipt Date(s): May 17, 2007

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-07-006.html>

**Institutional Clinical and Translational Science Award (U54) (RFA-RM-07-007)**

NIH Roadmap Initiatives  
Application Receipt Date(s): October 24, 2008

<http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-007.html>

**Development of Assays for High-Throughput Drug Screening (R01) (PA-07-320)**

National Institute of Diabetes and Digestive and Kidney Diseases  
National Cancer Institute  
National Institute of Allergy and Infectious Diseases  
National Institute of Mental Health

Application Receipt/Submission Date(s): Multiple dates, see announcement.

<http://grants.nih.gov/grants/guide/pa-files/PA-07-320.html>

**Development of Animal Models and Related Biological Materials For Research (R21) (PA-07-336)**

National Center for Research Resources

Application Receipt/Submission Date(s): Multiple dates, see announcement.

<http://grants.nih.gov/grants/guide/pa-files/PA-07-336.html>

**International Research Collaboration - Basic Biomedical (FIRCA-BB) (R03) (PAR-07-335)**

John E. Fogarty International Center  
National Center for Complementary and Alternative Medicine  
National Institute on Aging  
National Institute on Alcohol Abuse and Alcoholism  
National Institute of Biomedical Imaging and Engineering  
National Institute on Drug Abuse  
National Institute on Deafness and Other Communication Disorders  
National Institute of Dental and Craniofacial Research  
National Institute of Environmental Health Sciences  
National Institute of Neurological Disorders and Stroke

Application Receipt/Submission Date(s): May 21, 2007; September 21, 2007; and January 22, 2008

<http://grants.nih.gov/grants/guide/pa-files/PAR-07-335.html>

**Psychosocial/Behavioral Interventions and Services Research in Autism Spectrum Disorders (R34) (PA-07-343)**

National Institute of Mental Health  
National Institute of Child Health and Human Development  
National Institute on Deafness and Other Communication Disorders  
National Institute of Neurological Disorders and Stroke  
National Institute of Nursing Research

Application Receipt/Submission Date(s): Multiple dates, see announcement.

<http://grants.nih.gov/grants/guide/pa-files/PA-07-343.html>

**Bioengineering Research Partnerships (BRP)[R01] (PAR-07-352)**

National Institute of Biomedical Imaging and Engineering  
National Cancer Institute  
National Eye Institute  
National Human Genome Research Institute  
National Heart, Lung, and Blood Institute

National Institute on Aging  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
National Institute of Child Health and Human Development  
National Institute on Deafness and Other Communication Disorders  
National Institute of Dental and Craniofacial Research  
National Institute of Environmental Health Sciences  
National Institute of Neurological Disorders and Stroke  
Application Receipt/Submission Date(s): Multiple dates, see announcement.  
<http://grants.nih.gov/grants/guide/pa-files/PAR-07-352.html>

**MARC Undergraduate Student Training in Academic Research, Institutional National Research Service Award (NRSA) Research Training Grant (T34) (PAR-07-337)**

National Institute of General Medical Sciences  
Application Receipt/Submission Date(s): May 25, 2007, 2008, 2009  
<http://grants.nih.gov/grants/guide/pa-files/PAR-07-337.html>

**Pre-application Technical Assistance Meeting for: RFA-HG-07-005 Genome Wide Studies in Biorepositories with Electronic Medical Record Data (U01)**

The purpose of the meeting is to provide technical assistance for the application process and to answer any questions regarding the application process and responsiveness issues. We anticipate recording the meeting and a link to it will be made available, within 2-3 days of the meeting, on the Office of Population Genetics web site at <http://www.genome.gov/19518660>. The meeting is open to any individual or organization intending to apply but is not a prerequisite to applying. For more information regarding this meeting, follow the link:  
<http://grants1.nih.gov/grants/guide/notice-files/NOT-HG-07-013.html>

**Innovations in Biomedical Computational Science and Technology**

The NIH is interested in promoting research and developments in computational science and technology that will support rapid progress in areas of scientific opportunity in biomedical research. As defined here, biomedical computing or biomedical information science and technology includes database design, graphical interfaces, querying approaches, data retrieval, data visualization and manipulation, data integration through the development of integrated analytical tools, and tools for electronic collaboration, as well as computational and mathematical research including the development of structural, functional, integrative, and analytical models and simulations. More information regarding this notice is available at:  
<http://grants.nih.gov/grants/guide/pa-files/PAR-07-344.html>

**NEW TSC PUBLICATIONS**

Alaraj AM, Valyi-Nagy T, Roitberg B (2007) Double phakomatosis; neurofibromatosis type-1 and tuberous sclerosis. Acta Neurochir (Wien) 2007 Apr 5 [Epub ahead of print]

Cai SL, Walker CL (2006) TSC2, a key player in tumor suppression and cystic kidney disease. Nephrol Ther 2 Suppl 2:S119-22

