



TSC ALERT

Edited by Vicky Holets Whittemore, Ph.D. & Cheryl Dunigan, Ph.D.

April 2004

Welcome to the April 2004 edition of *TSC Alert* – an online research newsletter for individuals interested in Tuberous Sclerosis Complex (TSC) research and clinical care. This online newsletter contains information of interest to the TSC research and health care community. Please forward this newsletter to colleagues who are interested in TSC. To be added/deleted to/from the mailing list for *TSC Alert* and/or to submit information for the May 2004 *TSC Alert* contact: Vicky.Whittemore@tsalliance.org

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IMPORTANT DEADLINES:

May 4, 2004: Deadline for submission of grant applications for the Tuberous Sclerosis Complex Research Program (TSCRP) through the Congressionally Directed Medical Research Program. Applicants do not have to be U.S. citizens or perform research in the U.S. in order to apply for funding. See information below, or on the Web site at: <http://cdmrp.army.mil/funding/04tsrp.htm>

August 1, 2004: Deadline for submission of poster abstracts for late breaking research will be accepted until August 1st 2004.

'TSC genes - function and dysfunction - from molecular biology to therapeutic advances'

September 16-18, 2004
Queens' College
University of Cambridge
Cambridge, UK

Chairmen: Professor Patrick Bolton & Dr John Yates
Sponsored by the Tuberous Sclerosis Association

Pivotal roles for the TSC genes in cell biology have come from new research since 2001. In turn, this knowledge has increased understanding of the clinical manifestations of Tuberous Sclerosis. The 2004 conference will present new research around two main themes 'Normal function of TSC genes' and 'Clinical dysfunction caused by TSC gene mutations'. There will be plenary sessions on each theme, poster presentations and an opportunity to talk about any late breaking research.

GRANT ANNOUNCEMENTS:

Department of Defense Tuberous Sclerosis Complex Research Program Funding Opportunities for Fiscal Year 2004

Deadline: May 4, 2004

This year the TSCRP will provide three funding mechanisms for all research on TSC. They are:

- **Concept Awards:** The intent of the Concept Award is to fund the exploration of an initial concept or theory that could give rise to a testable hypothesis. These awards are to encourage the exploration of untested, high-risk questions relevant to Tuberous Sclerosis and are not intended to support the next step in an already established research project. Presentation of preliminary data is not consistent with the intent of this award mechanism.
- **Idea Development Awards:** Idea Development Awards are intended to encourage innovative research directed toward improved prevention, diagnosis, and/or treatment of tuberous sclerosis. All Idea Development Award proposals *must include preliminary data* relevant to tuberous sclerosis research and the proposed project.
- **Natural History Development Awards:** The intent of Natural History Development Award is to provide support for the development of a multi-institutional natural history study that will ascertain and analyze sufficient numbers of patients with tuberous sclerosis (TS) to yield a substantial normative data set and provide quantitative data on TS-related tumor growth and/or other manifestations of TS. The Natural History Development Award proposal should include plans for the establishment of the research team, the development of tools for data management and trial/research administration, the definition of recruitment strategies, and the development of the clinical protocol and other essential components of the study included in a Manual of Operations and Procedures. An additional goal of these awards is the formation of a consortium of investigators with the potential to carry out clinical trials and to expand cooperative research into the various clinical manifestations of this disease.

For more information, visit the CDMRP website at: <http://cdmrp.army.mil>

Bernard D'Souza International Fellowship Award

Deadline: May 1, 2004

The Child Neurology Society is now accepting applications for the 2004 Bernard D'Souza International Fellowship Award, which will sponsor all expenses for a child neurologist from a developing country to attend the 33rd Meeting of the CNS to be held in Ottawa, Canada, October 13-16, 2004. This will be preceded, or followed, by a visit to a selected training program in North America. The purpose of the award is to promote child neurology in developing countries. Applicants must have trained in a developing country, should be practicing child neurology in an academic environment and should be prepared to present a scientific paper in English. Preference will be shown to applicants less than age 45 years.

