



TSC ALERT

Edited by Vicky H Whittemore, PhD

July 2006

Welcome to the July 2006 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 August 2006 *TSC Alert* contact: vwhittemore@tsalliance.org

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SAVE THE DATE

May 24-26, 2007

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

Venue: Grand Hotel Palazzo Carpegna, Rome, Italy

Information: curatolo@uniroma2.it

September 23-25, 2007

Tuberous Sclerosis Complex: From Genes to New Therapeutics

International TSC Research Conference organized by the Tuberous Sclerosis Alliance

Loews Annapolis Hotel, Annapolis, MD

More information coming soon!

September 11-14, 2008

International TSC Conference

Organized by the Tuberous Sclerosis Association, U.K.

Brighton, U.K.

More information coming soon!

FUNDING OPPORTUNITIES

Tuberous Sclerosis Alliance RFPs

Letter of Intent Deadline: August 1, 2006 (LOI required)

Grant Application Deadline: November 1, 2006

The Tuberous Sclerosis Alliance announces the availability of awards for the following grant mechanisms:

- Predoctoral Awards
- Postdoctoral Awards
- Junior Investigator Awards
- Senior Investigator Awards
- Clinical Trial Development Awards
- Pilot Clinical Trial Awards
- Conference Awards

Additional information on the RFPs and LOI forms are available on the TS Alliance Web site at: <http://www.tsalliance.org>

Milken Family Foundation Translational Research Award to Fund Epilepsy Research Deadline: September 1, 2006

Administered by the Epilepsy Therapy Development Project <http://www.epilepsytdp.org/>

The Milken Family Foundation Translational Research Award is designed to advance the development of novel therapies for the treatment of epilepsy.

All grant proposals must demonstrate a clear and concise research plan integrating laboratory science with the clinical research, the probability of success, and the estimated timeframe for development. Preference is given to those proposals that already have a commercial partner committed to the research project. Other areas of consideration include but are not limited to seed funding for preliminary work necessary to explore novel approaches; projects, which if successful, offer a clear path to further development; proposals that support the commercialization of academic research projects; and research to bring new approaches and therapy to children.

Any individual holding an M.D., Ph.D., or equivalent degree is eligible to submit a proposal. Proposals for research originating from outside the United States are welcome.

Two grants in the amount of \$50,000 each will be awarded.

Visit the Web site of the Epilepsy Therapy Development Project for complete program guidelines and application procedures. <http://fconline.foundationcenter.org/pnd/10002796/epilepsytdp>

Understanding and Treating Tuberous Sclerosis Complex (R01) (PAS-06-205)

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

Tuberous Sclerosis Alliance

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

<http://grants.nih.gov/grants/guide/pa-files/PAS-06-205.html>

Understanding and Treating Tuberous Sclerosis Complex (R21) (PAS-06-206)

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
Tuberous Sclerosis Alliance
Application Receipt/Submission Date(s): Multiple dates, see announcement.
<http://grants.nih.gov/grants/guide/pa-files/PAS-06-206.html>

Monoclonal Antibodies for Neuroscience Research: Request for Mammalian Nervous System Targets (NOT-NS-06-008)

National Institute of Neurological Disorders and Stroke
National Institute of Mental Health
NOT-NS-06-008)
National Institute of Neurological Disorders and Stroke
National Institute of Mental Health
<http://grants.nih.gov/grants/guide/notice-files/NOT-NS-06-008.html>

NINDS Clinical Trial Planning Grant (R34) (PAR-06-460)

National Institute of Neurological Disorders and Stroke
Application Receipt/Submission Date(s): August 18, 2006; December 18, 2006; April 18, 2007; August 20, 2007; December 18, 2007; April 18, 2008; August 18, 2008; December 18, 2008; April 20, 2009
<http://grants.nih.gov/grants/guide/pa-files/PAR-06-460.html>

NINDS Cooperative Program in Translational Research PAR-05-158 – Pre-Application Consultation with Program Staff (NOT-NS-06-010)

National Institute of Neurological Disorders and Stroke
<http://grants.nih.gov/grants/guide/notice-files/NOT-NS-06-010.html>

Using Metabolomics to Investigate Biological Pathways and Networks (R01) (RFA-RM-06-010)

National Institute of Diabetes and Digestive and Kidney Diseases
Application Receipt Date(s): October 20, 2006
<http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-06-010.html>

NIAMS Clinical Trial Outcomes Instrument Development Grant Program (U01) (RFA-AR-06-006)

National Institute of Arthritis and Musculoskeletal and Skin Diseases
Application Receipt Date(s): August 29, 2006
<http://grants.nih.gov/grants/guide/rfa-files/RFA-AR-06-006.html>

**NARSAD: The Mental Health Research Association Seeks Applicants for Young Investigator Award Program
Deadline: July 25, 2006**

NARSAD: the Mental Health Research Association is a private, not-for-profit public charity organized for the purpose of raising funds for scientific research into the causes, cures, treatments, and prevention of severe psychiatric brain and behavior disorders, such as schizophrenia and depression.

