



TSC ALERT

Edited by Vicky H Whittemore, PhD

July 2005

Welcome to the July 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 August 2005 *TSC Alert* contact: vwhittemore@tsalliance.org

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GRANT ANNOUNCEMENTS

TUBEROUS SCLEROSIS ALLIANCE REQUEST FOR APPLICATIONS

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

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

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

Deadlines for TS Alliance Research Grants Program:

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

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

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

NIH RELEASES TUBEROUS SCLEROSIS COMPLEX PROGRAM ANNOUNCEMENT

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

BRAIN TUMOR FUNDERS' COLLABORATIVE**Deadline for pre-proposal: August 8, 2005**

The James S. McDonnell is partnering with seven other non-profit philanthropic and advocacy organizations to form the Brain Tumor Funders' Collaborative (BTFC). Our goal is to bridge the "translational gap" that prevents laboratory science from yielding new medical treatments for brain cancer. We are pooling our resources in a new, joint funding initiative: we will provide up to three \$2 million multi-year grants to support collaborative, innovative and novel approaches to brain tumor research. The deadline for submission of a brief pre-proposal is August 8, 2005. Further information and application guidelines are available at <http://www.braintumorfunders.org>

CHARLES E. CULPEPER SCHOLARSHIPS IN MEDICAL SCIENCE**Deadline: August 17, 2005**

Goldman Philanthropic Partnerships is currently accepting applications for its 2006 Charles E. Culpeper Scholarships in Medical Science Program designed to support the career development of academic physicians.

Up to three awards of \$108,000 per year for three years will be made to U.S. medical schools or equivalent U.S. educational institutions on behalf of candidates who are U.S. citizens or aliens who have been granted permanent U.S. residence (proof required), who have received their MD degree from a U.S. medical school or the equivalent of an MD degree from an educational institution equivalent to a U.S. medical school in 1997 or later, and who are judged worthy of support by virtue of the quality of their research proposals and their potential for successful careers in academic medicine. All scientific research relevant to human health is eligible for consideration; research that has relevance to cures for human disease is highly encouraged. No institution may nominate more than one candidate.

In selecting awardees, emphasis will be on identifying young physician scientists with clear potential for making substantial contributions to science as academic physicians. Since January 1988, 59 physician scientists have been selected as Charles E. Culpeper Medical Scholars.

Deadline for applications is Wednesday, August 17, 2005. Awards will be announced in January 2006, for activation on or about July 1, 2006. Application forms and instructions may be obtained on the Web at www.goldmanpartnerships.org or by contacting Amanda Morton, Charles E. Culpeper Program Manager, Goldman Philanthropic Partnerships, 155 North Pfingsten Road, Suite 109, Deerfield, IL 60015, telephone: (847)948-5512, fax: (847)948-5516.

PARENTS AGAINST CHILDHOOD EPILEPSY, INC. (PACE)

Deadline: September 15, 2005

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

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

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

For more information: www.paceusa.org

E-mail: pacenyemail@aol.com

Phone: 212-665-PACE (7223)

FAX: 212-327-3075

ROBERT S. MORISON FELLOWSHIP FOR ACADEMIC CLINICIAN SCIENTISTS IN EPILEPSY

The American Epilepsy Society (AES) is proud to announce its partnership with The Grass Foundation to offer the Robert S. Morison Fellowship for the training of academic clinician scientists in epilepsy. This two year post-doctoral fellowship will be awarded to a promising young investigator possessing an MD degree who intends to continue training in basic science in an epilepsy research laboratory. The fellowship was created in honor of the contributions of Dr. Morison, one of the founding Trustees of The Grass Foundation. Albert and Ellen Grass started The Grass Foundation in the 1950's and have made many contributions to the scientific and social aspects of epilepsy. The Fellowship will be \$40,000 per year for two years for salary with an additional \$10,000 (maximum) per year to be used for institutional fringe benefits plus \$1,000 for the fellow to travel to the AES Annual Meeting to present his/her results. The award will be announced and presented during the AES Annual Meeting. The next available fellowship will be funded July 1, 2006 through June 30, 2008. The application deadline will be September 1, 2005 and notification will be made by December 10, 2005. Physicians interested in being considered for a Robert S. Morison Fellowship should apply for either a Postdoctoral Fellowship or a Research and Training Fellowship for Clinicians administered by the Epilepsy Foundation. For application information go to <http://www.epilepsyfoundation.org/research/grants.cfm>

**Please note in the application the desire to be considered for a Morison Fellowship.

The Morison Fellowship will be selected by the AES/Epilepsy Foundation Clinical Grant Selection Committee from among qualified applicants for the Postdoctoral Fellowships and Research and

Training Fellowships. Applicants for this fellowship can at the same time be considered for a fellowship in the category under which he/she applied.

