



# TSC ALERT

## March 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>2</b>
<b>NEW TSC PUBLICATIONS</b> .....	<b>5</b>
<b>RESEARCH RESOURCES</b> .....	<b>9</b>
<b>CONFERENCES AND SEMINARS</b> .....	<b>9</b>
<b>TSC CLINICAL TRIALS AND STUDIES</b> .....	<b>12</b>
<b>TSC INFORMATION</b> .....	<b>15</b>

## **ABSTRACT SUBMISSION DEADLINES**

### **TSC Conference in Rome (May 2007): Final Call for Abstracts**

The organization of the International Research Symposium on TSC to be held in Rome next May is proceeding smoothly. We have received more than 30 abstracts, and the preliminary scientific program with the list of speakers are available for view on the website <http://www.ptsroma.it/tsc2007>. However, we are still looking for your contribution, and last minute presentations can be sent over **until the March 31, 2007**. Details concerning registration and hotel accommodation are available on the website.

Hope to see you in Rome in May-  
Prof. Paolo Curatolo  
Past President, International Child Neurology Association  
Pediatric Neurology & Psychiatry Unit  
Neuroscience Department  
Tor Vergata University of Rome  
email: [curatolo@uniroma2.it](mailto:curatolo@uniroma2.it)

### **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>

### **McKnight Neuroscience of Brain Disorders Award**

This award provides \$100,000 a year for three years to a scientist working to translate basic research into treatments, preventions, and cures for human diseases. Letters of intent are due April 2, 2007. For more information, please visit [www.mcknight.org/neuroscience](http://www.mcknight.org/neuroscience)

### **NIH Director's New Innovator Awards**

The Office of the Director, NIH, plans to issue a Request for Applications (RFA) in the spring of 2007, with review and funding expected by September 30, 2007, for NIH Director's New Innovator Awards.

This new program extends the concept of the NIH Director's Pioneer Awards

(<http://nihroadmap.nih.gov/pioneer/>) to support new investigators of exceptional creativity who

propose innovative approaches that have the potential to produce an unusually high impact on significant problems in biomedical and behavioral research. The NIH Director's New Innovator Awards will provide grant support to highly innovative new investigators who have not yet obtained a traditional R01 grant. Applicants must hold an independent research position at a domestic institution, and be within 10 years of their terminal degree (1997 or later). The proposed research may be in any scientific area relevant to the mission of NIH (biological, behavioral, clinical, social, physical, chemical, computational, engineering and mathematical sciences). The project description in the grant application will be briefer than that required for R01s and will emphasize the significance of the project, what makes the approaches exceptionally innovative, how the applicant will address risks and challenges, and the applicant's qualifications for this award. The review criteria will emphasize the importance and potential impact of the scientific problem, the novelty and innovativeness of the approach, and evidence of the applicant's potential for creative and innovative research. Presentation of preliminary data relevant to the project will be allowed, but is not required. Letters of reference are not required and will not be accepted. Awards will be made for up to \$300K direct costs per year plus applicable Facilities and Administrative costs, for five years. It is anticipated that approximately 14-16 awards will be made.

### **Announcing the NIH Director's Bridge Awards (NOT-OD-07-056)**

National Institutes of Health

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-056.html>

### **Notice of Intent to Issue a PA on Investigator-Initiated Multi-Site Clinical Trials (NOT-HL-07-108)**

National Heart, Lung, and Blood Institute

<http://grants.nih.gov/grants/guide/notice-files/NOT-HL-07-108.html>

### **Assay Development for High Throughput Molecular Screening (R21) (RFA-RM-07-008)**

NIH Roadmap Initiatives

Application Receipt Date(s): May 16, 2007

<http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-008.html>

**Implementation of NIH Fiscal Policy for Non-Competing Grant Awards - " FY 2007" (NOT-OD-07-049)**

National Institutes of Health

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-049.html>

**Notice of Legislative Mandates in Effect for FY 2007 (NOT-OD-07-050)**

National Institutes of Health

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-050.html>

**Salary Limitation on Grants, Cooperative Agreements, and Contracts (NOT-OD-07-051)**

National Institutes of Health

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-051.html>

**Request for Information (RFI): To Solicit Input for the National Institute of General Medical Sciences (NIGMS) Strategic Plan for 2008-2012 (NOT-GM-07-102)**