Chen H, Sun XF, Wu JS (2006) [Clinicopathologic study of subependymal giant cell astrocytoma.] Zhonghua Bing Li Xue Za Zhi 35(11):656-9 [Article published in Chinese]

Chong DY, Hirunwiwatkul P, McKeever PE, Trobe JD (2007) Papilledema in Obstructive Hydrocephalus Caused by Giant Cell Astrocytoma of Tuberous Sclerosis. J Neuroophthalmol 27(1):50-54

Deistung A, Mentzel HJ, Rauscher A, Witoszynskij S, Kaiser WA, Reichenbach JR (2006) Demonstration of paramagnetic and diamagnetic cerebral lesions by using susceptibility weighted phase imaging (SWI). Z Med Phys 16(4):261-7

- Feng Z, Hu W, de Stanchina E, Teresky AK, Jin S, Lowe S, Levine AJ (2007) The Regulation of AMPK {beta}1, TSC2, and PTEN Expression by p53: Stress, Cell and Tissue Specificity, and the Role of These Gene Products in Modulating the IGF-1-AKT-mTOR Pathways. *Cancer Res* 67(7):3043-53
- Fleury RN, Damante JH, Soares CT, Sant'ana E, Junior EJ, Moreira CR (2007) Malignant fibrous histiocytoma (undifferentiated high-grade pleomorphic sarcoma) occurring in tuberous sclerosis: a case report. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 103(4):e54-9 [Epub 2006 Sep 26]
- Florice F, Higaki K, Maki H, Nanba E, Ninomiya H, Ohno K (2007) Antisense suppression of TSC1 gene product, hamartin, enhances neurite outgrowth in NGF-treated PC12h cells. *Brain Dev* 2007 Mar 19 [Epub ahead of print]
- Gulati P, Thomas G (2007) Nutrient sensing in the mTOR/S6K1 signalling pathway. *Biochem Soc Trans* 35(Pt 2):236-8
- Hall DJ, Grewal SS, de la Cruz AF, Edgar BA (2007) Rheb-TOR signaling promotes protein synthesis, but not glucose or amino acid import, in *Drosophila*. *BMC Biol* 5(1):10 [Epub ahead of print]
- Hansen T, Katenkamp K, Bittinger F, Kirkpatrick CJ, Katenkamp D (2007) D2-40 labeling in lymphangiomyoma/lymphangiomyomatosis of the soft tissue: further evidence of lymphangiogenic tumor histogenesis. *Virchows Arch* 450(4):449-53 [Epub 2007 Feb 15]
- Holmes GL, Stafstrom CE, The Tuberous Sclerosis Study Group (2007) Tuberous Sclerosis Complex and Epilepsy: Recent Developments and Future Challenges. *Epilepsia* 2007 Mar 26 [Epub ahead of print]
- Hunzicker-Dunn M, Maizels ET (2006) FSH signaling pathways in immature granulosa cells that regulate target gene expression: branching out from protein kinase A. *Cell Signal* 18(9):1351-9 [Epub 2006 Apr 17]
- Jansen FE, Van Huffelen AC, Van Rijen PC, Leijten FS, Jennekens-Schinkel A, Gosselaar P, Van Nieuwenhuizen O; On behalf of the Dutch Collaborative Epilepsy Surgery Programme (2007) Epilepsy surgery in tuberous sclerosis: The Dutch experience. *Seizure* 2007 Apr 3 [Epub ahead of print]
- Krymskaya VP (2007) Targeting the phosphatidylinositol 3-kinase pathway in airway smooth muscle: rationale and promise. *BioDrugs* 21(2):85-95
- Lux AL (2007) Is hypsarrhythmia a form of non-convulsive status epilepticus in infants? *Acta Neurol Scand* 115(4):37-44
- Masoumi H, Kinney HC, Chadwick AE, Rubio A, Krous HF (2007) Sudden unexpected death in childhood associated with cardiac rhabdomyoma, involuting adrenal ganglioneuroma, and megalencephaly: another expression of tuberous sclerosis? *Pediatr Dev Pathol* 10(2):129-33
- Matsuyama K, Ohsawa I, Ogawa T (2007) Do children with tuberous sclerosis complex have superior musical skill? - A unique tendency of musical responsiveness in children with TSC. *Med Sci Monit* 13(4):CR156-164 [Epub ahead of print]
- Misirlioglu ED, Aliefendioglu D, Alpan N, Guven A, Peltek N (2006) Case 3: fetal intracardiac tumour - a feature of a genetic disease? *Acta Paediatr* 95(6):758, 761
- Momose S, Kobayashi T, Tada N, Itoyama S, Hino O (2007) N-terminal hamartin-binding and C-terminal GAP domain of tuberin can separate in vivo. *Biochem Biophys Res Commun* 356(3):693-8 [Epub 2007 Mar 13]