NARSAD's Young Investigator Award Program provides support for the most promising young scientists conducting neurobiological research. One- and two-year awards up to \$30,000 per year are provided to enable promising investigators to either extend research fellowship training or begin careers as independent research faculty. Basic and/or clinical investigators are supported, but research must be relevant to schizophrenia, major affective disorders, or other serious mental illnesses.

To be eligible, applicants must have a doctoral-level degree (e.g., M.D. [minimum PGY-IV], Ph.D., Psy.D., etc.) and already be employed in research training, or be in a faculty or independent research position. The award is intended to support post-doctoral fellows and assistant professors

(or equivalent). Predoctoral students and investigators who hold the rank of associate professor or equivalent are not eligible to apply.

Fifteen Young Investigators are selected each year to present at NARSAD's annual Scientific Symposium in New York City. Young Investigators are also eligible to be selected for NARSAD's Freedman Award for Outstanding Basic Research and its Klerman Award for Outstanding Clinical Research.

Program guidelines and application materials for the 2007 award are available at the NARSAD Web site. RFP Link:

<http://fconline.foundationcenter.org/pnd/10003060/narsad>

NEW TSC PUBLICATIONS

Arvais EW, Romanelli A, Hou X, David JS (2006) AKT-independent phosphorylation of TSC2 and activation of mTOR and ribosomal protein S6 kinase signaling by prostaglandin F2a. *J Biol Chem* 2006 Jul 1 [Epub ahead of print] <http://www.jbc.org/cgi/reprint/M605371200>

Berbel Tornero O, Ferris I Tortajada J, Donat Colomer J, Ortega Garcia JA, Verdeguer Miralles A (2006) [Risk factors associated with neonatal tumors. Experience of a pediatric environmental health specialty unit in Valencia (Spain).] *An Pediatr (Barc)* 64(5):439-48 [Article in Spanish]

Cai SL, Tee AR, Short JD, Bergeron JM, Kim J, Shen J, Guo R, Johnson CL, Kiguchi K, Walker CL (2006) Activity of TSC2 is inhibited by AKT-mediated phosphorylation and membrane partitioning. *J Cell Biol* 173(2):279-89

Connolly MB, Hendson G, Steinbok P (2006) Tuberous sclerosis complex: a review of the management of epilepsy with emphasis on surgical aspects. *Childs Nerv Syst* 2006 Jun 13 [Epub ahead of print]

Di Paolo S, Teutonico A, Leogrande D, Capobianco C, Schena PF (2006) Chronic Inhibition of Mammalian Target of Rapamycin Signaling Downregulates Insulin Receptor Substrates 1 and 2 and AKT Activation: A Crossroad between Cancer and Diabetes? *J Am Soc Nephrol* 2006 Jun 28 [Epub ahead of print]

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Ess KC (2006) The Neurobiology of Tuberous Sclerosis Complex. *Semin Pediatr Neurol* 13(1):37-42

Freilinger A, Rosner M, Hengstschlager M (2006) Tuberin negatively affects BCL-2's cell survival function. *Amino Acids* 30(4):391-6

Geier DA, Geier MR (2006) An evaluation of the effects of thimerosal on neurodevelopmental disorders reported following DTP and Hib vaccines in comparison to DTPH vaccine in the United States. *J Toxicol Environ Health A* 69(15):1481-95

Goncharova EA, Goncharov D, Lim PN, Noonan D, Krymskaya VP (2006) Modulation of cell migration and invasiveness by tumor suppressor TSC2 in lymphangiomyomatosis. *Am J Respir Cell Mol Biol* 34(4):473-80 Epub 2005 Dec 30

Guerrini R, Marini C (2006) Genetic malformations of cortical development. *Exp Brain Res* 2006 May 25 [Epub ahead of print]