AMERICAN SKIN ASSOCIATION

Deadline: October 3, 2005

The following grants are available from the American Skin Association:

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

For more information, contact the American Skin Association at:

346 Park Ave South, 4th Fl.

New York, NY 10010

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

FAX: (212)889-4959

E-mail: info@americanskin.org

Web site: www.americanskin.org

PROBES FOR MICROIMAGING THE NERVOUS SYSTEM (SBIR/STTR AWARD) (PA-05-120)

National Institute of Mental Health

National Institute on Aging

National Institute of Biomedical Imaging and Engineering National Institute on Deafness and Other Communication Disorders

National Institute of Neurological Disorders and Stroke

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

<http://grants.nih.gov/grants/guide/pa-files/PA-05-120.html>

PHARMACOLOGIC AGENTS AND DRUGS FOR MENTAL DISORDERS (SBIR/STTR AWARD) (PA-05-121)

National Institute of Mental Health

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

<http://grants.nih.gov/grants/guide/pa-files/PA-05-121.html>

DEVELOPMENT OF PET AND SPECT LIGANDS FOR BRAIN IMAGING (SBIR/STTR AWARD) (PA-05-122)

National Institute of Mental Health

National Institute on Aging

National Institute on Drug Abuse

National Institute on Deafness and Other Communication Disorders National Institute of Neurological Disorders and Stroke

Application Receipt Date(s):

Multiple dates, see announcement.

<http://grants.nih.gov/grants/guide/pa-files/PA-05-122.html>

SMALL GRANT PROGRAM FOR CONFERENCE SUPPORT (PAR-05-123)

Agency for Healthcare Research and Quality
Office of Extramural Research, Education, and Priority Populations
Application Receipt Date(s): Multiple dates, see announcement.
<http://grants.nih.gov/grants/guide/pa-files/PAR-05-123.html>

HIGH-END INSTRUMENTATION GRANT PROGRAM (PAR-05-124)

National Center for Research Resources
Application Receipt Date(s): September 20, 2005
<http://grants.nih.gov/grants/guide/pa-files/PAR-05-124.html>

COMPLEMENTARY AND ALTERNATIVE MEDICINE CAREER TRANSITION AWARD (K22) (PAR-05-129)

National Center for Complementary and Alternative Medicine
Office of Dietary Supplements
Application Receipt Date(s): Multiple dates, see announcement.
<http://grants.nih.gov/grants/guide/pa-files/PAR-05-129.html>

NINR MENTORED RESEARCH SCIENTIST DEVELOPMENT AWARD FOR UNDERREPRESENTED OR DISADVANTAGED INVESTIGATORS (K01)(PAR-05-135)

National Institute of Nursing Research
Application Receipt Date(s): Multiple dates, see announcement.
<http://grants.nih.gov/grants/guide/pa-files/PAR-05-135.html>

VENTER CENTER, UW, HOPKINS TO SUPPORT NEW NHLBI SEQUENCING, GENOTYPING SERVICE

Deadline for Applications: November 1, 2005

By a GenomeWeb News reporter

NEW YORK, June 27 (GenomeWeb News) - The National Heart, Lung, and Blood Institute is sponsoring a free DNA resequencing and genotyping service for certain investigators, the institute said today.

The University of Washington and the J. Craig Venter Institute will perform the DNA resequencing while Johns Hopkins University will provide the genotyping services. The Constella Group will be providing "logistical efforts."

The NHLBI bills the service, called the RS&G Service, as a successor to programs such as its Mammalian Genotyping Service, which is "now in its final round." "With the new RS&G Service, investigators can now move from their genomic regions of interest to the specific genes involved in a disease," NHLBI said in a statement.

To be eligible for the new service, researchers must be conducting "ongoing studies associated with genetic components involved in the cause, variable outcome, and progression of diseases associated with the heart, lungs, blood vessels and blood; as well as sleep disorders," the institute said in the statement.

Additional information about the new service can be found [here](#). The submission deadline for 2005 is Nov. 1.

NICHD INSTITUTIONAL PREDOCTORAL TRAINING PROGRAM IN REPRODUCTIVE, PERINATAL, AND PEDIATRIC EPIDEMIOLOGY (PAR-05-130)

National Institute of Child Health and Human Development

Application Receipt Date(s): May 10, 2006, May 10, 2007, May 10, 2008

<http://grants.nih.gov/grants/guide/pa-files/PAR-05-130.html>

NEW TSC PUBLICATIONS

NEW TSC COGNITIVE/BEHAVIOR GUIDELINES PUBLISHED A recent collaboration between two organizations dedicated to serving individuals affected by tuberous sclerosis complex (TSC) produced new guidelines addressing cognitive and behavioral issues relating to the disorder. The resulting article entitled, "Consensus clinical guidelines for the assessment of cognitive and behavioural problems in Tuberous Sclerosis," appears in *European Children and Adolescent Psychiatry* (14:183-190). The guidelines were first developed at a TSC Brain/Behavior Workshop in Cambridge, UK, sponsored by the United States-based Tuberous Sclerosis Alliance (TS Alliance) and the United Kingdom-based Tuberous Sclerosis Association.