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- Ono M, Boethig D, Akin E, Goerler H, Breyman T (2007) Coexistent cardiac rhabdomyoma with mitral valve anomaly in patients with tuberous sclerosis: a case report. Thorac Cardiovasc Surg 55(2):120-1
- Pulsifer MB, Winterkorn EB, Thiele EA (2007) Psychological profile of adults with tuberous sclerosis complex. Epilepsy Behav 2007 Mar 26 [Epub ahead of print]
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- Schillinger F, Montagnac R (2006) [Renal lesions in tuberous sclerosis] Nephrol Ther 2 Suppl 2:S123-6 [Article published in French]
- Svajdler M, Bohus P, Goc V, Tkacova V (2007) [Perivascular epithelioid cell tumor (PEComa) of the liver: a case report and review of the literature] Cesk Patol 43(1):18-22 [Article published in Czech]
- Urano J, Sato T, Matsuo T, Otsubo Y, Yamamoto M, Tamanoi F (2007) Point mutations in TOR confer Rheb-independent growth in fission yeast and nutrient-independent mammalian TOR signaling in mammalian cells. Proc Natl Acad Sci U S A 104(9):3514-9 [Epub 2007 Feb 20]
- Vendrell E, Ribas M, Valls J, Sole X, Grau M, Moreno V, Capella G, Peinado MA (2007) Genomic and transcriptomic prognostic factors in R0 Dukes B and C colorectal cancer patients. Int J Oncol 30(5):1099-107
- Weber RG, Hoischen A, Ehrler M, Zipper P, Kaulich K, Blaschke B, Becker AJ, Weber-Mangal S, Jauch A, Radlwimmer B, Schramm J, Wiestler OD, Lichter P, Reifenberger G (2007) Frequent loss of chromosome 9, homozygous CDKN2A/p14(ARF)/CDKN2B deletion and low TSC1 mRNA expression in pleomorphic xanthoastrocytomas. Oncogene 26(7):1088-97 [Epub 2006 Aug 7]
- Wu EH, Wu KK, Wong YH (2007) Tuberlin: A Stimulus-Regulated Tumor Suppressor Protein Controlled by a Diverse Array of Receptor Tyrosine Kinases and G Protein-Coupled Receptors. Neurosignals 15(5):217-227
- Yao JC (2007) Molecular targeted therapy for carcinoid and islet-cell carcinoma. Best Pract Res Clin Endocrinol Metab 21(1):163-72

## **RESEARCH RESOURCES**

### **Online Resource for Epilepsy Research**

AES along with several other funding organizations maintains a web site listing epilepsy research funding opportunities. The site has information on upcoming deadlines, eligibility criteria, links to more information and samples of funded programs. Participating organizations are AES, CURE, Epilepsy Foundation, Epilepsy Therapy Development Project, NINDS, FACES, The Milken Family Foundation, PACE, and the Tuberous Sclerosis Alliance. For more information:

<http://www.aesnet.org/erc/index.cfm>

## **CONFERENCES AND SEMINARS**

**April 12, 2007; 5:00 – 7:00 PM**

**LAM/TSC Seminar Series**

**SPECIAL PANEL – FOCUS ON RENAL AMLs in LAM/TSC – Improving Clinical Care//  
Insights into the Underlying Disease Pathogenesis**

MODERATOR: Elizabeth Thiele, MD, PhD

SPEAKERS: Elahna Paul, MD, PhD; Stuart Silverman, MD and Elizabeth Henske, MD

New Research Building - Harvard Medical School, 77 Avenue Louis Pasteur, Rm. 350, Boston, MA

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

**April 18-19, 2007**

**Workshop on Autism and the Environment: Challenges and Opportunities for Research**

The Forum on Neuroscience and Nervous Systems Disorders, Institutes of Medicine

National Academy of Sciences Building (500 5th Street, NW), Room 100, Washington, D.C.

For more information: <http://www.iom.edu/CMS/3740/35684/39826.aspx>

**April 19-22, 2007**

**2007 LAM International Research Conference**

The LAM Foundation

Cincinnati, OH

<http://www.thelamfoundation.org>

**May 1, 2007**

**Managing Incidental Findings in Human Subjects Research: From Imaging to Genomics**

Cowles Auditorium, Hubert H. Humphrey Center, University of Minnesota

Minneapolis, MN

Online registration, full agenda, discount airfare and hotel rates, and other information are available at <http://www.lifesci.consortium.umn.edu/conferences/incidentalfindings.php> or register by: Phone 612-625-0055, Fax 612-624-9143, E-mail [lawvalue@umn.edu](mailto:lawvalue@umn.edu).