National Institute of General Medical Sciences

<http://grants.nih.gov/grants/guide/notice-files/NOT-GM-07-102.html>

**NHLBI Creates A New Clinical Research Guide (NOT-HL-07-002)**

National Heart, Lung, and Blood Institute

<http://grants.nih.gov/grants/guide/notice-files/NOT-HL-07-002.html>

**Notice of a FAQ Website for RFA-HL-07-009, NHLBI Ancillary Studies in Clinical Trials (R01) (NOT-HL-07-007)**

National Heart, Lung, and Blood Institute

<http://grants.nih.gov/grants/guide/notice-files/NOT-HL-07-007.html>

**Special Emphasis Notice: AHRQ Announces Interest in Research Implementation Small Research (R03) Grants (NOT-HS-07-002)**

Agency for Healthcare Research and Quality

<http://grants.nih.gov/grants/guide/notice-files/NOT-HS-07-002.html>

**Request for Information (RFI): Tools and Resources for Research on Neuronal Plasticity (Neuroscience Blueprint) (NOT-MH-07-106)**

National Institutes of Health

National Center for Complementary and Alternative Medicine

National Center for Research Resources

National Eye Institute

National Institute on Aging

National Institute on Alcohol Abuse and Alcoholism

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 Environmental Health Sciences

National Institute of General Medical Sciences

National Institute of Justice

National Institute of Nursing Research

Office of Behavioral and Social Science Research

<http://grants.nih.gov/grants/guide/notice-files/NOT-MH-07-106.html>

**Developmental Psychopharmacology (R21) (PA-07-222)**

National Institute of Mental Health

National Institute of Child Health and Human Development

National Institute on Drug Abuse

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

<http://grants.nih.gov/grants/guide/pa-files/PA-07-222.html>

**Pilot and Feasibility Studies on Oral Health Promotion Research across the Life Span (R21) (PA-07-223)**

National Institute of Dental and Craniofacial Research

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

<http://grants.nih.gov/grants/guide/pa-files/PA-07-223.html>

**Multidisciplinary Translational Research in Critical Care (R01) (PA-07-233)**

National Heart, Lung, and Blood Institute

National Institute on Aging

National Institute of Child Health and Human Development

National Institute of Diabetes and Digestive and Kidney Diseases

National Institute of General Medical 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/PA-07-233.html>

**Planning Grant for Oral Health Promotion across the Life Span (R21) (PAR-07-224)**

National Institute of Dental and Craniofacial Research

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

<http://grants.nih.gov/grants/guide/pa-files/PAR-07-224.html>

**Centers of Biomedical Research Excellence (COBRE) [P20] (PAR-07-229)**

National Center for Research Resources

Application Receipt/Submission Date(s): October 24, 2007; October 29, 2008; October 28, 2009

<http://grants.nih.gov/grants/guide/pa-files/PAR-07-229.html>

**CDC Grants for Public Health Research Dissertation (R36) (PAR-07-231)**

Centers for Disease Control and Prevention

Office of Public Health Research

Application Receipt/Submission Date(s): April 10, August 10, annually.

<http://grants.nih.gov/grants/guide/pa-files/PAR-07-231.html>

**Molecular Probes for Microscopy of Cells (R01) (PAR-07-234)**

National Institute of General Medical Sciences

Application Receipt/Submission Date(s): May 25, 2007, August 29, 2007, May 27, 2008 and August 29, 2008

