



TSC ALERT

Edited by Vicky H Whittemore, PhD

October 2005

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

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GRANT ANNOUNCEMENTS

UNDERSTANDING AND TREATING TUBEROUS SCLEROSIS COMPLEX

Participating Organizations

National Institutes of Health (NIH), (<http://www.nih.gov/>)

Tuberous Sclerosis Alliance (TS Alliance), (<http://www.tsalliance.org>)

Components of Participating Organizations

National Institute of Neurological Disorders and Stroke (NINDS), (<http://www.ninds.nih.gov>)

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), (<http://www.niddk.nih.gov/>)

National Institute of Mental Health (NIMH), (<http://www.nimh.nih.gov>)

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), (<http://www.niams.nih.gov>)

National Cancer Institute (NCI), (<http://www.nci.nih.gov>)

Letters of Intent Receipt Date(s): Not Applicable

Application Receipt Dates(s): Standard dates apply, please see <http://grants.nih.gov/grants/funding/submissionschedule.htm> for details

Peer Review Date(s): Standard dates apply, please see <http://grants.nih.gov/grants/funding/submissionschedule.htm> for details

Council Review Date(s): Standard dates apply, please see <http://grants.nih.gov/grants/funding/submissionschedule.htm> for details

Earliest Anticipated Start Date: April 2006

Additional Information To Be Available Date (Url Activation Date): Not Applicable

Expiration Date: March 2, 2008

BIOLOGY OF RNA INTERFERENCE: STABILITY, DELIVERY AND PROCESSING BY TISSUES (RFA-HL-05-019)

Letter of Intent Receipt Date: December 21, 2005

Application Receipt Date: January 18, 2006

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-05-019.html>

NOTICE OF INTENT TO PUBLISH A REQUEST FOR APPLICATIONS (RFA) TITLED: SOCIAL NEUROSCIENCE (NOT-DA-05-011)

National Institute on Drug Abuse

<http://grants.nih.gov/grants/guide/notice-files/NOT-DA-05-011.html>

NOTICE OF INSTITUTIONAL CLINICAL AND TRANSLATIONAL SCIENCE AWARD RFA AND PRE-SUBMISSION MEETING (NOT-RM-05-013)

NIH Roadmap Initiatives

National Center for Research Resources

<http://grants.nih.gov/grants/guide/notice-files/NOT-RM-05-013.html>

COMPLETION OF A COMPREHENSIVE MOUSE KNOCKOUT RESOURCE (RFA-HG-05-007)

National Human Genome Research Institute

National Cancer Institute

National Center for Research Resources

National Eye Institute

National Heart, Lung, and Blood Institute

National Institute on Aging

National Institute on Alcohol Abuse and Alcoholism

National Institute of Arthritis and Musculoskeletal and Skin Diseases

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 Mental Health

National Institute of Neurological Disorders and Stroke

Application Receipt Date(s): November 22, 2005

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-05-007.html>

A DATA COORDINATION CENTER FOR THE KNOCKOUT MOUSE PROJECT (KOMP) (RFA-HG-05-008)

National Human Genome Research Institute

Application Receipt Date(s): November 22, 2005

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-05-008.html>

COLLABORATIVE RESEARCH ON MENTAL AND NEUROLOGICAL DISORDERS (RFA-MH-06-003)

National Institute of Mental Health

National Institute of Neurological Disorders and Stroke

Application Receipt Date(s): November 18, 2005

<http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-06-003.html>

NINDS EXPLORATORY/DEVELOPMENTAL PROJECTS IN TRANSLATIONAL RESEARCH (PAR-05-157)

National Institute of Neurological Disorders and Stroke

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

<http://grants.nih.gov/grants/guide/pa-files/PAR-05-157.html>

NINDS COOPERATIVE PROGRAM IN TRANSLATIONAL RESEARCH (PAR-05-158)

National Institute of Neurological Disorders and Stroke

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

<http://grants.nih.gov/grants/guide/pa-files/PAR-05-158.html>

NINDS COOPERATIVE SMALL BUSINESS AWARDS IN TRANSLATIONAL RESEARCH (SBIR) (PAR-05-159)

National Institute of Neurological Disorders and Stroke

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

<http://grants.nih.gov/grants/guide/pa-files/PAR-05-159.html>

NINDS MENTORED RESEARCH AND CLINICAL SCIENTIST DEVELOPMENT AWARDS IN TRANSLATIONAL RESEARCH (PAR-05-160)