**May 9-12, 2007**

**68<sup>th</sup> Annual Meeting of the Society for Investigative Dermatology**

The Century Plaza Hotel, Los Angeles, CA

For more information: [www.sidnet.org](http://www.sidnet.org)

**May 10, 2007; 5:00 – 7:00 PM**

**LAM/TSC Seminar Series**

SPEAKERS: Celeste Simon, PhD and Lief Ellison, MD, PhD

The HIF1 Signaling Pathway and Therapeutic Targets Relevant to LAM/TSC

New Research Building - Harvard Medical School, 77 Avenue Louis Pasteur, Rm. 350, Boston, MA

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

**May 24-26, 2007**

**Tuberous Sclerosis Complex International Research Conference 2007 in Rome (Italy)**

Venue: Grand Hotel Palazzo Carpegna, Rome, Italy

Information: <http://www.ptsroma.it/tsc2007/>

**June 24-26, 2007**

**Epileptology: Comprehensive Review and Practical Exercises**

Renaissance Quail Hollow Resort, Painesville, OH

For more information: [www.clevelandclinicmeded.com/Epileptology07](http://www.clevelandclinicmeded.com/Epileptology07)

**June 27-29, 2007**

**17<sup>th</sup> International Cleveland Clinic Epilepsy Symposium: Epilepsy Surgery**

InterContinental Hotel & Bank of America Conference Center, Cleveland, OH

For more information: [www.clevelandclinicmeded.com/EpilSurg07](http://www.clevelandclinicmeded.com/EpilSurg07)

**September 6-8, 2007**

**4th Annual World Congress of the International Brain Mapping & Intraoperative Surgical Planning Society (IBMISPS)**

Washington Plaza Hotel, Washington, D.C.

Deadline for submission of abstracts: June 30, 2007

Information and Registration: [www.ibmisps.org](http://www.ibmisps.org)

**September 23-25, 2007**

**Tuberous Sclerosis Complex: From Genes to New Therapeutics**

International TSC Research Symposium organized by the Tuberous Sclerosis Alliance

Loews Annapolis Hotel, Annapolis, MD

More information coming soon on the TS Alliance website at [www.tsalliance.org](http://www.tsalliance.org)

**October 23-27, 2007**

**57<sup>th</sup> Annual Meeting of the American Society of Human Genetics**

San Diego Convention Center, San Diego, CA

Deadline for submission of abstracts: June 7, 2007

For more information: [www.ashg.org](http://www.ashg.org)

**November 3-4, 2007**

**Advances in Tuberous Sclerosis: From Pathway to Therapy**

Sydney Children's Hospital, Randwick, NSW, Australia

For more information, contact Dr. David Mowat at [d.mowat@unsw.edu.au](mailto:d.mowat@unsw.edu.au) or Dr John Lawson at

[John.Lawson@unsw.edu.au](mailto:John.Lawson@unsw.edu.au)

**November 27-29, 2007**

**2007 National Prevention and Health Promotion Summit**

Hyatt Regency Capitol Hill

Washington D.C.

Conference Contact Information: <http://www.cdc.gov/cochp/conference/index.htm>

**November 30 - December 4, 2007**

**American Epilepsy Society**

Philadelphia Convention Center, Philadelphia, PA

Deadline for Submission of Abstracts: June 4, 2007

For more information and to submit an abstract, go to: [www.AESNET.org](http://www.AESNET.org)

**September 11-14, 2008**

**International TSC Conference**

Organized by the Tuberous Sclerosis Association, U.K.

Brighton, U.K. More information coming soon!

**NEWS**

**Secretary's Advisory Committee on Genetics, Health, and Society**

**REQUEST FOR PUBLIC COMMENT**

**Draft Report on Pharmacogenomics**

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The Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) is requesting public comment on a draft report to the Secretary of Health and Human Services (HHS), Realizing the Promise of Pharmacogenomics: Opportunities and Challenges. The draft report is available electronically at [http://www4.od.nih.gov/oba/sacghs/public\\_comments.htm](http://www4.od.nih.gov/oba/sacghs/public_comments.htm)

SACGHS identified the emerging field of pharmacogenomics as a high study priority because it holds significant promise for improving the productivity of the drug development pipeline, increasing the safety and effectiveness of drugs by reducing adverse reactions, and ultimately resulting in more efficient use of drugs. The draft report describes these opportunities, while also identifying the challenges associated with pharmacogenomics product development and integration into clinical and public health practice.

The draft report describes opportunities and challenges in pharmacogenomics in three major areas: 1) research and development; 2) "gatekeepers," i.e., those who are involved in facilitating the progression of pharmacogenomics; and 3) implementation of pharmacogenomics to improve outcomes in clinical and public health practice. Draft recommendations also are presented in each area.

SACGHS is requesting comments on all aspects of the draft report and recommendations. In particular, the Committee would welcome your feedback on the following questions:

- \*Are the discussions of topics and issues accurate and complete?
- \*Have any significant opportunities, challenges, or other issues been missed?
- \*Does the draft report adequately describe the range of perspectives on the issues?
- \*Are the draft recommendations specific enough?
- \*Are there other strategies for addressing the issues?
- \*Which draft recommendations should be of highest priority for the Federal government to address?
- \*Appendix A of the report identifies major pharmacogenomics activities in the public and private sectors. Are there other relevant initiatives that should be included in the list?

Comments received by June 1, 2007 will be considered by SACGHS in preparing the final report.