<http://grants.nih.gov/grants/guide/pa-files/PAR-07-234.html>

**Continued Development and Maintenance of Software (R01) (PAR-07-235)**

National Center for Research Resources

National Cancer Institute

National Human Genome Research Institute

National Heart, Lung, and Blood Institute

National Institute on Alcohol Abuse and Alcoholism

National Institute of Biomedical Imaging and Engineering

National Institute on Drug Abuse

National Institute of General Medical Sciences

National Institute of Mental Health

## **NEW TSC PUBLICATIONS**

Au KS, Williams AT, Roach ES, Batchelor L, Sparagana SP, Delgado MR, Wheless JW, Baumgartner JE, Roa BB, Wilson CM, Smith-Knuppel TK, Cheung MY, Whittemore VH, King TM, Northrup H (2007) Genotype/phenotype correlation in 325 individuals referred for a diagnosis of tuberous sclerosis complex in the United States. *Genet Med* 9(2):88-100

Baram TZ (2007) Models for infantile spasms: An arduous journey to the holy grail... *Ann Neurol*. 2007 Feb 21 61(2):89-91 [Epub ahead of print]

Byrd LM, Jadoon B, Lieberman I, Johnston T (2007) Chronic Pain and Obstetric Management of a Patient with Tuberous Sclerosis. *Pain Med* 8(2):199-203

Cao Y, Kamioka Y, Yokoi N, Kobayashi T, Hino O, Onodera M, Mochizuki N, Nakae J (2006) Interaction of FoxO1 and TSC2 induces insulin resistance through activation of the mammalian target of rapamycin/p70 S6K pathway. *J Biol Chem* 281(52):40242-51 [Epub 2006 Oct 31]

Cause-Mariscal A, Palot M, Visseaux H, Daigremont-Botmans C, Malinovsky JM (2007) Labor analgesia and cesarean section in women affected by tuberous sclerosis: report of two cases. *Int J Obstet Anesth* 2007 Mar 2 [Epub ahead of print]

Chakrabarti PP, Daumke O, Suveyzdis Y, Kotting C, Gerwert K, Wittinghofer A (2006) Insight into Catalysis of a Unique GTPase Reaction by a Combined Biochemical and FTIR Approach. *J Mol Biol* 2006 Nov 10 [Epub ahead of print]

Chandra PS, Salamon N, Nguyen ST, Chang JW, Huynh MN, Cepeda C, Leite JP, Neder L, Koh S, Vinters HV, Mathern GW (2007) Infantile spasm-associated microencephaly in tuberous sclerosis complex and cortical dysplasia. *Neurology* 68(6):438-45

Cook SJ, Morley SJ (2007) Nutrient-responsive mTOR signalling grows on Sterile ground. *Biochem J* 403(1):e1-3

Cottier JP, Toutain A, Hommet C, Sembely C, Bosq M, Texier N, Herbreteau D, Sirinelli D (2006) [Cortical malformations and epilepsy: Role of MR imaging] *J Radiol* 87(11 Pt 1):1621-34 [Article published in French]

D'Armiento J, Imai K, Schiltz J, Kolesnekova N, Sternberg D, Benson K, Pardo A, Selman M, Smolarek T, Vundavalli M, Sonnet J, Szabolcs M, Chada K (2007) Identification of the benign mesenchymal tumor gene HMGA2 in lymphangiomyomatosis. *Cancer Res* 67(5):1902-9

Dallos G, Chmel R, Alfoldy F, Torok S, Telkes G, Diczhazi C, Perner F, Jaray J, Langer RM (2006) Bourneville-Pringle disease for kidney transplantation: a single-center experience. *Transplant Proc* 38(9):2823-4

De Wilde H, Benatar A (2007) Cardiac rhabdomyoma with long-term conduction abnormality: Progression from pre-excitation to bundle branch block and finally complete heart block. *Med Sci Monit* 2007 Jan 18 13(2):CS21-23 [Epub ahead of print]

Garzon JC, Ng CS, Lee TW, Yim AP (2007) Video-assisted Thoracic Surgery for Pneumothorax in LAM. *Heart Lung Circ* 2007 Mar 7 [Epub ahead of print]

Gayatri N, Ferrie C, Cross H (2007) Corticosteroids including ACTH for childhood epilepsy other than epileptic spasms. *Cochrane Database Syst Rev* 1):CD005222

Grosse C, Bankier A (2007) Imaging of emphysema. *Radiologe* 2007 Jan 16 [Epub ahead of print] [Article published in German]