National Institute of Neurological Disorders and Stroke

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

<http://grants.nih.gov/grants/guide/pa-files/PAR-05-160.html>

NEUROSCIENCE BLUEPRINT INTERDISCIPLINARY CENTER CORE GRANTS (RFA-NS-06-003)

NIH Blueprint for Neuroscience Research

National Institute of Neurological Disorders and Stroke

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 Mental Health

National Institute of Nursing Research

Application Receipt Date(s): January 19, 2006

<http://grants.nih.gov/grants/guide/rfa-files/RFA-NS-06-003.html>

MENTAL RETARDATION AND DEVELOPMENTAL DISABILITIES RESEARCH CENTERS 2006 (RFA-HD-05-030)

National Institute of Child Health and Human Development

Application Receipt Date(s): December 21, 2005

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HD-05-030.html>

CENTERS OF EXCELLENCE IN GENOMIC SCIENCE (CEGS) (PAR-05-163)

National Human Genome Research Institute

National Institute of Mental Health

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

<http://grants.nih.gov/grants/guide/pa-files/PAR-05-163.html>

DEVELOPMENT AND IMPROVEMENT OF INBRED ES CELL LINES FOR USE IN GENERATION OF MOUSE MUTANTS (RFA-DA-06-009)

The long-range goal of KOMP is to generate a public resource composed of null mutations, each marked with a useful reporter, in every gene in the mouse genome in the C57BL/6 genetic background. The purpose of this RFA is to develop C57BL/6 ES cell lines that are efficient for high-throughput gene targeting and in successfully generating mice that can transmit the targeted mutation through the germline, both steps being necessary to create knockout mice on a C57BL/6 background. This RFA is a companion to two other RFAs ([HG-05-007](#) and [HG-05-008](#)), all three of which are part of the NIH Knockout Mouse Project (KOMP). For more information, please see: <http://grants.nih.gov/grants/guide/rfa-files/RFA-DA-06-009.html>

There is an informational meeting for potential applicants to this RFA. Details are below. If you would like to call in to the meeting, please contact Dr. Jane Peterson at petersoj@mail.nih.gov

Applicant Information Meeting:

October 6, 2005, 2-4 p.m.
NIH main Campus, Bldg 50
1st Floor Conference Center
National Institutes of Health (NIH)
9000 Rockville Pike
Bethesda, Maryland 20892

MENTORED RESEARCH SCIENTIST DEVELOPMENT AWARD (K01)(PA-06-001)

National Institutes of Health
National Center for Complementary and Alternative Medicine
National Cancer Institute
National Center for Research Resources
National Human Genome Research Institute
National Institute on Aging
National Institute on Alcohol Abuse and Alcoholism
National Institute of Allergy and Infectious Diseases
National Institute of Arthritis and Musculoskeletal and Skin Diseases
National Institute of Biomedical Imaging and Engineering
National Institute of Child Health and Human Development
National Institute on Drug Abuse
National Institute on Deafness and Other Communication Disorders
National Institute of Diabetes and Digestive and Kidney Diseases
National Institute of Environmental Health Sciences
National Institute of Mental Health
National Institute of Neurological Disorders and Stroke
National Institute of Nursing Research
Office of Dietary Supplements
Application Receipt Date(s): Multiple dates, see announcement.
<http://grants.nih.gov/grants/guide/pa-files/PA-06-001.html>

NEW TSC PUBLICATIONS

Alexopoulos A, Lachhwani DK, Gupta A, Kotagal P, Harrison AM, Bingaman W, Wyllie E (2005) Resective surgery to treat refractory status epilepticus in children with focal epileptogenesis. *Neurology* 64(3):567-70

Beer TW (2005) Cutaneous Angiomyolipomas are HMB45 Negative, Not Associated with Tuberous Sclerosis, and Should Be Considered as Angioleiomyomas with Fat. *Am J Dermatopathol* 27(5):418-21

Black JL, Ge Q, Boustany S, Johnson PR, Poniris MH, Glanville AR, Oliver BG, Moir LM, Burgess JK (2005) In vitro studies of lymphangioliomyomatosis. *Eur Respir J* 26(4):569-76

Fukunaga M (2005) Perivascular epithelioid cell tumor of the uterus: report of four cases. *Int J Gynecol Pathol* 24(4):341-6

Hay N (2005) The Akt-mTOR tango and its relevance to cancer. *Cancer Cell* 8(3):179-83

Iida K, Otsubo H, Mohamed IS, Okuda C, Ochi A, Weiss SK, Chuang SH, Snead OC 3rd (2005) Characterizing magnetoencephalographic spike sources in children with tuberous sclerosis complex. *Epilepsia* 46(9):1510-7