The deadline for receipt of applications for the award is **May 1, 2004**. The application and complete selection criteria can be obtained by contacting:

Geoffrey Miller, M.D.
Chair, International Affairs Committee
Child Neurology Society
Neurology Section
Texas Children's Hospital
6621 Fannin, CC1710
Houston, Texas 77030
Phone: 832-822-1779
Fax: 832-822-1717
E-mail: [gmiller@bcm.tmc.edu](mailto:gmilller@bcm.tmc.edu)

LAM Foundation Postdoctoral Fellowships

Deadline: September 1

The LAM Foundation is offering postdoctoral fellowships for the study of the cellular and molecular basis of the abnormal smooth muscle proliferation that occurs in the disease, Lymphangiomyomatosis (LAM.) The LAM Post Doctoral 3 year Fellowship Awards provide a maximum of \$150,000 (\$50,000 per year, renewable for up to two additional years). Pilot Project Awards of up to \$25,000 are also available for the initiation of innovative research projects. Candidates must have at least two years of experience, an MD, PhD, or equivalent degree, and perform the work in a laboratory with established expertise in smooth muscle biology or the genetics of tuberous sclerosis. Examples of competitive proposals include those that focus on the genetic regulation of smooth muscle growth or the development of a smooth muscle cell line that is representative of LAM lesion. Mechanistic, hypothesis driven approaches of all types are welcomed. Formalin-fixed LAM tissues, dispersed LAM lung cells, genetic probes and other reagents are available. The deadline for fall applications is **September 1st** and funding begins January 15th of the following year. You may write to The LAM Foundation at 10105 Beacon Hills Drive, Cincinnati, Ohio, 45241 or email lam@one.net. For your convenience, you will find the terms and application form under [Funding for Scientists](#) on the LAM Foundation Web site.



NIH ANNOUNCEMENTS:

Genetic and Rare Diseases Information Center - New Services in Spanish

http://rarediseases.info.nih.gov/html/resources/info_cntr_esp.html

Established by the National Human Genome Research Institute (NHGRI) and the Office of Rare Diseases (ORD), the Genetic and Rare Diseases Information Center employs experienced information specialists to answer questions from the general public, including patients and their families, health care professionals and biomedical researchers.

By Telephone

Monday - Friday, 12:00 p.m. to 6:00 p.m. Eastern Time
(888) 205-2311 (Phone)
(888) 205-3223 (TTY)

By E-mail or Fax

(Answered within 5 to 10 working days)
gardinfo@nih.gov
(240) 632-9164 (Fax)

By U.S. Mail

(Answered within 5 to 10 working days)
The Genetic and Rare Diseases Information Center
P.O. Box 8126
Gaithersburg, MD 20898-8126

For information on rare cancers, please contact the [National Cancer Institute's Cancer Information Service \(CIS\)](#) toll-free at (800) 4-CANCER.

Note: The Genetic and Rare Diseases Information Center does not give medical advice, provide treatment, or diagnose illness.

SCIENTISTS COMPARE RAT GENOME WITH HUMAN, MOUSE: Analysis Yields New Insights into Medical Model, Evolutionary Process An international research team, supported by the National Institutes of Health (NIH), today announced it has completed a high-quality, draft sequence of the genome of the laboratory rat, and has used that data to explore how the rat's genetic blueprint stacks up against those of mice and humans.

In a paper published in the April 1 issue of the journal "Nature", the Rat Genome Sequencing Project Consortium describes its efforts to produce and analyze a draft sequence of the Brown Norway strain of the laboratory rat (*Rattus norvegicus*). The project, led by the Human Genome Sequencing Center at Baylor College of Medicine in Houston, was primarily funded by the National Heart, Lung and Blood Institute (NHLBI), \$58.5 million, and the National Human Genome Research Institute (NHGRI), \$60 million.