Han EK, Levenson JD, McGonigal T, Shah OJ, Woods KW, Hunter T, Giranda VL, Luo Y (2007) Akt inhibitor A-443654 induces rapid Akt Ser-473 phosphorylation independent of mTORC1 inhibition. *Oncogene* 2007 Mar 5 [Epub ahead of print]

Hattori A, Hayano J, Fujimoto S, Ando N, Mizuno K, Kamei M, Kobayashi S, Ishikawa T, Togari H (2007) Cardiac vagal activation by adrenocorticotrophic hormone treatment in infants with West syndrome. *Tohoku J Exp Med* 211(2):133-9

Hayashi AA, Proud CG (2007) The rapid activation of protein synthesis by growth hormone requires signaling through the mammalian target of rapamycin, mTOR. *Am J Physiol Endocrinol Metab* 2007 Feb 6 [Epub ahead of print]

Hossain Z, Ali SM, Ko HL, Xu J, Ng CP, Guo K, Qi Z, Ponniah S, Hong W, Hunziker W (2007) Glomerulocystic kidney disease in mice with a targeted inactivation of Wwtr1. *Proc Natl Acad Sci U S A* 104(5):1631-6 [Epub 2007 Jan 24]

Hsu YC, Chern JJ, Cai Y, Liu M, Choi KW (2007) Drosophila TCTP is essential for growth and proliferation through regulation of dRheb GTPase. *Nature* 445(7129):785-8

Huyghe E, Zairi A, Nohra J, Kamar N, Plante P, Rostaing L (2007) Gonadal impact of target of rapamycin inhibitors (sirolimus and everolimus) in male patients: an overview. *Transpl Int* 20(4):305-11

Inomoto C, Umemura S, Sasaki Y, Yasuda M, Terachi T, Osamura RY (2007) Renal cell carcinoma arising in a long pre-existing angiomyolipoma. *Pathol Int* 57(3):162-6

Jaworski J, Sheng M (2006) The growing role of mTOR in neuronal development and plasticity. *Mol Neurobiol* 34(3):205-19

Karnak I, Alehan D, Ekinci S, Buyukpamukcu N (2007) Cardiac rhabdomyoma as an unusual mediastinal mass in a newborn. *Pediatr Surg Int* 2007 Mar 9 [Epub ahead of print]

Kaur S, Lal L, Sassano A, Majchrzak-Kita B, Srikanth M, Baker DP, Petroulakis E, Hay N, Sonenberg N, Fish EN, Plataniias LC (2007) Regulatory effects of mammalian target of rapamycin-activated pathways in type I and II interferon signaling. *J Biol Chem* 282(3):1757-68 [Epub 2006 Nov 17]

Kebria M, Black D, Borelli C, Modica I, Hensley M, Chi DS (2007) Primary retroperitoneal lymphangiomyomatosis in a postmenopausal woman: a case report and review of the literature. *Int J Gynecol Cancer* 17(2):528-32

Kozlowski P, Roberts P, Dabora S, Franz D, Bissler J, Northrup H, Au KS, Lazarus R, Domanska-Pakiela D, Kotulska K, Jozwiak S, Kwiatkowski DJ (2007) Identification of 54 large deletions/duplications in TSC1 and TSC2 using MLPA, and genotype-phenotype correlations. *Hum Genet* 2007 Feb 8 [Epub ahead of print]