Comments should be addressed to Reed V. Tuckson, MD, SACGHS Chair, and sent to Suzanne Goodwin by email at [goodwins@od.nih.gov](mailto:goodwins@od.nih.gov) or fax at 301-496-9839, or mail to:

Reed V. Tuckson, MD  
Chair  
Secretary's Advisory Committee on Genetics, Health, and Society  
NIH Office of Biotechnology Activities  
6705 Rockledge Drive, Suite 750  
Bethesda, MD, 20892 (20817 for non-US Postal Service mail)

### **Final Report Available: *Policy Issues Associated with Undertaking a New Large U.S. Population Cohort Study of Genes, Environment, and Disease***

The LPS report, *Policy Issues Associated with Undertaking a New Large U.S. Population Cohort Study of Genes, Environment, and Disease*, describes the preliminary questions that should be addressed to help policymakers decide whether the U.S. Government should undertake a new LPS of genes, environment, and disease. It identifies five areas that require further analysis and consideration by the Secretary of Health and Human Services prior to making a decision as to whether a new LPS could take place: research policy; research logistics; regulatory and ethical considerations; public health, social, and economic implications; and public engagement. The report also concludes that the Secretary should initiate a thorough consideration of the full range of policy issues outlined in the report and that the public at large, the scientific community, a relevant Government agencies and policymakers, and the private sector stakeholders should be engaged in the process. The report is available at: <http://www4.od.nih.gov/oba/SACGHS.HTM>

### **HHS SECRETARY LEAVITT ANNOUNCES STEPS TOWARD A FUTURE OF "PERSONALIZED HEALTH CARE"**

HHS Secretary Mike Leavitt today outlined a course for achieving gene-based medical care combined with health information technology, which he called "Personalized Health Care." He said the

initiative has the potential to transform the quality, safety and value of health care for patients in the future.

"Personalized health care will combine the basic scientific breakthroughs of the human genome with computer-age ability to exchange and manage data," Secretary Leavitt said. "Increasingly it will give us the ability to deliver the right treatment to the right patient at the right time -- every time."

In a speech before the annual meetings of the Personalized Medicine Coalition, at the National Press Club, the Secretary outlined steps already under way to develop the needed information, as well as new steps he is undertaking to build the foundation for personalized health care and ensure that gene-based medical data and health information technology are used appropriately.

"Every one of us is biologically unique. We've always known that, but we haven't had the knowledge or the tools to deliver health care at that kind of individual level. That's what's changing," Secretary Leavitt said.

Gene-based medicine can help individuals identify their particular susceptibilities to disease while they are well and take effective preventive steps. In the future, it will help detect the onset of disease much earlier, enabling treatment to prevent disease progression, and can help bring about medical products that are tailored more precisely to the needs of each individual.

Health information technology, including powerful new tools for managing vast amounts of information, will be needed both to continue building basic scientific knowledge and to make the new knowledge useable and accessible for patient care.

Secretary Leavitt emphasized how much work remains to build a system that can deliver personalized health care. He has identified this issue as one of his priorities for the next two years.

"The Human Genome Project was a dramatic success, but it has correctly been called a race to the starting line," he said. "The work that remains is sweeping, from the most fundamental science to the details of health care practice."

Secretary Leavitt announced new steps that HHS is taking to lay the foundation for a personalized health care future:

- \*HHS is engaged in a broad review of the implications for privacy protection as health information technology is increasingly adopted, including needs for genetic information, and the anticipated effect on the confidentiality, privacy and security of individually identifiable health information.

- \*HHS will review existing structures for ensuring that genetic tests are accurate, valid and useful. The objective will be to ensure that responsibilities are clearly and appropriately assigned among HHS agencies to support useful genetic testing for patients.

- \*HHS will develop consistent policies for its agencies regarding access to and security of federally supported research. The goal will be to ensure open information access for researchers, to support progress, while still rewarding discovery and innovation.

- \*The President's budget for 2008 includes \$15 million in start-up funding to create a new electronic network that would draw together the nation's major health data repositories. This network of networks would enable researchers to match treatments and outcomes, and in that way learn from the nation's day-to-day medical practice and improve safety and effectiveness of medical treatments.

- \*The American Health Information Community (AHIC) will develop recommendations to identify health IT standards for including genetic test information on electronic health records. AHIC is charged with developing recommendations for establishing or identifying

consensus standards and for other specific actions toward achieving President Bush's goal that most Americans have electronic health records by 2014.

Current efforts at HHS agencies supporting personalized health care total \$277 million this year, and are proposed to grow to \$352 million in FY 2008. Current work at HHS agencies includes:

\*At the National Institutes of Health (NIH), genome-wide association studies are using information from years of clinical trials to find associations between genetic elements and health outcomes. A milestone event is expected this fall when research from the long-running Framingham Heart Study, involving some 10,000 volunteers who have been followed over two generations, may be posted at NIH's Genotype and Phenotype (dbGaP) Web site.