A high-resolution photo of the Brown Norway strain of the laboratory rat is available at: <http://www.genome.gov/10005141>

NHGRI and NHLBI are two of the 27 institutes and centers at the NIH, which is an agency of the Department of Health and Human Services. For more on comparative genomic analysis, go to: <http://www.genome.gov/10005835>

Additional information about NHGRI can be found at its Web site: <http://www.genome.gov>

Additional information about NHLBI can be found at its Web site: <http://www.nhlbi.nih.gov>

NIH ANNOUNCES MAY 2004 CONFERENCE ON THE HIPAA PRIVACY RULE AND RESEARCH (NOT-OD-04-036)

National Institutes of Health

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-036.html>

LARGE-SCALE CENTERS FOR THE PROTEIN STRUCTURE INITIATIVE (RFA-GM-05-001)

National Institute of General Medical Sciences

APPLICATION RECEIPT DATE: October 15, 2004

<http://grants.nih.gov/grants/guide/rfa-files/RFA-GM-05-001.html>

SPECIALIZED CENTERS FOR THE PROTEIN STRUCTURE INITIATIVE (RFA-GM-05-002)

National Institute of General Medical Sciences

National Center for Research Resources

APPLICATION RECEIPT DATE: October 15, 2004

<http://grants.nih.gov/grants/guide/rfa-files/RFA-GM-05-002.html>

RESEARCH ON AUTISM AND AUTISM SPECTRUM DISORDERS (PA-04-085)

National Institute of Mental Health

National Institute on Deafness and Other Communication Disorders

National Institute of Child Health and Human Development

National Institute of Neurological Disorders and Stroke

National Institute of Environmental Health Sciences

National Institute of Nursing Research

APPLICATION RECEIPT DATE(S): Multiple dates, see announcement

<http://grants.nih.gov/grants/guide/pa-files/PA-04-085.html>

HIGH THROUGHPUT TOOLS FOR BRAIN AND BEHAVIOR: SBIR (PA-04-086)

National Institute of Mental Health

National Institute of Neurological Disorders and Stroke

APPLICATION RECEIPT DATE(S): Multiple dates, see announcement

<http://grants.nih.gov/grants/guide/pa-files/PA-04-086.html>

GENE-ENVIRONMENT EFFECTS AND EPIGENESIS IN DEPRESSION (RFA-MH-05-006)

National Institute of Mental Health

National Institute on Alcohol Abuse and Alcoholism

National Institute on Drug Abuse

APPLICATION RECEIPT DATE: July 16, 2004

<http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-05-006.html>

NON-INVASIVE METHODS FOR DIAGNOSIS AND PROGRESSION OF DIABETES, KIDNEY, UROLOGICAL, HEMATOLOGICAL AND DIGESTIVE DISEASES (PA-04-088)

National Institute of Diabetes and Digestive and Kidney Diseases

APPLICATION RECEIPT DATE(S): Multiple dates, see announcement

<http://grants.nih.gov/grants/guide/pa-files/PA-04-088.html>

NIDDK SHORT-TERM TRAINING FOR MEDICAL STUDENTS (T35) (PAR-04-090)

National Institute of Diabetes and Digestive and Kidney Diseases

APPLICATION RECEIPT DATE(S): Multiple dates, see announcement

<http://grants.nih.gov/grants/guide/pa-files/PAR-04-090.html>

**CDC PUBLIC HEALTH RESEARCH: HEALTH PROTECTION RESEARCH INITIATIVE
MENTORED RESEARCH SCIENTIST DEVELOPMENT AWARD (KO1)(RFA -CD-04-001)**

Centers for Disease Control and Prevention

APPLICATION RECEIPT DATE: June 22, 2004

<http://grants.nih.gov/grants/guide/rfa-files/RFA-CD-04-001.html>

**CDC PUBLIC HEALTH RESEARCH: HEALTH PROTECTION RESEARCH INITIATIVE
INVESTIGATOR INITIATED RESEARCH (R01) (RFA -CD-04-002)**