- Kroll-Seger J, Kaminska A, Moutard ML, de Saint-Martin A, Guet A, Dulac O, Chiron C (2007) Severe relapse of epilepsy after vigabatrin withdrawal: for how long should we treat symptomatic infantile spasms? *Epilepsia* 48(3):612-3
- Lam AP, Corbridge TC (2007) Multiple cysts in the kidney and lungs in a patient with polycystic kidney disease and lymphangiomyomatosis. *ScientificWorldJournal* 7:80-2
- Leung AK, Robson WL (2007) Tuberous sclerosis complex: a review. *J Pediatr Health Care* 21(2):108-14
- Luat AF, Makki M, Chugani HT (2007) Neuroimaging in tuberous sclerosis complex. *Curr Opin Neurol* 20(2):142-150
- Lux AL (2007) Is hypsarrhythmia a form of non-convulsive status epilepticus in infants? *Acta Neurol Scand* 115(4):37-44
- Martignoni G, Pea M, Reghellin D, Zamboni G, Bonetti F (2007) Perivascular epithelioid cell tumor (PEComa) in the genitourinary tract. *Adv Anat Pathol* 14(1):36-41
- Mennel S, Meyer CH, Peter S, Schmidt JC, Kroll P (2007) Current treatment modalities for exudative retinal hamartomas secondary to tuberous sclerosis: review of the literature. *Acta Ophthalmol Scand* 85(2):127-132
- Mizuguchi M (2007) Abnormal giant cells in the cerebral lesions of tuberous sclerosis complex. *Congenit Anom (Kyoto)* 47(1):2-8
- Muhammed K, Mathew J (2007) Coexistence of two neurocutaneous syndromes: Tuberous sclerosis and hypomelanosis of Ito. *Indian J Dermatol Venereol Leprol* 73(1):43-5
- Muhler MR, Rake A, Schwabe M, Schmidt S, Kivelitz D, Chaoui R, Hamm B (2007) Value of fetal cerebral MRI in sonographically proven cardiac rhabdomyoma. *Pediatr Radiol* 2007 Mar 15 [Epub ahead of print]
- Paddenberg R, Stieger P, von Lilien AL, Faulhammer P, Goldenberg A, Tillmanns HH, Kummer W, Braun-Dullaeus RC (2007) Rapamycin attenuates hypoxia-induced pulmonary vascular remodeling and right ventricular hypertrophy in mice. *Respir Res* 2007 Feb 24 8(1):15 [Epub ahead of print]
- Papacostas SS, Papathanasiou ES, Myriantopoulou P, Stylianidou G (2007) Tuberous sclerosis successfully treated with levetiracetam monotherapy: 18 months of follow-up. *Pharm World Sci* 2007 Mar 1 [Epub ahead of print]
- Pelletier CL, Maggi LB Jr, Brady SN, Scheidenhelm DK, Gutmann DH, Weber JD (2007) TSC1 sets the rate of ribosome export and protein synthesis through nucleophosmin translation. *Cancer Res* 67(4):1609-17
- Rammeh Rommani S, Trabelsi A, Attia L, Msakni I, Koubaa A, Ben Jilani S, Zermani R (2006) Perivascular epithelioid cell tumor of the uterus: a case report. *Pathologica* 98(6):649-51
- Raznahan A, Higgins NP, Griffiths PD, Humphrey A, Yates JR, Bolton PF (2007) Biological markers of intellectual disability in tuberous sclerosis. *Psychol Med* 2007 Mar 5;:1-12 [Epub ahead of print]
- Schick V, Majores M, Fassunke J, Engels G, Simon M, Elger CE, Becker AJ (2007) Mutational and expression analysis of CDK1, cyclinA2 and cyclinB1 in epilepsy-associated glioneuronal lesions. *Neuropathol Appl Neurobiol* 33(2):152-62