The new guidelines outline the neuropsychiatric problems associated with TSC, the purpose of recommended assessments, developmentally appropriate stages for assessment, and specific areas that should be targeted for assessment. The article summarizes the guidelines in three tables, which can be found on the TS Alliance website at www.tsalliance.org

"We are thrilled that these clinical guidelines have been published as they will greatly assist individuals with TSC to obtain the assessments and services they need in the educational and mental health arenas" says Nancy Taylor, TS Alliance CEO.

Tuberous sclerosis complex (TSC), a genetic disorder characterized by abnormal growths in a wide range of organs, is estimated to affect nearly 50,000 people in the U.S. and more than 1 million worldwide. In the brain, abnormalities of differentiation, proliferation and migration can produce a range of neuropsychiatric features such as mental disabilities, autism and ADHD. Cognitive and behavioral features in TSC are often of greatest concern to families, yet limited clinical assessment and interventions are currently offered.

"Beginning in the 1970s, when parents of children with TSC first came together, the problems they most talked about were those of behavior and how these affected the lives of all family members," explains Ann Hunt, Head of Research for the UK Tuberous Sclerosis Association and senior author of the guidelines. "This was an area that had been sorely neglected by most pediatricians and psychiatrists, although many professionals were aware how severe these problems could be. It is great to finally offer consensus clinical guidelines for assessments that should enable individuals with TSC to access the appropriate services they need."

Petrus de Vries, MD, PhD, University of Cambridge, Cambridge, UK and primary author of the guidelines, states, "I truly hope that setting out guidelines for the assessment of cognitive and behavioral difficulties in TSC will not only raise awareness about the need to evaluate the complex neurodevelopmental profiles of individuals with TSC, but that it will also empower families and clinicians to identify and implement appropriate intervention and management strategies."

The complete reference is: de Vries P, Humphrey A, McCartney D, Prather P, Bolton P, Hunt A (2005) Consensus clinical guidelines for the assessment of cognitive and behavioural problems in Tuberous Sclerosis. *Eur Child Adolesc Psychiatry* 14(4):183-90

TSC Publications:

Chen CP, Liu YP, Huang JK, Chang TY, Chen MR, Chiu NC, Wang W (2005) Contribution of ultrafast magnetic resonance imaging in prenatal diagnosis of sonographically undetected cerebral tuberous sclerosis associated with cardiac rhabdomyomas. *Prenat Diagn* 2005 Jun 20 25(6):523-524 [Epub ahead of print]

Damsa C, Borrás L, Bianchi-Demicheli F, Andreoli A (2005) [Alpha-thalassems and bipolar disorders: a genetic link?] *Encephale* 31(1 Pt 1):72-5 [Article in French]

de Saint Aubain Somerhausen N, Gomez Galdon M, Bouffieux B, Courtin C, Theunis A, Vogeleer MN, Myant N (2005) Clear cell 'sugar' tumor (PEComa) of the skin: a case report. *J Cutan Pathol* 32(6):441-4

de Vries P, Humphrey A, McCartney D, Prather P, Bolton P, Hunt A (2005) Consensus clinical guidelines for the assessment of cognitive and behavioural problems in Tuberous Sclerosis. *Eur Child Adolesc Psychiatry* 14(4):183-90

El-Hashemite N, Kwiatkowski DJ (2005) IFN γ -Jak-Stat Signaling in Pulmonary LAM and Renal AML: A Potential Therapeutic Target. *Am J Respir Cell Mol Biol* 2005 Jun 30 [Epub ahead of print]

Gau CL, Kato-Stankiewicz J, Jiang C, Miyamoto S, Guo L, Tamanoi F (2005) Farnesyltransferase inhibitors reverse altered growth and distribution of actin filaments in Tsc-deficient cells via inhibition of both rapamycin-sensitive and -insensitive pathways. *Mol Cancer Ther* 4(6):918-26

Gemmill RM, Zhou M, Costa L, Korch C, Bukowski RM, Drabkin HA (2005) Synergistic growth inhibition by Iressa and Rapamycin is modulated by VHL mutations in renal cell carcinoma. *Br J Cancer* 92(12):2266-77

Goh S, Thiele EA (2005) Anorexia nervosa in a child with tuberous sclerosis complex. *J Child Neurol* 20(5):457-60

Hu X, Pandolfi PP, Li Y, Koutcher JA, Rosenblum M, Holland EC (2005) mTOR promotes survival and astrocytic characteristics induced by Pten/AKT signaling in glioblastoma. *Neoplasia* 7(4):356-68

Jiang WG, Sampson J, Martin TA, Lee-Jones L, Watkins G, Douglas-Jones A, Mokbel K, Mansel RE (2005) Tuberlin and hamartin are aberrantly expressed and linked to clinical outcome in human breast cancer: The role of promoter methylation of TSC genes. *Eur J Cancer*. 2005 Jun 10; [Epub ahead of print]