Centers for Disease Control and Prevention

APPLICATION RECEIPT DATE: June 22, 2004

<http://grants.nih.gov/grants/guide/rfa-files/RFA-CD-04-002.html>

**CDC PUBLIC HEALTH RESEARCH: HEALTH PROTECTION RESEARCH INITIATIVE
INSTITUTIONAL RESEARCH TRAINING GRANT (RFA -CD-04-003)**

Centers for Disease Control and Prevention

APPLICATION RECEIPT DATE: June 21, 2004

<http://grants.nih.gov/grants/guide/rfa-files/RFA-CD-04-003.html>

**CDC PUBLIC HEALTH RESEARCH: HEALTH PROTECTION RESEARCH INITIATIVE
CENTERS OF EXCELLENCE IN HEALTH PROMOTION ECONOMICS CENTER CORE
GRANT (P30) (RFA -CD-04-004)**

Centers for Disease Control and Prevention

APPLICATION RECEIPT DATE: June 21, 2004

<http://grants.nih.gov/grants/guide/rfa-files/RFA-CD-04-004.html>

MICROARRAY CENTERS FOR RESEARCH ON THE NERVOUS SYSTEM (RFA -NS-05-002)

National Institute of Neurological Disorders and Stroke

National Institute of Mental Health

APPLICATION RECEIPT DATE: August 9, 2004

<http://grants.nih.gov/grants/guide/rfa-files/RFA-NS-05-002.html>

MOLECULAR LIBRARIES SCREENING CENTERS NETWORK (MLSCN) (RFA -RM-04-017)

National Institutes of Health

APPLICATION RECEIPT DATE: August 24, 2004

<http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-017.html>

TSC TISSUE AVAILABILITY:

If you are interested in obtaining tissue for your research, please contact the Brain and Tissue Bank at 1-800-847-1539 or visit their Web site at: <http://som1.umaryland.edu/braintissuebank>

If you have specific needs for TSC tissue for your research, please contact Vicky Whittemore at vwhittemore1@comcast.net

RESOURCES:

GENE EXPRESSION PROFILING TECHNOLOGY CONSORTIUM

The National Institute of Neurological Disorders and Stroke (NINDS) and the National Institute of Mental Health (NIMH) of the NIH have established a consortium of three centers to provide NINDS/NIMH investigators with the opportunity to further their research through the use of gene expression profiling technology. The primary goal of this consortium is to further basic and translational research through acquisition and dissemination of high-quality expression array data. <http://arrayconsortium.tgen.org/np2/home.do>

NEWS:

OVATION PHARMACEUTICALS ACQUIRES NORTH AMERICAN RIGHTS FOR SABRIL (VIGABATRIN); TUBEROUS SCLEROSIS ALLIANCE TO PARTICIPATE IN TASK FORCE

Ovation Pharmaceuticals of Deerfield, Illinois announced that they have acquired exclusive North American rights from Aventis for sabril (vigabatrin) and Frisium/Mystan (clobazam). Vigabatrin has been proven to be a first-line therapeutic for infantile spasms, a common seizure type often associated with tuberous sclerosis complex (TSC).

Clinical consensus developed at the NIH/Tuberous Sclerosis Alliance Consensus Conference in 1998 identified vigabatrin as the drug of choice to treat infantile spasms. The United States Food and Drug Administration (FDA), however, have not approved vigabatrin, because of safety issues, specifically evidence of visual field loss, difficult if not impossible to detect by perimetric field studies in young or disabled children. Infantile spasms, if undetected and untreated can be associated with significant mental disabilities. Vigabatrin is a highly effective first-line therapy to treat infantile spasms in children with TSC.

Because vigabatrin has not been available in the United States, families and individuals with a prescription from a U.S. doctor have found it medically necessary to obtain the drug from many of the 40 countries in which vigabatrin has been approved. The FDA has issued advisories on the import of such critical therapeutics (www.fda.gov).