- Semela D, Piguet AC, Kolev M, Schmitter K, Hlushchuk R, Djonov V, Stoupis C, Dufour JF (2007) Vascular remodeling and antitumoral effects of mTOR inhibition in a rat model of hepatocellular carcinoma. *J Hepatol* 2007 Jan 17 [Epub ahead of print]
- Shawki HB, Muhammed SM, Reda AN, Abdulla TS, Ardalan DM (2007) Pulmonary lymphangioliomyomatosis. *Saudi Med J* 28(1):131-4
- Sieghart W, Fuereder T, Schmid K, Cejka D, Werzowa J, Wrba F, Wang X, Gruber D, Rasoul-Rockenschaub S, Peck-Radosavljevic M, Wacheck V (2007) Mammalian Target of Rapamycin Pathway Activity in Hepatocellular Carcinomas of Patients Undergoing Liver Transplantation. *Transplantation* 83(4):425-432
- Silva AA, Carlos R, Contreras E, Almeida OP, Lopes MA, Vargas PA (2007) Angiomyolipoma of the upper lip: case report and review of the literature. *Med Oral Patol Oral Cir Bucal* 12(2):E101-4
- Slodkowska J, Patera J, Breborowicz J, Jarzemska A, Korzeniewska-Kosela M, Siemiatkowska K, Radzikowska E, Przybylski G, Kozlowski W (2006) Extrapulmonary lymphangioliomyomatosis presented as the asymptomatic retroperitoneal tumours--two cases report. *Pol J Pathol* 57(4):205-7
- Storm PB, Magge SN, Kazahaya K, Sutton LN (2007) Cervical Chordoma in a Patient with Tuberous Sclerosis Presenting with Shoulder Pain. *Pediatr Neurosurg* 43(2):167-169
- Velisek L, Jehle K, Asche S, Veliskova J (2007) Model of infantile spasms induced by N-methyl-D-aspartic acid in prenatally impaired brain. *Ann Neurol* 2007 Feb 21 61(2):109-119 [Epub ahead of print]
- Wang H, Kubica N, Ellisen LW, Jefferson LS, Kimball SR (2006) Dexamethasone represses signaling through the mammalian target of rapamycin in muscle cells by enhancing expression of REDD1. *J Biol Chem* 281(51):39128-34 [Epub 2006 Oct 30]
- Wang Y, Greenwood JS, Calcagnotto ME, Kirsch HE, Barbaro NM, Baraban SC (2007) Neocortical hyperexcitability in a human case of tuberous sclerosis complex and mice lacking neuronal expression of TSC1. *Ann Neurol* 2007 Feb 5 [Epub ahead of print]
- Weissman KJ (2007) Mutasynthesis - uniting chemistry and genetics for drug discovery. *Trends Biotechnol* 2007 Feb 14 [Epub ahead of print]
- Witman PM (2006) More than just a bump: the hamartoma syndromes. *Adv Dermatol* 22:157-80
- Yasui S, Tsuzaki K, Ninomiya H, Floricel F, Asano Y, Maki H, Takamura A, Nanba E, Higaki K, Ohno K (2007) The TSC1 gene product hamartin interacts with NADE. *Mol Cell Neurosci* 2007 Feb 12 [Epub ahead of print]
- Yin XJ, Wang G, Khan-Dawood FS (2007) Requirements of phosphatidylinositol-3 kinase and mammalian target of rapamycin for estrogen-induced proliferation in uterine leiomyoma- and myometrium-derived cell lines. *Am J Obstet Gynecol* 196(2):176.e1-5
- Zhang H, Bajraszewski N, Wu E, Wang H, Moseman AP, Dabora SL, Griffin JD, Kwiatkowski DJ (2007) PDGFRs are critical for PI3K/Akt activation and negatively regulated by mTOR. *J Clin Invest* 2007 Feb 8 [Epub ahead of print]

## **RESEARCH RESOURCES**

### **TSCRCP Funded TSC Research Resources**

The Tuberous Sclerosis Complex Research Program (TSCRCP) in the Congressionally Directed Medical Research Program (CDMRP) in the Department of Defense (DoD) has posted a listing of the research resources that were developed utilizing funding from this program. For more information see:

<http://cdmrp.army.mil/tscrp/default.htm>

## **CONFERENCES AND SEMINARS**

### **March 26-27, 2007**

#### **Twelfth Meeting of the Secretary's Advisory Committee on Genetics, Health, and Society**

Marriott Inn and Conference Center University of Maryland-College Park 3501

University Boulevard East, Adelphi, MD 20783

<http://marriott.com/hotels/travel/wasum-the-inn-and-conference-center-university-of-maryland-university-college/>

The meeting is open to the public, and pre-registration is not required. Seating will be available on a first-come-first-serve basis. For directions, please visit <http://conferencecenters.com/WASUM>

For more information about the Committee and to obtain up-to-date information about the meeting, please visit <http://www4.od.nih.gov/oba/sacghs.htm>

### **March 29-30, 2007**

#### **Curing Epilepsy 2007: Translating Discoveries into Therapies**

Natcher Conference Center, Bethesda, MD

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

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

### **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 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/>

### **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)

### **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 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**

### **AES Launches Regional Symposia March 24, 2007 in Los Angeles**

The American Epilepsy Society has received an educational grant from Pfizer, Inc. to host a five-city series of symposia entitled: A Comprehensive Review of Epilepsy Management: A Case-Based CME Symposium. The symposia are chaired by AES Education Council Chair L. James Willmore, M.D.