\*At the Food and Drug Administration (FDA), the Critical Path initiative is organizing work across 76 science and regulatory areas to improve product development, especially for gene-oriented drugs and diagnostic tests. Regulatory guidance on the co-development of drugs and diagnostic products, which is an important stepping stone for gene-based medical care, will be published this fall.

\*The Centers for Disease Control and Prevention (CDC) has worked with the National Cancer Institute to define the leading 100 genetic variants of public health significance. CDC is using its National Health and Nutrition Examination Survey (NHANES), one of the nation's largest health surveys, to determine how common these variants are in the U.S. population. Results will be released this summer and will be important for researchers.

"In the future, we'll understand diseases at a new level," Secretary Leavitt said. "We'll know them as gene- or molecular-based diseases. And that will give us new kinds of treatments that will be effective for both the very specific condition and the individual patient."

More information about the Personalized Health Care initiative is available at [www.hhs.gov/myhealthcare](http://www.hhs.gov/myhealthcare)

### **New Journal: Paediatric and Perinatal Epidemiology**

Since January 2007, the journal *Paediatric and Perinatal Epidemiology* has been accepting submissions online. One of the major interests of the Journal is epidemiologic research on birth defects and on developmental disabilities. The web address for submission is <http://mc.manuscriptcentral.com/ppe>.

When submitting a manuscript for submission to a journal, please consider *Paediatric and Perinatal Epidemiology*. With their new electronic system (Manuscript Central) turnaround time from submission to an editor's decision is faster than ever. In addition, the procedure is much less cumbersome for authors, since all processes for authors, referees and editors are electronic. If you have any questions about the journal, please e-mail Dr John Kiely at [ppe.american.editors@gmail.com](mailto:ppe.american.editors@gmail.com).

### **Changing the Circadian Clock with the Seasons**

New research has revealed what keeps animals' internal clocks running on time through the long nights of winter, the long days of summer, and everything in between. The research shows that a specific network of brain cells is the key to synchronizing the circadian clock to environmental cues, and reveals an astonishing degree of flexibility within the system. This research was published in the April 06, 2007, issue of *Cell* by Michael Rosbash, Ph.D., HHMI investigator at Brandeis University. For the full story, go to: <http://www.hhmi.org/news/rosbash20070406>

## **TSC CLINICAL TRIALS AND STUDIES**

### **1. A Randomized, Controlled Trial of Ganaxolone in Patients With Infantile Spasms**

**Official Title:** A Double-Blind, Placebo-Controlled, Dose-Ranging Clinical Study to Evaluate the Safety, Tolerability, and Antiepileptic Activity of Ganaxolone in Treatment of Patients With Infantile Spasms

**Study Purpose:** The study is a two period (8-10 days/period), incomplete cross-over in which successive cohorts of 9 subjects are randomized, in a 2:1 ratio, to 1 of 2 sequences, A and B. In each cohort, Sequence A, comprised of 6 subjects, receives ascending doses of ganaxolone during period 1 and ganaxolone (at the maximal dose attained in period 1) and ascending doses of placebo during period 2. Sequence B, comprised of 3 subjects, receives ascending doses of placebo during period 1 and receives the maximum dose of placebo and ascending doses of ganaxolone during period 2. The dosing level in each subsequent cohort will be based upon experience gained from previous cohorts.

**Eligibility:** Male or female, 4 to 24 months of age (inclusive) with a diagnosis of IS with a 24 hour video EEG (vEEG) recording confirming the diagnosis and previously treated with 3 or fewer antiepileptic drugs (AEDs) are eligible for the study. The subject is able to continue treatment with concomitant AEDs (no more than 2; adrenocorticotrophic hormone [ACTH], corticosteroids, felbamate, and vigabatrin are not allowed concomitantly). A ketogenic diet is permitted if it can be maintained for the duration of the study.

Please refer to this study by ClinicalTrials.gov identifier NCT00441896  
Julia Tsai, PhD 203-315-5820 [jtsai@marinuspharma.com](mailto:jtsai@marinuspharma.com)  
Earl Giller, MD, PhD 203-315-5808 [egiller@marinuspharma.com](mailto:egiller@marinuspharma.com)

### **California**

Children's Hospital of Los Angeles, Los Angeles, CA, 90027, Recruiting  
Jenny Rodriguez 323-660-2450 Ext. 5812 [JRodriguez@chla.usc.edu](mailto:JRodriguez@chla.usc.edu)  
Wendy Mitchell, MD, Principal Investigator

Mattel Children's Hospital at UCLA, Los Angeles, CA, 90095, Not yet recruiting  
Angela Perez 310-206-4037 [aperez@mednet.ucla.edu](mailto:aperez@mednet.ucla.edu)  
Raman Sankar, MD, Principal Investigator