The announcement from Ovation Pharmaceuticals brings promise that renewed efforts to seek approval from the FDA can move forward. Aventis has not pursued further FDA approval of vigabatrin since 1998, following the FDA action to decline approval at that time due to safety concerns. However, the company continued to manufacture and distribute vigabatrin outside of the United States.

Ovation Pharmaceuticals sought to acquire North American rights to vigabatrin with the specific plan to seek approval from the FDA in order to make both vigabatrin and clobazam available nationally. Ovation will work closely with the FDA, the Tuberous Sclerosis Alliance (TS Alliance), Child Neurology Society and other organizations to support the approval process. The process may take two to three years. Ovation will be unable to distribute vigabatrin in the U.S. until the FDA gives its final approval.

In an effort to facilitate communication and assistance from the professional and patient community, Ovation has announced its partnership with a newly formed Rare Disease Task Force headed by Roy D. Elterman, M.D., a Dallas pediatric neurologist and founder of the U.S. Infantile Spasms Study Group. TS Alliance president Mike Coburn applauded Ovation's outreach to the medical and advocacy community commenting that "effective coordination and partnerships between groups representing the patient community, professionals and industry are critical if we are going to provide solutions to problems facing individuals with TSC and the healthcare providers treating individuals with TSC and other disorders." Coburn announced that TS Alliance Board Member and Director of the Massachusetts General Hospital Comprehensive Pediatric Epilepsy Program, Elizabeth Thiele, M.D., Ph.D. will represent the TS Alliance on the Rare Disease Task Force.

Ovation Pharmaceuticals, Inc. is a privately held specialty pharmaceutical company that acquires underpromoted branded pharmaceutical products and late-stage development products. Founded in August 2000, Ovation reinvigorates and grows products for underserved patient populations through targeted clinical, marketing and sales efforts and product life cycle management that focuses on developing new formulations, introducing new indications and pursuing significant product improvements. For more information visit www.ovationpharma.com/prod_acquisition.html

PARTICIPATE IN KETOGENIC DIET SURVEY

If any centers/countries would like to participate in a survey on the use of the ketogenic diet, please email Eric H. Kossoff, M.D. privately at: ekossoff@jhmi.edu. Notable needs are : Mexico/Central America, Northern/Central Africa, Eastern Europe, Russia, and France.

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NEW TSC PUBLICATIONS:

TSC Basic Science Highlight:

Birchenall-Roberts MC, Fu T, Bang OS, Dambach M, Resau JH, Sadowski CL, Bertolette DC, Lee HJ, Kim SJ, Ruscetti FW (2004) **Tuberous sclerosis complex 2 gene product interacts with human SMAD proteins: A molecular link of two tumor suppressor pathways.** J Biol Chem Apr 2 [Epub ahead of print] <http://www.jbc.org/cgi/reprint/M402790200v1>

The tuberous sclerosis complex (TSC) 2 gene product (tuberin) is a tumor suppressor protein whose absence or inactivation is associated with human malignancies of the brain, kidney, heart, skin, as well as mental retardation and autism. At the cellular level, tuberin is required as a critical regulator of cell growth (1), neuronal differentiation (2), and tumor suppression (3;4) (4). Researchers from the Basic Research Program, SAIC-Frederick, National Cancer Institute, in Frederick, MD, report a critical role for tuberin in late stage myeloid cell differentiation. Tuberin strongly augments TGF- β 1 signal transduction pathways, including SMAD activation. They also demonstrate that the amino-terminal region of tuberin interacts specifically with the MH2 domain of SMAD2 and SMAD3 proteins to regulate TGF- β 1-responsive genes such as Cip/p21. Inhibition of tuberin expression by Tsc2 antisense greatly reduces the ability of TGF- β to transcriptionally regulate Cip/p21, Kipp27 and cyclin A leading to an abrogation of the antiproliferative effects of TGF- β 1. Also, inhibition of tuberin expression during stimulation of monocytic differentiation with vitamin D3 and TGF- β 1 significantly impaired myeloid cell growth inhibition and differentiation. Together, the data demonstrate the presence of a novel activation process following TGF- β 1 stimulation that requires tuberin-dependent activity.