Jozwiak J (2005) Hamartin and tuberin: Working together for tumour suppression. *Int J Cancer* 2005 Oct 4 [Epub ahead of print]

Kalyanasundaram K, Parameswaran A, Mani R (2005) Perivascular epithelioid tumor of urinary bladder and vagina. *Ann Diagn Pathol* 9(5):275-8

- Karadag D, Mentzel HJ, Gullmar D, Rating T, Lobel U, Brandl U, Reichenbach JR, Kaiser WA (2005) Diffusion tensor imaging in children and adolescents with tuberous sclerosis. *Pediatr Radiol* 35(10):980-3 [Epub 2005 Jun 14]
- Kawai K, Shimizu H, Yagishita A, Maehara T, Tamagawa K (2004) Clinical outcomes after corpus callosotomy in patients with bihemispheric malformations of cortical development. *J Neurosurg* 101(1 Suppl):7-15
- Kolb TM, Duan L, Davis MA (2005) Tsc2 Expression Increases the Susceptibility of Renal Tumor Cells to Apoptosis. *Toxicol Sci* 2005 Sep 8 [Epub ahead of print]
- Kossoff EH, Thiele EA, Pfeifer HH, McGrogan JR, Freeman JM (2005) Tuberous sclerosis complex and the ketogenic diet. *Epilepsia* 46(10):1684-6
- Kpodonu J, Massad MG, Chaer RA, Caines A, Evans A, Snow NJ, Geha AS (2005) The US Experience with Lung Transplantation for Pulmonary Lymphangiomyomatosis. *J Heart Lung Transplant* 24(9):1247-53
- Kumasaka T, Seyama K, Mitani K, Souma S, Kashiwagi S, Hebisawa A, Sato T, Kubo H, Gomi K, Shibuya K, Fukuchi Y, Suda K (2005) Lymphangiogenesis-Mediated Shedding of LAM Cell Clusters as a Mechanism for Dissemination in Lymphangiomyomatosis. *Am J Surg Pathol* 29(10):1356-1366
- Lesma E, Grande V, Carelli S, Brancaccio D, Canevini MP, Alfano RM, Coggi G, Di Giulio AM, Gorio A (2005) Isolation and growth of smooth muscle-like cells derived from tuberous sclerosis complex-2 human renal angiomyolipoma: epidermal growth factor is the required growth factor. *Am J Pathol* 167(4):1093-103
- Lillo M, Marin M, Frutos L, Navarro T, Coronado M, Martin Curto L (2005)[Renal angiomyolipoma and fever: assessment with isotopic renogram and 67Ga scintigraphy.] *Rev Esp Med Nucl* 24(5):322-5 [Article in Spanish]
- Liu H, Coooke K, Frager D (2005) Bilateral massive renal angiomyolipomatosis in tuberous sclerosis. *AJR Am J Roentgenol* 185(4):1085-6
- Rocio M, Bos JL, Zwartkruis FJ (2005) Regulation of the small GTPase Rheb by amino acids. *Oncogene*. 2005 Sep 19 [Epub ahead of print]
- Rosner M, Freilinger A, Lubec G, Hengtschlager M (2005) The tuberous sclerosis genes, TSC1 and TSC2, trigger different gene expression responses. *Int J Oncol* 27(5):1411-24
- Ryu JH, Moss J, Beck GJ, Lee JC, Brown KK, Chapman JT, Finlay GA, Olson EJ, Ruoss SJ, Maurer JR, Raffin TA, Peavy HH, McCarthy K, Taveira-Dasilva A, McCormack FX, Avila NA, Decastro RM, Jacobs SS, Stylianou M, Fanburg BL (2005) The NHLBI Lymphangiomyomatosis Registry: Characteristics of 230 Patients at Enrollment. *Am J Respir Crit Care Med*. 2005 Oct 6 [Epub ahead of print]
- Shitara N (2005) [Tuberous sclerosis complex.] *Nippon Rinsho* 63 Suppl 9:170-6 [Article in Japanese]
- Stafstrom, CE (2005) Progress toward understanding epileptogenesis in tuberous sclerosis complex: two hits, no outs, and the eker rat is up to bat. *Epilepsy Curr* 5(4):136-8
<http://www.pubmedcentral.gov/articlerender.fcgi?tool=pubmed&pubmedid=16151521>
- Wei JJ, Chiriboga L, Arslan AA, Melamed J, Yee H, Mittal K (2005) Ethnic differences in expression of the dysregulated proteins in uterine leiomyomata. *Hum Reprod* 2005 Sep 19 [Epub ahead of print]
- Yu J, Baybis M, Lee A, McKhann G 2nd, Chugani D, Kupsky WJ, Aronica E, Crino PB (2005) Targeted gene expression analysis in hemimegalencephaly: activation of beta-catenin signaling. *Brain Pathol* 15(3):179-86