The program is geared toward the general neurologist, pediatrician, residents, nurses and pharmacists. These regional meetings will take place throughout the year. The symposia will feature an interdisciplinary panel, who will review the epidemiology, diagnosis and evaluation of epilepsy. Workshops geared specifically to the adult physician, the pediatric physician and professional in epilepsy will follow and will be geared toward guidelines and emerging trends in the treatment of epilepsy.

These workshops will provide a venue for participants to interact with experts in discussion of current issues and future directions in epilepsy management. The goal of the symposium is to enhance participants' knowledge base of epilepsy and its management, as well as optimize their skills in epilepsy care by demonstrating practical application of diagnostic tools and therapeutic options.

The first symposia in Los Angeles will also feature David M. Labiner, M.D.; Raman Sankar, M.D., Ph.D.; and Susan L. Yudovin, RN, MN, CPNP.

Future programs will be held in Houston (May 19), Atlanta, St. Louis, and Philadelphia (November 30).

For program and registration information, visit the AES Web site at [www.aesnet.org](http://www.aesnet.org) or [click here to download brochure in .pdf format.](#)

### **HHMI and Elsevier Announce Public Access Agreement**

The Howard Hughes Medical Institute (HHMI) and Elsevier have established an agreement to make author manuscripts of articles published in Elsevier and Cell Press journals publicly available six months following final publication. It takes effect for articles published after September 1, 2007. For the full story, go to <http://www.hhmi.org/news/hhmielsevier20070308.html>

### **Largest-Ever Search for Autism Genes Reveals New Clues**

<http://www.nimh.nih.gov/press/largest-ever-search-for-autism-genes-reveals-new-clues.cfm>

### **Half of Adults With Anxiety Disorders Had Psychiatric Diagnoses in Youth**

<http://www.nimh.nih.gov/press/anxietyhistory.cfm>

### **Study Tracks Prevalence of Eating Disorders**

<http://www.nimh.nih.gov/press/prevalence-of-eatingdisorders.cfm>

### **Common Gene Version Optimizes Thinking - but With a Possible Downside**

<http://www.nimh.nih.gov/press/darpp-32variations.cfm>

### **Autism Research Efforts Highlighted in Biological Psychiatry Special Issue**

[http://www.nimh.nih.gov/press/autism\\_biopsychiatry.cfm](http://www.nimh.nih.gov/press/autism_biopsychiatry.cfm)

### **Brain's Reward Circuit Activity Ebbs and Flows with a Woman's Hormonal Cycle**

<http://www.nimh.nih.gov/press/rewardcircuit.cfm>

### **Extreme Irritability: Is It Childhood Bipolar Disorder?**

<http://www.nimh.nih.gov/press/ped-bipolar-irritability.cfm>

### **New Tests May Help Researchers Detect Genetic Basis For Autism**

<http://www.nimh.nih.gov/press/moy-crawley-autism.cfm>

### **Clues to Making and Breaking Memories Included in List of Year's Top Science**

<http://www.nimh.nih.gov/press/sciencebreakthru-2006.cfm>

### **Adult Stem Cells Decide the Fate of Their Daughters**

Adult stem cells call the shots when it comes to their daughters' destinies. That's the take-home lesson from a new study of adult stem cells in the intestines of fruit flies. Allan C. Spradling, Ph.D., HHMI investigator at Carnegie Institution of Washington, and collaborators found that intestinal stem cells make important decisions about their fate by communicating directly with their daughter cells, instructing them to become one of two possible cell types. The studies bring researchers a bit closer to understanding how adult stem cells decide to make the cell type that best meets the current needs of the organism. This research was published in the February 16, 2007, issue of Science. For the full story, go to: <http://www.hhmi.org/news/spradling20070215.html>