TSC Clinical Science Highlight:

Kielinen M, Rantala H, Timonen E, Linna SL, Moilanen I (2004) **Associated medical disorders and disabilities in children with autistic disorder: a population-based study.** *Autism* 8(1):49-60

This is a population-based survey that was conducted among 152,732 Finnish children and adolescents aged under 16 years and living in northern Finland. Diagnoses and associated medical conditions were derived from the hospital and institutional records of this area. One hundred and eighty-seven children with DSM-IV autistic disorder were identified. Associated medical disorders or associated disorders of known or suspected genetic origin were found in 12.3 percent, including tuberous sclerosis, Down syndrome, fragile X syndrome, Klinefelter syndrome, XYY syndrome, chromosome 17 deletion, chromosome 46, XX, dup(8) (p) and mitochondriopathy. Other associated medical disorders identified were epilepsy, hydrocephalus, fetal alcohol syndrome and cerebral palsy. Hearing impairments were found in 8.6 percent and severe impairment of vision in 3.7 percent of the individuals with autistic disorder. Medical disorders seem to have a special impact on the genesis of autistic disorder and need to be thoroughly examined in each child with autistic disorder.

TSC Publications:

Adhvaryu K, Shanbag P, Vaidya M (2004) Tuberous sclerosis with hypothyroidism and precocious puberty. *Indian J Pediatr* 71(3):273-5

Akalin F, Baysoy G, Ozturk B, Yalcin Y, Ekici G, Yilmaz Y (2004) A case of tuberous sclerosis presenting with dysrhythmia in the first day of life. *Turk J Pediatr* 46(1):79-81

Birchenall-Roberts MC, Fu T, Bang OS, Dambach M, Resau JH, Sadowski CL, Bertolette DC, Lee HJ, Kim SJ, Ruscetti FW (2004) Tuberous sclerosis complex 2 gene product interacts with human SMAD proteins: A molecular link of two tumor suppressor pathways. *J Biol Chem* Apr 2 [Epub ahead of print]

Fesslova V, Villa L, Rizzuti T, Mastrangelo M, Mosca F (2004) Natural history and long-term outcome of cardiac rhabdomyomas detected prenatally. *Prenat Diagn* 24(4):241-8

Fingar DC, Blenis J (2004) Target of rapamycin (TOR): an integrator of nutrient and growth factor signals and coordinator of cell growth and cell cycle progression. *Oncogene* 23(18):3151-

Herguner MO, Karabay-Bayazit A, Noyan A, Altunbasak S, Anarat A (2004) Symptomatic kidney involvement in a child with tuberous sclerosis. *Turk J Pediatr* 46(1):76-8

Heywood G, Smyrk TC, Donohue JH (2004) Primary angiomyolipoma of the pancreas. *Pancreas* 28(4):443-5

Higuchi T, Abe M, Okada K, Nakajima Y, Ohnishi Y, Hagi C, Fukuda N, Kuno T, Takahashi S, Saito S, Nagura Y, Matsumoto K (2004) The Salvage of Graft Occlusion in a Maintenance Hemodialysis Patient with Tuberous Sclerosis by Percutaneous Transluminal Angioplasty using Intravascular Ultrasound: Case Report. *Ther Apher* 8(2):164-7

Jansen FE, Van Nieuwenhuizen O, Van Huffelen AC (2004) Tuberous sclerosis complex and its founders. *J Neurol Neurosurg Psychiatry* 75(5):770

Jones KA, Jiang X, Yamamoto Y, Yeung RS (2004) Tuberin is a component of lipid rafts and mediates caveolin-1 localization: role of TSC2 in post-Golgi transport. *Exp Cell Res* 295(2):512-24