Kagawa K, Chugani DC, Asano E, Juhasz C, Muzik O, Shah A, Shah J, Sood S, Kupsky WJ, Mangner TJ, Chakraborty PK, Chugani HT (2005) Epilepsy surgery outcome in children with tuberous sclerosis complex evaluated with alpha-[11C]methyl-L-tryptophan positron emission tomography (PET). *J Child Neurol* 20(5):429-38

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*. 2005 Jun 14; [Epub ahead of print]

Kida Y, Yamaguchi K, Suzuki H, Kanda E, Ando M, Ohashi K, Funata N, Saito H (2005) Tuberous sclerosis, associated with renal cell carcinoma and angiomyolipoma, in a patient who developed endstage renal failure after nephrectomy. *Clin Exp Nephrol* 9(2):179-82

Kunzi T, Walther F, Marti HP, Frey FJ, Vogt B (2005) Intrarenal arterial aneurysms with haematuria in a patient with tuberous sclerosis complex. *Nephrol Dial Transplant* 2005 Jun 14 [Epub ahead of print]

Mak BC, Kenerson HL, Aiche LD, Barnes EA, Yeung RS (2005) Aberrant β -Catenin Signaling in Tuberous Sclerosis. *Amer J Pathol* 167:107-116

Nellist M, Burgers PC, van den Ouweland AM, Halley DJ, Luijckx TM (2005) Phosphorylation and binding partner analysis of the TSC1-TSC2 complex. *Biochem Biophys Res Commun* 2005 Jun 14 [Epub ahead of print]

Pollock-Barziv SM, Cohen MM, Maclean H, Downey GP (2005) Patients' perceptions versus medical testing of function in women with lymphangiomyomatosis (LAM). *Respir Med* 2005 Jul;99(7):901-9 Epub 2005 Jan 25

Shields JA, Eagle RC Jr, Shields CL, Marr BP (2005) Aggressive retinal astrocytomas in 4 patients with tuberous sclerosis complex. *Arch Ophthalmol* 123(6):856-63

Sofer A, Lei K, Johannessen CM, Ellisen LW (2005) Regulation of mTOR and Cell Growth in Response to Energy Stress by REDD1. *Mol Cell Biol* 25(14):5834-45

Wu EH, Wong YH (2005) Activation of muscarinic M(4) receptor augments NGF-induced pro-survival Akt signaling in PC12 cells. *Cell Signal* 2005 Jun 22 [Epub ahead of print]

Yapici Z, Dincer A, Eraksoy M (2005) Proton spectroscopic findings in children with epilepsy owing to tuberous sclerosis complex. *J Child Neurol* 20(6):517-22

Zaroff CM, Isaacs K (2005) Neurocutaneous syndromes: Behavioral features. *Epilepsy Behav* 2005 Jun 28 [Epub ahead of print]

CONFERENCES

TSC SPECIAL INTEREST GROUP (SIG) TO BE HELD AT AMERICAN EPILEPSY SOCIETY MEETING

Thanks to the efforts of Drs. Frances Jensen and Greg Holmes, there will be a TSC SIG at the upcoming American Epilepsy Society meeting that will be held in Washington, DC on December 2-6, 2005. The TSC SIG will be held on Saturday, December 3, 2005 from 2:00 – 4:30 pm. Speakers will be: Drs. Greg Holmes, Elizabeth Thiele, Frances Jensen and Peter Crino. See you there!

AN INVITATION FROM OUR GERMAN TSC COLLEAGUES:

We would like to invite you to [the Tuberous Sclerosis Complex \(TSC\) International Research Conference 2006](#) that will take place from **May 3rd to May 5th, 2006**, in Berlin, Germany. The conference will be organized by the German Tuberous Sclerosis Association (TSD)

e.V.) together with the Epilepsy Centre of the federal states of Berlin and Brandenburg and the Epilepsy Centre Bethel, both operated by the »von Bodelschwing'sche Anstalten« Bielefeld-Bethel.

Both basic research and applied clinical research will be discussed. Subjects include the molecular functions of TSC, animal models, translational research and clinical problems in different organ systems. There will be enough remaining time for informal discussion. We will also organize a poster exhibition.

We are sure to offer a scientific meeting in an exciting and emerging field and we will be pleased by your participation. The German capital Berlin will invite you to an attractive stay, to which we will contribute with an appealing side program.