### **District of Columbia**

Children's National Medical Center, Washington, DC, 20010, Not yet recruiting  
Mirinda Gillespie 202-884-2635 [mgillesp@cnmc.org](mailto:mgillesp@cnmc.org)  
Joan Conry, MD, Principal Investigator

### **Florida**

Miami Children's Hospital, The Brain Institute, Miami, FL, 33155, Recruiting  
Amelia Halac, MD 305-663-6802 [Amelia.Halac@mch.com](mailto:Amelia.Halac@mch.com)  
Michael Duchowny, MD, Principal Investigator

### **New York**

Montefiore Medical Center- Albert Einstein College of Medicine, Bronx, NY, 10467, Not yet recruiting  
Chris O'Dell, RN 718-920-4378 [codell@sprynet.com](mailto:codell@sprynet.com)  
Shlomo Shinnar, MD, PhD, Principal Investigator

### **Tennessee**

Le Bonheur Children's Medical Center, Memphis, TN, 38105, Recruiting  
Michelle Ellis, RN, CCRP 901-287-5330 [EllisMi@lebonheur.org](mailto:EllisMi@lebonheur.org)  
James Wheless, MD, Principal Investigator

### **Texas**

Dallas Pediatric Neurology Associates, Dallas, TX, 75230, Not yet recruiting

Karen Mansfield 972-566-4609 [kamansfield99@aol.com](mailto:kamansfield99@aol.com)  
Roy D Elterman, MD, Principal Investigator

Texas Children's Hospital, Houston, TX, 77030, Not yet recruiting  
Angus Wilfong, MD 832-822-1765 [awilfong@bcm.tmc.edu](mailto:awilfong@bcm.tmc.edu)  
Angus Wilfong, MD, Principal Investigator

### **Virginia**

Virginia Commonwealth University Health System, Richmond, VA, 23298, Not yet recruiting  
Kathy O'Hara, RN 804-828-0445 [ko'hara@mcvh-vcu.edu](mailto:ko'hara@mcvh-vcu.edu)  
John (Jack) M Pellock, MD, Principal Investigator

### **Wisconsin**

Children's Hospital of Wisconsin, Milwaukee, WI, 53201, Not yet recruiting  
Rhonda Werner 414-266-7539 [RWerner@chw.org](mailto:RWerner@chw.org)  
Mary Zupanc, MD, Principal Investigator

### **More Information**

[information about ganaxolone](#)

**Sponsored by: Marinus Pharmaceuticals**

**Information provided by:** Marinus Pharmaceuticals

**ClinicalTrials.gov Identifier:** NCT00441896

### **For more information about the trial:**

<http://www.clinicaltrials.gov/ct/show/NCT00441896?order=96>

## **2. Sirolimus (Rapamycin) in Treating Patients with Angiomyolipoma of the Kidney**

**Official Title:** Phase II Study of Sirolimus in Patients with Angiomyolipoma of the Kidney Secondary to Tuberous Sclerosis or Lymphangiomyomatosis

### **Study Purpose:**

**Rationale:** Drugs used in chemotherapy, such as sirolimus, work in different ways to stop the growth of tumor cells, either by killing the cells or by stopping them from dividing.

**Purpose:** This phase II trial is studying how well sirolimus works in treating individuals with angiomyolipoma of the kidney.

### **Eligibility:**

Ages Eligible for Study: 18 Years - 65 Years

**Genders Eligible for Study:** Both

### **Location and Contact Information:**

Please refer to this study by ClinicalTrials.gov identifier NCT00126672

### **Connecticut**

Connecticut Children's Medical Center, Hartford, Connecticut, 06106, United States; Recruiting  
Francis J. DiMario, MD 860-545-9460

### Massachusetts

Massachusetts General Hospital, Boston, Massachusetts, 02114, United States; Recruiting Elizabeth Thiele, MD, PhD 617-726-6540

### New York

New York University Medical Center, New York, New York, 10016, United States; Recruiting Daniel K. Miles, MD 212-263-8318

### Ohio

Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, 45229-3039, United States; Recruiting David Franz, MD 513-636-4222

### Pennsylvania

University of Pennsylvania Medical Center, Philadelphia, Pennsylvania, 19104-4283, United States; Recruiting Peter Crino, MD, PhD 215-349-5312

### Texas

University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, 75390, United States; Recruiting Arthur I. Sagalowsky, MD 214-645-8797 [arthur.sagalowsky@utsouthwestern.edu](mailto:arthur.sagalowsky@utsouthwestern.edu)

Study chairs or principal investigators: Sandra Dabora, MD, PhD, Study Chair, Brigham and Women's Hospital

For more information about this clinical trial, visit: <http://www.cancer.gov/clinicaltrials/DFCI-04298>

### 3. Siblings Wanted for a Modifier Gene Research Study



The Herscot Center for Tuberous Sclerosis Complex and the Center for Human Genetic Research at the Massachusetts General Hospital are trying to identify additional genes that play a role in neurological problems in TSC.