Jozwiak S, Kwiatkowski D, Kotulska K, Larysz-Brysz M, Lewin-Kowalik J, Grajkowska W, Roszkowski M (2004) Tuberin and hamartin expression is reduced in the majority of subependymal giant cell astrocytomas in tuberous sclerosis complex consistent with a two-hit model of pathogenesis. *J Child Neurol* 19(2):102-6

Khan N, Javed A, Wazir S, Yousaf M (2003) Tuberous sclerosis--rare presentation as pneumothorax. *J Ayub Med Coll Abbottabad* 15(4):60-2

Kielinen M, Rantala H, Timonen E, Linna SL, Moilanen I (2004) Associated medical disorders and disabilities in children with autistic disorder: a population-based study. *Autism* 8(1):49-60

Kimball SR, Jefferson LS (2004) Molecular mechanisms through which amino acids mediate signaling through the mammalian target of rapamycin. *Curr Opin Clin Nutr Metab Care* 7(1):39-44

Pan D, Dong J, Zhang Y, Gao X Tuberous sclerosis complex: from *Drosophila* to human disease. *Trends Cell Biol* 14(2):78-85

Rossello Barbara M, Mus Malleu A, Rebassa Llul M, Casals Armada J. [Giant angiomyolipoma in a case of tuberous sclerosis.] *Actas Urol Esp* 28(2):133-7 [Article in Spanish]

Sarnat HB, Flores-Sarnat L (2004) Integrative classification of morphology and molecular genetics in central nervous system malformations. *Am J Med Genet* 126A(4):386-92

Wu J, Khalil FK, Keehn CA, Saeed S, Morgan MB (2004) Hamartin and tuberin immunohistochemical expression in cutaneous fibroepithelial polyps. *J Cutan Pathol* 31(5):383-7

TSC-Related Articles:

Atkins MB, Hidalgo M, Stadler WM, Logan TF, Dutcher JP, Hudes GR, Park Y, Liou SH, Marshall B, Boni JP, Dukart G, Sherman ML (2004) Randomized phase II study of multiple dose levels of CCI-779, a novel mammalian target of rapamycin kinase inhibitor, in patients with advanced

refractory renal cell carcinoma. *J Clin Oncol* 22(5):909-18

Best JL, Acheson JF (2004) The natural history of Vigabatrin associated visual field defects in patients electing to continue their medication. *Eye*. 2004 Apr 16 [Epub ahead of print]

Daniel C, Pippin J, Shankland SJ, Hugo C (2004) The Rapamycin derivative RAD inhibits mesangial cell migration through the CDK-inhibitor p27(KIP1). *Lab Invest* Apr 5 [Epub ahead of print]

Evans SE, Colby TV, Ryu JH, Limper AH (2004) Transforming growth factor-beta 1 and extracellular matrix-associated fibronectin expression in pulmonary lymphangioleiomyomatosis. *Chest* 125(3):1063-70

Juhasz C, Chugani HT (2003) Imaging the epileptic brain with positron emission tomography. *Neuroimaging Clin N Am* 13(4):705-16, viii

Kivity S, Lerman P, Ariel R, Danziger Y, Mimouni M, Shinnar S (2004) Long-term cognitive outcomes of a cohort of children with cryptogenic infantile spasms treated with high-dose adrenocorticotrophic hormone. *Epilepsia* 45(3):255-62

Kondo Y, Hollingsworth EF, Kondo S (2004) Molecular targeting for malignant gliomas (Review). *Int J Oncol* 24(5):1101-9

Krawczyk P, Czekajska-Chehab E, Kieszko R, Siwiec J, Wegrzyn-Szkutnik I, Gryglicka B, Milanowski J (2004) Difficulties in the diagnosis of rare immunological diseases manifesting with cystic lung disease and spontaneous pneumothorax: Case reports. *Heart Lung* 33(1):21-5

Lekmine F, Sassano A, Uddin S, Smith J, Majchrzak B, Brachmann SM, Hay N, Fish EN, Plataniias LC (2004) Interferon-gamma engages the p70 S6 kinase to regulate phosphorylation of the 40S S6 ribosomal protein. *Exp Cell Res* 295(1):173-82