For additional information, visit the conference Web site at: <http://www.tsc2006.org>

August 28 – September 1, 2005

26th International Epilepsy Congress

Le Palais des Congres de Paris

Paris, France

<http://www.epilepsycongress.org>

September 11-14, 2005

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

Jiuhua Spa and Resort, Beijing, China

www.chinamed.com.cn/birthdefects

September 26-27, 2005

Access to Quality Testing for Rare Diseases: A National Conference

Doubletree Executive Meeting Center and Hotel

Rockville, MD

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

October 7-12, 2005

4th World Congress of Cellular and Molecular Biology

Poitiers, France

<http://www.cmbworldcongress2005.com>

October 14-18, 2005

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

The Westin Copley Place, Boston, MA

<http://www.ispg.net>

October 18-23, 2005

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

Sheraton Centre Toronto

Toronto, Canada

<http://www.aacap.org>

October 25-29, 2005

American Society of Human Genetics

Salt Lake City, UT

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

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

November 12-16, 2005

Society for Neuroscience

Washington, DC Convention Center

Washington, DC

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

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

December 2-6, 2005

American Epilepsy Society & American Clinical Neurophysiology Society

Washington, DC Convention Center

Washington, DC

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

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

May 3-5, 2006

TSC International Research Conference 2006

Spandau, Ev. Johannesstift

Hotel "Christophorus Haus"

Berlin, Germany

<http://www.tsc2006.org>

March 31 – April 2, 2006

LAM Foundation 2006 Research Conference

Hilton Netherlands Cincinnati Hotel

Cincinnati, OH

<http://lam.uc.edu>

July 2-6, 2006

7th European Congress of Epileptology

Helsinki Fair Centre, Helsinki, Finland

<http://www.epilepsyhelsinki2006.org>

SAVE THE DATE!

July 14-16, 2006

National TSC Conference

Organized by the Tuberous Sclerosis Alliance

[Indian Lakes Resort](#)

Chicago, Illinois

<http://www.tsalliance.org>

March 2007

NINDS Epilepsy Conference

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

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

NEWS

TUBEROUS SCLEROSIS ALLIANCE ANNOUNCES NEW GRANT AWARDS

The TS Alliance announces the following grant awards for FY'06 (listed alphabetically by PI):

Development of New Molecular Testing for the TSC1 and TSC2 Genes

Kit-Sing Au, PhD; University of Texas Medical School at Houston; Houston, TX

Total Award: \$220,150

Supplemental Funding for TSC Multicenter Rapamycin Clinical Trial

Sandra Dabora, MD, PhD; Brigham & Women's Hospital, Boston, MA

Total Award: \$151,619

Role of NMDA Receptors in Tuberous Sclerosis Complex

Frances Jensen, MD; Children's Hospital and Harvard Medical School; Boston, MA

Total Award: \$100,000

Identification of Rheb-GEFs and Rheb Effectors by RNAi Screens in Drosophila

Lutz Kockel, PhD; Sponsor: Norbert Perrimon; Harvard Medical School; Boston, MA

Total Award: \$150,000

Response of Tuberous Sclerosis Skin Tumors to Rapamycin

Shaowei Li, MD, PhD; Uniformed Services University of the Health Sciences; Bethesda, MD

Total Award: \$150,000

TSC Translational Research Training Award

Lynsey Meikle; Sponsor: David Kwiatkowski, MD, PhD; Brigham & Women's Hospital/Harvard; Boston, MA

Total Award: \$150,000

TSC1 and TSC2 Variation Database

Sue Povey, MD, Bchir, MD; University College London, London UK

Total Award: \$93,500

Neuronal Connectivity in TSC2-Deficient Mice

Mustafa Sahin, MD, PhD; Children's Hospital; Boston, MA

Total Award: \$150,000

TSC1 Knockout Mouse – Research Resource Development

Stephen Rockwood; The Jackson Laboratory; Bar Harbor, ME

Total Award: \$5,000

TS ALLIANCE TO SUPPORT DEVELOPMENT OF A NEW TSC VARIATION DATABASE

Responding to the needs of the TSC research and clinical communities, the TS Alliance will support the development and maintenance of a new TSC1 and TSC2 Variation Database. Professor Sue Povey at the University College London in London, UK will oversee this project. Prof. Povey has a long-standing interest in TSC, playing a key role in the research that identified the TSC1 and TSC2 genes. The aim of this project is to establish a comprehensive, accessible, accurate and up-to-date record of all documented genetic variation in the two genes TSC1 and TSC2, and to identify whether the changes recorded are thought to be pathological. This will have immediate value to diagnostic services for individuals with TSC and their families worldwide. It is the long-term goal to link as many of the records to a detailed clinical database to elucidate possible genotype-phenotype correlations, and to identify the clinical consequences of specific variations in the TSC genes. More information will be forthcoming on the TS Alliance Web site as it becomes available.

CURE FUNDS RESEARCH ON TSC Citizens United for Research in Epilepsy (CURE) announced that they funded the following research grant:

Pathogenesis of Cortical Lesions in a Model of Tuberous Sclerosis

Arnold R. Kriegstein, MD, PhD – University of California, San Francisco

This research will focus on observation of the proliferation and migration of the genetically abnormal progenitor cells in the cerebral cortex in order to gain insight into how these gene defects influence cortical development. Hopefully, these studies will effect the development of new therapies to treat epilepsy in individuals with TSC, and potentially other causes of epilepsy.