CONFERENCES

October 19-20, 2005

Eighth Meeting of the Secretary's Advisory Committee on Genetics, Health, and Society

Bethesda North Marriott Hotel, North Bethesda, MD

An agenda has been posted online at:

<http://www4.od.nih.gov/oba/SACGHS/meetings/October2005/SACGHSOct2005premeeting.htm>

Public Comments:

SACGHS welcomes public perspectives on any of the issues to be covered during the meeting as well as on issues important to members of the public. If you wish to provide comments at the meeting, please contact Amanda Sarata by email at sarataa@od.nih.gov or by phone at 301-496-9838 to sign up. Please indicate whether you will be speaking as an individual or on behalf of an organization, and if the latter, your affiliation with that organization. Written public comments also may be submitted to SACGHS via sarataa@od.nih.gov. In order to be considered by SACGHS at the October meeting, written comments should be submitted no later than October 17, 2005.

The meeting is open to the public, and pre-registration is not required. Seating will be available on a first-come-first-serve basis.

Webcast: The meeting will be webcast. Information on how to access the webcast will be available on the day of the meeting at:

<http://www4.od.nih.gov/oba/SACGHS/meetings/October2005/SACGHSOct2005premeeting.htm>

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>

October 18-23, 2005

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

Sheraton Centre Toronto

Toronto, Canada

<http://www.aacap.org>

October 25-29, 2005

American Society of Human Genetics

Salt Lake City, UT

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

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

October 28–November 1, 2005

Fifth Annual Cold Spring Harbor Laboratory/Wellcome Trust Conference on Genome Informatics

Cold Spring Harbor, NY

The focus for this conference is large-scale genome informatics. Biology is an experimental science that is experiencing an explosion of new data. This requires biologists to increase the scale and sophistication in the information technology used for their research. The conference scope encompasses the management and the analysis of these data, such as whole genome comparisons within and among species and strains, the analysis of results from high throughput experiments to uncover cellular pathways and molecular interactions, and the design of effective algorithms to identify regulatory sequence motifs. For more information and to register, please see:

<http://meetings.cshl.edu/meetings/info05.shtml>

November 9-12, 2005

8th Annual Conference on Computational Genomics

University Park Hotel @ MIT in Cambridge, MA

Co-sponsored with The Institute for Genomic Research, this conference brings together practitioners of the science of computational genomics and promotes interaction between the fields of computer science and molecular biology in support of genomics. Each annual conference brings new and established investigators together with students intending to enter the field, creating an invigorating environment for discovery and collaboration. Topics include comparative genomics, sequence alignment and assembly, gene expression analysis, proteomics, systems biology, and gene finding and genome annotation. For more information on this event and to register, please visit:

<http://www.jax.org/courses/events/coursedetails.do?id=137&detail=scope>

November 12-16, 2005

Society for Neuroscience

Washington, DC Convention Center

Washington, DC

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

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

December 2-6, 2005

American Epilepsy Society & American Clinical Neurophysiology Society

Washington, DC Convention Center

Washington, DC

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

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

January 5-7, 2006

Genetics Society of America meeting: GENETIC ANALYSIS: From Model Organisms to Human Biology

Abstract Deadline: November 14, 2005

Location: San Diego, CA

The genome sequences have firmly reestablished the fact that all organisms are built from the same set of genes, underscoring the importance of model organisms for understanding gene function. This rich information resource along with the fantastic experimental opportunities offered by model organisms promise new insights into biology. If we are fully to realize this potential, investigators working with different organisms, including humans, must communicate with each other and exchange ideas. The meeting is intended to provide a forum for sharing this information. The meeting will highlight both human and model organism genetics in a complementary way. For more information on the meeting see:

<http://www.gsa-modelorganisms.org/>

January 8 - 13, 2006

Keystone Symposium on Genome Sequence Variation and the Inherited Basis of Common Disease and Complex Traits