Lim KE, Tsai YH, Hsu YI Y, Hsu Wc W (2004) Pulmonary lymphangioleiomyomatosis: high-resolution CT findings in 11 patients and compared with the literature. *Clin Imaging* 28(1):1-5

Lotze TE, Wilfong AA (2004) Zonisamide treatment for symptomatic infantile spasms. *Neurology* 62(2):296-8

Newton HB (2004) Molecular neuro-oncology and development of targeted therapeutic strategies for brain tumors. *Expert Rev Anticancer Ther* 4(1):105-28

Oshiro N, Yoshino K, Hidayat S, Tokunaga C, Hara K, Eguchi S, Avruch J, Yonezawa K (2004) Dissociation of raptor from mTOR is a mechanism of rapamycin-induced inhibition of mTOR function. *Genes Cells* 9(4):359-66

Pechet TT, Meyers BF, Guthrie TJ, Battafarano RJ, Trulock EP, Cooper JD, Patterson GA (2004) Lung transplantation for lymphangioleiomyomatosis. *J Heart Lung Transplant* 23(3):301-8

Pitts S, Oberstein EM, Glassberg MK (2004) Benign metastasizing leiomyoma and lymphangioleiomyomatosis: sex-specific diseases? *Clin Chest Med* 25(2):343-60

Riesterer O, Zingg D, Hummerjohann J, Bodis S, Pruschy M (2004) Degradation of PKB/Akt

protein by inhibition of the VEGF receptor/mTOR pathway in endothelial cells. Oncogene Apr 5
[Epub ahead of print]

CONFERENCES:

For a complete listing of conferences, visit the TS Alliance website at:
<http://216.33.101.121/Research/upcoming%20conferences.asp>

September 16-18, 2004

TSC International Research Conference 2004

TSC Genes - Function and Dysfunction - From Molecular Biology to Therapeutic Advances

Organized by the Tuberous Sclerosis Association of Great Britain
Queens' College, University of Cambridge, Cambridge UK

**Deadline for Submission of Poster Abstracts for late breaking research will be accepted
until August 1, 2004.**

See Tuberous Sclerosis Association Web site for additional information and forms at:
<http://www.tuberous-sclerosis.org/research/conference/index.shtml>

For any queries please contact Ann Hunt at: research@tuberous-sclerosis.org
or telephone/fax: 44 (0)1993 881238

ARCHIVED ISSUES OF TSC ALERT:

December 2002 TSC Alert

<http://www.tsalliance.org/research/tsc%20alert.asp>

January 2003 TSC Alert

<http://www.tsalliance.org/Research/TSC%20Alert012203.asp>

February 2003 TSC Alert

<http://www.tsalliance.org/Research/TSC%20Alert021003.asp>

March 2003 TSC Alert

<http://www.tsalliance.org/Research/TSC%20Alert030403.asp>

April 2003 TSC Alert

<http://www.tsalliance.org/Research/TSC%20Alert040103.asp>

May 2003 TSC Alert

<http://www.tsalliance.org/Research/TSC%20Alertdefault.asp>

June 2003 TSC Alert

<http://www.tsalliance.org/Research/TSC%20Alert060103.asp>

July 2003 TSC Alert

<http://www.tsalliance.org/Research/TSC%20Alert72703.asp>

August 2003 TSC Alert

<http://www.tsalliance.org/Research/TSC080103.asp>

September 2003 TSC Alert

<http://www.tsalliance.org/Research/TSC%20Alert091503.asp>

October 2003 TSC Alert - Coming soon!

November 2003 TSC Alert

<http://www.tsalliance.org/Research/TSC%20Alert112403.asp>

December 2003 TSC Alert

<http://www.tsalliance.org/Research/TSC%20Alertdefault.asp>

January 2004 TSC Alert

<http://www.tsalliance.org/Research/TSC%20Alert%20default.asp>

February/March 2004 TSC Alert

Coming soon!