FDA APPROVES KEPPRA® FOR USE IN CHILDHOOD EPILEPSY UCB Pharma, Inc. announced that the FDA has approved Keppra® (levetiracetam) as add-on therapy in the treatment of partial-onset seizures in children four years of age and older with epilepsy. The FDA approved this new pediatric indication for Keppra® under a six month priority review. The approval of Keppra® (levetiracetam) for children was based on findings from one multi-center, randomized, double-blind, placebo-controlled pivotal study conducted at 60 sites in North America, in 198 children 4 to 16 years of age with partial onset seizures with or without secondary generalization uncontrolled by standard AEDs. Study participants were taking one or two other AEDs at entry. The study consisted of an 8-week baseline period and a 4-week titration period, followed by a 10-week evaluation period.

When measuring efficacy, those taking Keppra® had a significantly larger reduction (26.8%) in weekly seizure frequency over placebo, on average. Additionally, responder rates (the portion of patients achieving a 50% or greater reduction in seizures) for patients taking Keppra were 44.6% versus 19.6% for placebo (both with a p=0.0002 compared to placebo).

In pediatric patients, 4 to 16 years of age, the most common adverse events associated with Keppra® in combination with other AEDs were somnolence, accidental injury, hostility, nervousness and asthenia. Keppra® is associated with somnolence, fatigue, and behavioral abnormalities as well as hematological abnormalities. For more information, visit the AES Press room at <http://www.aesnet.org/Visitors/About/Pressroom/Keppra.cfm>

PREGABALIN APPROVED BY FDA The American Epilepsy Society (AES) Practice Committee reports that Pfizer Inc. has received U.S. Food and Drug Administration (FDA) approval to market pregabalin (Lyrica") for adjunctive treatment of partial onset seizures in adults with epilepsy. The most common side effects across all pregabalin (Lyrica") clinical trials were dizziness, somnolence, dry mouth, peripheral edema, blurred vision, weight gain and difficulty with concentration/attention. Lyrica will be designated a controlled substance, recommended for classification in the category with lowest potential for abuse or misuse relative to controlled substances in other categories. Lyrica will be available in pharmacies in the fall. The FDA approved Lyrica in December 2004 for the management of diabetic peripheral neuropathy and postherpetic neuralgia. More information is located on our website in the online Press Room at <http://www.aesnet.org/Visitors/About/Pressroom/Pfizer.cfm>

MESSAGE FROM THE SECRETARY'S ADVISORY COMMITTEE ON GENETICS, HEALTH AND SOCIETY Public concern about the potential misuse of genetic information in health insurance and employment is the Secretary's Advisory Committee on Genetics, Health and Society's (SACGHS) highest priority. As you may know, the Committee undertook several initiatives to address this important issue. Specifically, the Committee:

- 1) Held a hearing in October 2004 to hear from members of the public, healthcare providers and stakeholders about their experiences with genetic discrimination;
- 2) Developed a DVD highlighting the testimony received at the October hearing;
- 3) Requested, gathered, and compiled written public comments on genetic discrimination, specifically from individuals who either have experienced discrimination or have concerns and fears about it;
- 4) Commissioned an analysis of the adequacy of current law in protecting against genetic discrimination in health insurance and employment;
- 5) Conducted outreach to key stakeholders, including patient and consumer advocates and the business and health insurance communities; and
- 6) Conveyed this information to the Secretary of Health and Human Services and urged further Secretarial efforts to bring about the enactment of Federal genetic nondiscrimination legislation.

The Committee's letter to the Secretary as well as the DVD, compilation of public comments, and the legal analysis can be accessed on the SACGHS website at: <http://www4.od.nih.gov/oba/sacghs/reports/reports.html>.

SACGHS was established to serve as a forum for deliberation on the ethical, legal and social issues at the intersection of genetics, health and society and to advise the Secretary of Health and Human Services about these issues. Further information about the Committee and its meetings, reports and recommendations is available at <http://www4.od.nih.gov/oba/SACGHS.HTM>.

If you have any questions, please contact Amanda Sarata at sarataa@od.nih.gov or 301-496-9838

MOST COMMON LUNG CANCERS MAY BEGIN IN NEWLY DISCOVERED CELLS The most common form of lung cancer may begin in a group of newly isolated lung stem cells, according to new studies by HHMI researcher, Tyler Jacks, Ph.D., Massachusetts Institute of Technology. The identification of the new stem cells could lead to earlier diagnosis of lung cancer in people. The discovery is a handsome payoff for a laborious effort to build a better mouse model of lung

cancer. This research was published in the June 17, 2005, issue of Cell. For the full story, go to <http://www.hhmi.org/news/jacks4.html>