**We would like to enroll TSC siblings over 2 years of age that differ in their expression of**  
**autism** or **infantile spasms** or **uncontrollable seizures**

Participants will have:

- clinical evaluation by a neurologist specialized in TSC (Dr. Elizabeth Thiele)
- blood drawn
- brain MRI
- EEG
- neuropsychological testing (only for siblings differing in autism)

The whole study will take about 2 days to complete. There is no direct cost to the participants.

Travel and lodging will be reimbursed for participants who live more than 2 hours away from Boston.

For more information contact Susana Camposano 617-726 0240 (M-F, 8-5),  
[scamposano@partners.org](mailto:scamposano@partners.org)

#### **4. TSC and TSC/LAM Protocols at the National Institutes of Health**

The Clinical Research Nurses can be reached toll-free at 1-877-NIH-LUNG, # 3 on the menu or locally through 301-496-3632.

#### **5. Individuals with Seizures Sought**

Scientists at the National Institute of Neurological Disorders and Stroke (NINDS) seek people age 5 and older with seizures for participation in research studies. People with seizures that are not controlled by standard antiepileptic drugs are eligible. However, those with other medical conditions, particularly if on-going therapy is needed, may be excluded. The scientists will record seizures with video-EEG (electroencephalogram) monitoring, and will conduct non-invasive brain imaging tests such as positron emission tomography (PET) and magnetic resonance imaging (MRI) scans. The studies may last several months, with an inpatient stay of up to 2 weeks and 10-15 outpatient visits of about an hour each.

Before patients enter the study, they will be screened in the outpatient clinic. The screening will include a history, a neurological examination, an EEG, and an MRI scan, if needed. Even if patients decide not to enter the study after the initial screening, the investigators may be able to make suggestions for further seizure evaluation or treatment.

The studies will take place at the National Institutes of Health (NIH) Clinical Center in Bethesda, MD. All study-related expenses will be paid by the NIH. There is no cost for participation or for any tests associated with the research.

For further information, contact Dr. William Theodore, Chief, Clinical Epilepsy Section, NINDS, NIH, Building 10, Room 5N250, 10 Center Drive MSC 1408, Bethesda, MD 20892-1408; telephone: 301-496-1923. Please refer to study number 01-N-0139.

#### **6. Everolimus (RAD001) Therapy of Giant Cell Astrocytoma in Patients with Tuberous Sclerosis Complex**

The purpose of the study is to evaluate the safety and potential side effects of everolimus (an experimental drug) on a person with Tuberous Sclerosis Complex who also has been diagnosed with a brain tumor (astrocytoma). The hypothesis is that the drug will cause the tumor size to decrease, and may have beneficial activity separate from effects on tumors in patients.

##### **Eligibility**

Ages Eligible for Study: 3 Years and above,  
Genders Eligible for Study: Both

##### **Inclusion Criteria:**

- Age three years and older
- If female and of child bearing potential, documentation of negative pregnancy test prior to enrollment and, where applicable, use of appropriate, non-estrogen containing birth control contraceptive regimen while on study that is to be continued 3 months after discontinuation of everolimus. Use of barrier methods alone will not constitute an acceptable contraceptive regimen.
- Clinically definite diagnosis of tuberous sclerosis (modified Gomez criteria or positive genetic test)
- Presence of giant cell astrocytoma as defined by imaging characteristics and serial increase in size of lesion on 2 or more MRI scans

- Adequate renal function (creatinine < 1.5 mg/dl)

Exclusion Criteria:

- Serious intercurrent medical illness or other uncontrolled medical disease which could compromise participation in the study
- Significant hematologic or hepatic abnormality
- Continuous requirement for supplemental oxygen
- Intercurrent infection at initiation of oxygen
- Recent surgery (within 2 months of initiation of everolimus)
- Pregnant or lactating women
- Use of an investigational drug within the last 30 days
- Must be adequately recovered from the acute toxicities of any prior therapy
- Clinical evidence of impending herniation or focal neurologic deficit related to the subject's astrocytoma

**Location and Contact Information**

Please refer to this study by ClinicalTrials.gov identifier NCT00411619

Jenny Leonard, R.N., CFNP

Cincinnati Children's Hospital Medical Center, Cincinnati, OH 45229

Phone: 513-636-4222

E-mail: [tsclinic@cchmc.org](mailto:tsclinic@cchmc.org)

David N Franz, M.D., Principal Investigator

Darcy A Krueger, M.D., Ph.D., Sub-Investigator

Marguertie M Care, M.D., Sub-Investigator

Anna W Byars, Ph.D, Sub-Investigator

Kerry Crone, M.D., Sub-Investigator

Katherine Holland-Bouley, M.D., Ph.D., Sub-Investigator

For more information, see: <http://www.clinicaltrials.gov/ct/show/NCT00411619?order=1>

**TSC INFORMATION**

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

This is the April 2007 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 May 2007 *TSC Alert* contact: [vwhitemore@tsalliance.org](mailto:vwhitemore@tsalliance.org)

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