Abstract Deadline: October 4, 2005

Early Registration Deadline: November 7, 2005

Location: Big Sky Resort, Montana

Common human diseases and most other traits vary in a continuous manner, modified by multiple genes and environmental influences. Rapidly expanding information about genome sequence variation is making it possible for the first time to do well-powered searches for the inherited contributors to common diseases and other complex phenotypes. Success will provide insight into the genetic architecture of quantitative characters, the evolutionary history of trait variation, and the etiology of common human diseases. This meeting aims to bring together investigators from population genetics, genomics, quantitative genetics, epidemiology and medical research to examine these problems from a variety of perspectives. For more information and to register, please visit:

<http://www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=787&CFID=1196412&CFTOKEN=19360022>

May 3-5, 2006

TSC International Research Conference 2006

Spandau, Ev. Johannesstift
Hotel "Christophorus Haus"
Berlin, Germany
<http://www.tsc2006.org>

March 31–April 2, 2006

LAM Foundation 2006 Research Conference

Hilton Netherlands Cincinnati Hotel
Cincinnati, OH
<http://lam.uc.edu>

July 2-6, 2006

7th European Congress of Epileptology

Helsinki Fair Centre, Helsinki, Finland
<http://www.epilepsyhelsinki2006.org>

SAVE THE DATE! July 14-16, 2006

Embracing the Possibilities: 2006 National TSC Conference

Presented by the Tuberous Sclerosis Alliance
[Indian Lakes Resort](http://www.indianlakesresort.com)
Chicago, Illinois
<http://tsalliance.easycqi.com/pages.aspx?content=330>

October 30–November 2, 2006

World Congress on Autism

Cape Town, South Africa
Call for Papers closes 30th September 2005
Early Bird Registration Closes June 30th 2006
Please visit www.autismcongress.com

March 2007

NINDS Epilepsy Conference

Follow-up to 2000 Conference "Curing Epilepsy: Focus on the Future"
<http://www.ninds.nih.gov>

NEWS

ANTI-EPILEPTIC DRUG ALERTS Two alerts were posted for tiagabine and oxcarbazepine. The tiagabine (Gabitril) advisory can be found at <http://www.fda.gov/cder/drug/advisory/gabitril.htm>

The trileptal (oxcarbazepine) advisory can be found at http://www.fda.gov/medwatch/SAFETY/2005/trileptal_hcp.pdf

HUMAN BRAIN IS STILL EVOLVING Howard Hughes Medical Institute researcher, Bruce T. Lahn, Ph.D., The University of Chicago, has analyzed sequence variations in two genes that regulate brain size in human populations have found evidence that the human brain is still evolving. They speculate that if the human species continues to survive, the human brain may continue to evolve, driven by the pressures of natural selection. Their data suggest that major variants in these genes arose at roughly the same times as the origin of culture in human populations as well as the advent of agriculture and written language. This research was published in the September 09, 2005, issue of Science. For the full story, go to <http://www.hhmi.org/news/lahn4.html>

NERVE CELLS POSSESS A PREVIOUSLY UNKNOWN FORM OF PLASTICITY Researchers have discovered a new form of synaptic plasticity, the changes to nerve cells in the brain that underlie learning and memory. The phenomenon, the scientists say, may help govern how a single neuron integrates and processes multiple stimuli. This research by Lily Y. Jan, Ph.D and Yuh Nung Jan, Ph.D., University of California, San Francisco, and Robert B. Darnell, M.D., Ph.D., The Rockefeller University, was published in the October 07, 2005, issue of Cell. For the full story, go to <http://www.hhmi.org/news/jan2.html>

NEURAL STEM CELLS ARE LONG-LIVED New studies in mice have shown that immature stem cells that proliferate to form brain tissues can function for at least a year -- most of the life span of a mouse -- and give rise to multiple types of neural cells, not just neurons. The discovery may bode well for the use of these neural stem cells to regenerate brain tissue lost to injury or disease. This research by Alexandra L. Joyner, Ph.D. at New York University School of Medicine was published in the October 06, 2005, issue of Nature. For the full story, go to <http://www.hhmi.org/news/joyner.html>

COMPUTERS MAKE BIG STRIDES IN PREDICTING PROTEIN STRUCTURE Computers can predict the detailed structure of small proteins nearly as well as experimental methods, at least some of the time, according to new studies by HHMI researcher David Baker, Ph.D. at the University of Washington School of Medicine. The findings provide a glimmer of hope that scientists eventually may be able to determine the structure of proteins from their genomic sequences, a problem that has seemed insurmountable. This research was published in the September 16, 2005, issue of Science. For the full story, go to <http://www.hhmi.org/news/baker4.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.