DEVELOPMENTAL STUDIES HYBRIDOMA BANK The Developmental Studies Hybridoma Bank (DSHB), a national resource, was established under the auspices of the National Institute of Child Health and Human Development to supply investigators with monoclonal antibodies at cost (e.g., 1 ml of supernatant costs \$25.00). Ten monoclonal antibodies purchased from the DSHB cost the same as one average antibody purchased commercially. Monoclonal antibodies can be ordered in the form of tissue culture supernatant, concentrate, or ascites fluid. Select hybridoma cells lines are also available. Our stock includes antibodies directed against human antigens as well as those of several major model organisms including *C. elegans*, *Drosophila*, *Xenopus*, chicken, zebrafish, rat and mouse. Some of the more popular antibodies are directed against homeobox domain proteins (e.g., sonic hedgehog, PAX 6, armadillo and Islet-1), cell lineage markers (e.g., QH1), neural-specific proteins (e.g., nestin, NCAM and neurofilaments), cytoskeletal proteins (e.g., tubulin, myosins, actin and actin-binding proteins), extracellular matrix proteins (e.g., 15 different antibodies to 9 types of collagen), cell surface proteins (e.g., CD antigens, cadherins and integrins) and many more. In addition, the DSHB provides antibodies used in ChIP-chip technology (c-myc), cell growth studies (BrdU) and stem cell identification protocols (SSEA-1, SSEA-3, SSEA-4 and FORSE-1). Last year the DSHB filled over 7,100 orders for researchers world-wide. The DSHB continually welcomes new monoclonal antibody contributions. Investigators find this the most cost-effective means of making their antibodies available to the research community. The Bank is directed by Dr. David R. Soll.

To view our on-line catalog, visit our website at <http://www.uiowa.edu/~dshbwww>

If you would like to receive the 2005 DSHB catalog, or if you wish to contribute monoclonals to the DSHB for distribution, please contact:

The Developmental Studies Hybridoma Bank

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NIH AWARDS FOUR MICROARRAY CENTERS \$25M FOR NEUROSCIENCE RESEARCH

By a GenomeWeb staff reporter NEW YORK, June 20 (GenomeWeb News) - The National Institutes of Health has awarded a consortium of four microarray core facilities a total of \$25 million over five years to support gene expression analysis as part of the [NIH Neuroscience Blueprint](#).

The centers in the NIH Neuroscience Microarray Consortium are located at the University of California at Los Angeles, the Translational Genomics Research Institute, Yale University, and Duke University. Each center provides access to different array platforms.

The Microarray Consortium supports around 10,000 investigators, according to a statement issued by TGen. It was initially funded in 2002 with \$9 million from the National Institute of

Neurological Disorders and Stroke and the National Institute of Mental Health. The new award is supported by these two institutes as well as thirteen other NIH Neuroscience Blueprint institutes.

The consortium worked with 5 AM Solutions, a software company based in Phoenix, Ariz., to create a central database for the data it is generating. Further information about the consortium is available [here](#)

COLLABORATIVE RESEARCH NETWORK TO IDENTIFY SMALL MOLECULES The National Institutes of Health recently announced it is awarding \$88.9 million in grants to nine institutions over three years to establish a collaborative research network that will use high-tech screening methods to identify small molecules that can be used as research tools. Small molecules have great potential to help scientists in their efforts to learn more about key biological processes involved in human health and disease. A principal investigator at one of the nine sites is a National Advisory Neurological Disorders and Stroke Council member, Dr. Ray Dingledine. For more, see <http://www.nih.gov/news/pr/jun2005/nimh-15.htm>

BIOINFORMATICS REVEALS NEW GENE REGULATION SYSTEM Using bioinformatics and comparative genomics, an HHMI international research scholar has identified a new system for regulating genes that are essential to bacterial replication. The Russian scientist scanned gene sequences and proteomes of several taxonomic groups of bacteria, identifying not only a highly conserved signal sequence, but also its regulatory transcription factor, the repressor nature of the signal, and other genes regulated by the same system. The research by Mikhail Gelfand, PhD, DSc from the Institute for Information Transmission Problems in Moscow, Russia was published in the July issue of Trends in Genetics, published early online. For the full story, go to <http://www.hhmi.org//news/gelfand.html>

HHS TO LAUNCH CHANGED MEDICARE APPEALS PROCESS: New Procedures Will Increase Access and Avoid Case Backlogs New procedures mandated by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 will soon offer quicker resolution to appeals by Medicare beneficiaries, providers and suppliers.

The Medicare hearings function, currently handled by the Social Security Administration (SSA), will transition on July 1, 2005 to the Office of Medicare Hearings and Appeals (OMHA) located within the Department of Health and Human Services (HHS). The changes will help ensure that fee-for-service Medicare claims appeals are resolved within the 90-day timeframe mandated by the Medicare, Medicaid, and SCHIP Benefits Improvement and Protection Act of 2000 (BIPA).

"As HHS assumes responsibility for handling Medicare hearings, we are committed to making the appeals process better, faster and more convenient for seniors and other people with Medicare," HHS Secretary Mike Leavitt said. "Our goal is to eliminate the need for an aged or disabled beneficiary to travel if other resources are available closer to home."