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- Humphrey A, Neville BG, Clarke A, Bolton PF (2006) Autistic regression associated with seizure onset in an infant with tuberous sclerosis. *Dev Med Child Neurol* 48(7):609-11
- Hussain N, Curran A, Pilling D, Malluci CL, Ladusans EJ, Alfirevic Z, Pizer B (2006) Congenital subependymal giant cell astrocytoma diagnosed on fetal MRI. *Arch Dis Child* 91(6):520
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- Kairi-Vassilatou E, Grapsa D, Kontogianni-Katsarou K, Smyrniotis V, Hasiaskos D, Agatha AK (2006) Clinicopathological features of unusual vascular lesions of the pelvis, retroperitoneum and colon in females: a report of five cases and review of the literature. *Eur J Gynaecol Oncol* 27(3):250-5
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<http://www.jbc.org/cgi/reprint/M605273200v1>
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- Keri JE, Avashia N (2006) An adolescent girl with tuberous sclerosis complex and acne. *Pediatr Ann* 35(6):433-5
- Kingsley PB, Shah TC, Woldenberg R (2006) Identification of diffuse and focal brain lesions by clinical magnetic resonance spectroscopy. *NMR Biomed* 2006 Jun 8 19(4):435-462 [Epub ahead of print]
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Mitogen-Activated Protein Kinase and Akt Pathways in Glioblastoma. Clin Cancer Res 12(13):3935-3941

Represas CR, Duran MT, Tizon JC, Amigo LP, Garcia-Tejedor JL, Cervino MM (2006) [32 year old woman with progressive dyspnea.] Rev Clin Esp 206(4):193-4 [Article in Spanish]

Rosser T, Panigrahy A, McClintock W (2006) The Diverse Clinical Manifestations of Tuberous Sclerosis Complex: A Review. Semin Pediatr Neurol 13(1):27-36

Septer S, Thompson ES, Willemsen-Dunlap A (2006) Anesthesia concerns for children with tuberous sclerosis. AANA J 74(3):219-25

Shields WD (2006) Infantile Spasms: Little Seizures, BIG Consequences. Epilepsy Curr 6(3):63-9

Sood S, Chugani HT (2006) Functional neuroimaging in the preoperative evaluation of children with drug-resistant epilepsy. Childs Nerv Syst 2006 Jun 24 [Epub ahead of print]

Suryawan A, Escobar J, Frank JW, Nguyen HV, Davis TA (2006) Developmental Regulation of the Activation of Signaling Components Leading to Translation Initiation in Skeletal Muscle of Neonatal Pigs. Am J Physiol Endocrinol Metab 2006 Jun 6 [Epub ahead of print]

Swierczynska M, Mastalerz L, Papla B, Sladek K, Nizankowska-Mogilnicka E (2005) A case of emphysema suggesting cystic lung disease in computer tomography.] Przegl Lek 62(12):1558-60 [Article in Polish]

Williamson DL, Bolster DR, Kimball SR, Jefferson LS (2006) Time course changes in signaling pathways and protein synthesis in C2C12 myotubes following AMPK activation by AICAR. Am J Physiol Endocrinol Metab 291(1):E80-9

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CONFERENCES & SEMINARS

December 1-5, 2006

2006 AES Annual Meeting/North American Regional Epilepsy Congress

San Diego Convention Center

Abstract submissions accepted March 6 – June 5, 2006

For more information: <http://www.aesnet.org/Visitors/AnnualMeeting/index.cfm>

****TSC SIG will take place on Saturday, December 2, 2006**

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://www.ninds.nih.gov>

April 19-22, 2007

2007 LAM International Research Conference

The LAM Foundation

Cincinnati, OH

<http://www.thelamfoundation.org>

May 24-26, 2007

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More information coming soon!

NEWS

CURE Funds TSC Research Project

Citizens United for Research in Epilepsy (CURE) announced their research grant awards for 2006. Among the grants that were approved The Rhode Island Award to Nikolaus J. Sucher, M.D. at Children's Hospital & Harvard Medical School, Boston, MA entitled "A role for the mTOR pathway in NMDA receptor mediated epileptogenesis: a molecular investigation of protein interactions". The NMDA receptor is crucial for the normal function of the brain. The receptor is a protein complex that is composed of multiple subunits, some of which may be critical for the development of epilepsy in patients with Tuberous Sclerosis (TSC). This study will investigate the molecular details of the interaction and function of selected proteins, which may suggest novel targets for the treatment of TSC and epilepsy.

Researchers Find the Snooze Button With help from some drowsy fruit flies, a team of researchers from the Howard Hughes Medical Institute has identified a region of the fruit fly's brain that is crucial to controlling sleep. The findings support the idea that one of sleep's essential roles is to limit sensory input so the brain can organize and crystallize the day's memories for storage and future retrieval. This research by Amita Sehgal, Ph.D., HHMI investigator, University of Pennsylvania School of Medicine, was published in the June 08, 2006, issue of Nature. For the full story, go to: <http://www.hhmi.org/news/sehgal20060608.html>

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.