### **Alternative Ways of Reading DNA Have Spurred Evolution**

Humans are substantially more complex than the tiny worm *Caenorhabditis elegans*, yet both organisms have about the same number of genes. Why is human DNA so much more versatile? In a new article published in the journal *Genome Research*, Howard Hughes Medical Institute researcher Philip Green, Ph.D. at the University of Washington and his collaborators conclude that roughly 40-50 percent of human and mouse genes have alternative promoters. Promoters tell specialized enzymes where to start reading the DNA message that is used to produce a protein. The data suggest that alternative promoters are critically important to the functioning of higher organisms. For the full story, go to: <http://www.hhmi.org/news/green20070215.html>

### **How Cells Connect Their Plumbing**

Researchers have uncovered an important aspect of how cells create the junctions that allow them to communicate directly with one another. These gap junctions are protein channels through which cells exchange molecules and charged atoms among each other, helping to coordinate processes ranging from embryonic development to the heartbeat. A new understanding of how cells target the components of these channels to the appropriate location on the cell surface could reveal important insights into processes that have gone awry in heart failure and cancer. This research by Lily Y. Jan, Ph.D. and Yuh Nung Jan, Ph.D., HHMI investigators at the University of California, San Francisco was published in the February 08, 2007, issue of Cell. For the full story, go to:

<http://www.hhmi.org//news/jan20070208.html>

### **Unscrambling the Gibbon Genome**

The arboreal, branch-swinging antics of the gibbon are nothing compared to the acrobatics its genome has undergone during evolution. While the genomes of humans and other primates still resemble that of their common ancestor, the massive genomic scrambling of the gibbon genome has rendered it a complex puzzle. Solving that puzzle, scientists believe, could help reveal how evolution experiments with genomic rearrangement, as well as how chromosomes can become unstable in cancer and other genetic diseases. Now, Howard Hughes Medical Institute researcher Evan E. Eichler, Ph.D. from the University of Washington School of Medicine and his colleagues have mapped in the finest detail yet the many chromosomal breaks and rearrangements that have reshaped the white-cheeked gibbon's genome as it evolved. For the full story, go to:

<http://www.hhmi.org//news/eichler20070216.html>

### **New Functional Atlas Gives the 411 on Gene Partners**

Sometimes it helps to have a "cheat sheet" when you are working on a problem as difficult as deciphering the relationships among hundreds of thousands of genes. At least that's the idea behind a powerful new technique developed by Howard Hughes Medical Institute (HHMI) researchers to analyze how genes function together inside cells. This research was published in the February 21, 2007, issue of Nature by Jonathan S. Weissman, Ph.D., HHMI investigator at the University of California, San Francisco. For the full story, go to:

<http://www.hhmi.org//news/weissman20070221.html>

### **Watching a Biological Jigsaw Puzzle Come Together**

Scientists have recorded the action involved in assembling telomerase, an enzyme used by cells to protect their genes during the potentially dangerous process of DNA replication. Using a sophisticated technique for tracking structural changes in individual molecules in real time, they have revealed how three of the protein and RNA components of the enzyme come together, altering their shapes along the way to ensure that the next piece will fit. This research was published in the February 25, 2007, issue of Nature by Xiaowei Zhuang, Ph.D., HHMI investigator at Harvard University. For the full story, go to: <http://www.hhmi.org//news/zhuang20070225.html>

## **TSC CLINICAL TRIALS AND STUDIES**

### **1. Sirolimus 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 [david.franz@chmcc.org](mailto:david.franz@chmcc.org)

**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>

**2. Siblings Wanted for a Modifier Gene Research Study**

MASSACHUSETTS  
GENERAL HOSPITAL



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)

### **3. 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.

### **4. 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.

### **5. 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

Marguerite 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 March 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 April 2007 *TSC Alert* contact: [vwhitemore@tsalliance.org](mailto:vwhitemore@tsalliance.org)

Archived issues of the TSC Alert can be found at: <http://www.tsalliance.org/pages.aspx?content=25>