HHS anticipates it can reduce hearing timeframes to comply with the BIPA requirements by using video conferencing technology (VTC) with a state-of-the-art electronic hearings process to provide significantly more access points than currently exist. HHS has access to VTC sites in over 1,000 cities nationwide. Both VTC and in-person hearings will be offered as appropriate to best meet the needs of all parties. To the extent that an in-person hearing is required, that hearing will be granted in the location most convenient to the parties. HHS Administrative Law Judges will travel to various locations around the country to conduct in-person hearings, as needed, which may include the use of local government facilities or other available sites.

More information on the new Medicare appeals function is available from OMHA Web site at www.hhs.gov/omha

HEALTH INSURANCE COVERAGE FOR CHILDREN UP IN 2004; NUMBER OF UNINSURED ADULTS STABLE Health insurance coverage for children showed continued improvement in 2004, and the percentage of working-age adults without insurance coverage, which had been climbing in recent years, did not increase last year, according to a new report from the Centers for Disease Control and Prevention (CDC).

The data, based on CDC's National Health Interview Survey, provides estimates of insurance coverage for the United States in 2004. For the first time, the latest survey also includes statistics on insurance coverage for the nation's 10 largest states.

The report, which tracks insurance coverage since 1997, finds that the improvement in coverage for children reflects an increase in public coverage—including the State Children's Health Insurance Program—for poor and near-poor children.

For more information, visit <http://www.cdc.gov/od/oc/media/pressrel/r050629.htm>

FDA REVIEWS DATA FOR ANTIDEPRESSANT USE IN ADULTS In response to recent scientific publications that report the possibility of increased risk of suicidal behavior in adults treated with antidepressants, the U.S. Food and Drug Administration (FDA) has issued a Public Health Advisory (PHA) to update patients and healthcare providers with the latest information on this subject.

Even before the publication of these recent reports, FDA had already begun the process of reviewing available data to determine whether there is an increased risk of suicidal behavior in adults taking antidepressants. The Agency has asked manufacturers to provide information from their trials using an approach similar to that used in the evaluation of the risk of suicidal behavior in the pediatric population taking antidepressants. This effort will involve hundreds of clinical trials and may take more than a year to complete.

In the meantime, the PHA advises health care providers and patients to be aware of the following:

Adults being treated with antidepressant medicines, particularly those being treated for depression, should be watched closely for worsening of depression and for increased suicidal thinking or behavior. Close observation of adults may be especially important when antidepressant medications are started for the first time or when doses for the specific drugs prescribed have been changed. Adults whose symptoms worsen while being treated with antidepressants, including an increase in suicidal thinking or behavior, should be evaluated by their health care professional. These recommendations are consistent with warnings already present in approved labeling for antidepressants used by adults.

FDA will provide updated information as it becomes available. The Public Health Advisory is available on line at <http://www.fda.gov/cder/drug/advisory/SSRI200507.htm>

NIH PUBLIC ACCESS POLICY IMPLEMENTED Beginning May 2, 2005, investigators funded in full or in part by NIH will be asked to submit the final manuscript, upon acceptance for

publication, to PubMed Central (PMC). PMC is the NIH digital repository of full-text, peer-reviewed biomedical, behavioral, and clinical research journals. It is a publicly accessible, permanent, and searchable electronic archive available at <http://www.pubmedcentral.nih.gov/>. Through this archive of peer-reviewed, NIH-funded research publications, health care providers, educators, and scientists will be more readily able to exchange and search for research publications, and the public will have greater access to health-related publications. An added benefit of using PMC is that articles returned by a search are automatically linked to a variety of research-related resources in other National Library of Medicine databases, such as DNA and protein sequences, protein structures, small molecules (PubChem) and taxonomy. These databases also provide linkages to a broad collection of other biological and health-related resources. Additional information is available at <http://www.nih.gov/about/publicaccess/Finalpublicaccessimplementation031505.htm>

STRUCTURE OF BIOLOGICAL "TRANSISTOR" DETAILED IN HIGHER ORGANISMS

HHMI researcher Roderick MacKinnon, M.D. at Rockefeller University, is unveiling the first detailed view of the architecture of a natural "transistor" that ensures the proper flow of potassium ions in cells. The research group, which had previously determined the structure of voltage-sensing membrane channels in primitive bacteria, has now advanced their understanding to channels in higher organisms, including mammals.

The advance, which was made possible, in part, by some clever chemistry that permitted fragile protein crystals to grow in a more "native" environment, is likely to offer new insights into how the channels function in the brain and heart. These channels control the flow of potassium ions through the cell membrane in response to voltage changes across the cell membrane. This research was published in the July 08, 2005, issue of Science. For the full story, go to <http://www.hhmi.org//news/mackinnon9.html>

EMPLOYMENT OPPORTUNITIES

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

TSC INFORMATION

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