



TSC ALERT

Edited by Vicky Holets Whittemore, Ph.D. & Cheryl Dunigan, Ph.D.
October 2003

Welcome to the October 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 2003 *TSC Alert* contact: Vicky.Whittemore@tsalliance.org

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GRANT ANNOUNCEMENTS:

TUBEROUS SCLEROSIS ALLIANCE: Letter of Intent Deadline Announced

Letters of Intent (LOIs) will be accepted until **November 15, 2003**. Invited applicants will be selected from the submitted LOIs and asked to submit a complete application, due January 15, 2004. Funding to begin July 1, 2004.

Focus: Research related to the Tuberous Sclerosis Complex (TSC). Researchers focused on preclinical and clinical studies relevant to TSC are particularly invited to apply. LOIs describing other areas of research relevant to TSC will also be considered.

Additional information can be obtained at: <http://www.tsalliance.org> or by calling Dr. Cheryl Dunigan at the TS Alliance at 1-800-225-6872.

DEPARTMENT OF DEFENSE TUBEROUS SCLEROSIS COMPLEX RESEARCH PROGRAM ANNOUNCES AWARDS

The Department of Defense Tuberos Sclerosis Complex Research Program (TSCRCP) was established in Fiscal Year 2002 (FY02) by Joint Appropriations Conference Committee Report No. 107-350, which provided \$1M for tuberous sclerosis research. A Program Announcement was released in March of 2002, with proposals received by September 5, 2002. Following peer and programmatic reviews, institutions began receiving funds during the summer of 2003.

Award Recipients of TSCRCP **Idea Development Awards** were:

- David Gutmann, M.D., Ph.D., Washington University in St. Louis, \$374,002 for his research proposal entitled "Mouse Models of TSC-Related Epilepsy."
- Elizabeth Henske, M.D., Fox Chase Cancer Center, \$398,751 for her research proposal entitled "TSC1 And TSC2 Gene Homologs in Schizosaccharomyces Pombe."
- Naoto Ito, Ph.D., Massachusetts General Hospital, \$420,569 for his research proposal entitled "Functions of TSC in the Nervous System in Drosophila Melanogaster."

Congress appropriated \$2 million for the TSCRCP in FY03. Proposals were requested through a Program Announcement in March 2003 and proposals were received in August 2003. The two tiers of review will be completed by December 2003. FY03 award negotiations will begin in January 2004 and be completed by September 30, 2004.

Congress appropriated \$3 million to continue the TSCRCP in FY04. For more information about the TSCRCP awards, technical and public abstracts about the research, previous TSCRCP Program Announcements, and other CDMRP-sponsored programs and events, please visit the CDMRP web site (<http://cdmrp.army.mil>).

The TSCRCP program is administered by the U.S. Army Medical Research and Materiel Command through the Office of the Congressionally Directed Medical Research Programs (CDMRP).

McKNIGHT ENDOWMENT FUND FOR NEUROSCIENCE

The McKnight Endowment Fund for Neuroscience supports innovative research designed to bring science closer to the day when diseases of the brain can be accurately diagnosed, prevented, and treated. To this end, the McKnight Endowment Fund for Neuroscience invites letters of intent for the 2004 McKnight Technological Innovations in Neuroscience Awards. Up to four awards are made annually, each providing \$100,000 for two years. <http://www.mcknight.org/neuroscience/>

GRASS FOUNDATION

Investigators on the threshold of an independent career in neuroscience are eligible for fellowships doing cutting edge research in neurobiology on a project of their choice. The deadline for applications is December 15, 2003. For more information, please visit The Grass Foundation Web site (<http://www.grassfoundation.org>).

GENETIC SERVICES PROGRAM INITIATIVE

HRSA has announced funding opportunities for the following projects:

Project 1: Regional Genetics and Newborn Screening Collaboratives

Project 2: Consumer Based Family History Tool and Education Process

Projects 3 and 4: Translating Medical Genetics Into Services (# 3 Delivering Genetic Services and #4 Translational Public Policy)

Projects 5 and 6: Newborn Screening Public Health Infrastructure (#5 Quality Assessment of NBS and #6 Community Practice Resource Center)

Genetic Services Projects direct URL:

<http://www.hrsa.gov/grants/preview/guidancemchb/hrsa04055.htm>

Medical Home for Children with Special Health Care Needs direct URL:

<http://www.hrsa.gov/grants/preview/guidancemchb/hrsa04046.htm>

Linked from <http://www.hrsa.gov/grants/preview> and

<http://www.hrsa.gov/grants/preview/mch.htm#hrsa04056>

For assistance contact: Joni Johns at jjohns@hrsa.gov or 301-443-2088

NIH ANNOUNCEMENTS:

ANNOUNCEMENT OF US-JAPAN BRAIN RESEARCH COLLABORATIVE PROGRAM (BRCP) - THE US COMPONENT

National Institute of Neurological Disorders and Stroke

National Institute of Mental Health

National Institute on Drug Abuse

National Institute on Deafness and Other Communication Disorders

National Institutes of Dental and Craniofacial Research

INDEX: NEUROLOGICAL DISORDERS, STROKE; MENTAL HEALTH; DRUG ABUSE; DEAFNESS, OTHER COMMUNICATION DISORDERS; DENTAL, CRANIOFACIAL RESEARCH

<http://grants.nih.gov/grants/guide/notice-files/NOT-NS-03-024.html>

EXPLORATORY AND DEVELOPMENTAL RESEARCH GRANTS FOR INVESTIGATIONS IN RARE DISEASES (R21) (PA-03-171)

National Heart, Lung, and Blood Institute

Office of Rare Diseases

INDEX: HEART, LUNG, BLOOD; RARE DISEASES

<http://grants.nih.gov/grants/guide/pa-files/PA-03-171.html>

PRELIMINARY INVESTIGATIONS LEADING TO OPTIMAL TRIALS IN NEUROLOGY (PAR-03-174)

National Institute of Neurological Disorders and Stroke

INDEX: NEUROLOGICAL DISORDERS, STROKE

<http://grants.nih.gov/grants/guide/pa-files/PAR-03-174.html>

NEUROTECHNOLOGY RESEARCH, DEVELOPMENT, AND ENHANCEMENT (PA-04-006)

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 on Drug Abuse
National Institute on Aging
National Institute of Biomedical Imaging and Bioengineering
National Institute of Diabetes and Digestive and Kidney Diseases
INDEX: MENTAL HEALTH; DEAFNESS, OTHER COMMUNICATION DISORDERS; CHILD HEALTH,
HUMAN DEVELOPMENT; NEUROLOGICAL DISORDERS, STROKE; DRUG ABUSE; AGING;
BIOMEDICAL
IMAGING, BIOENGINEERING; DIABETES, DIGESTIVE, KIDNEY DISEASES
<http://grants.nih.gov/grants/guide/pa-files/PA-04-006.html>

NIH Support for Conferences and Scientific Meetings
<http://grants2.nih.gov/grants/guide/pa-files/PA-03-176.html>

NIAMS SMALL GRANT PROGRAM FOR NEW INVESTIGATORS
National Institute of Arthritis and Musculoskeletal and Skin Diseases
INDEX: ARTHRITIS, MUSCULOSKELETAL, SKIN DISEASES
<http://grants.nih.gov/grants/guide/pa-files/PA-04-002.html>

COLLABORATIVE ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES SCIENCE AWARD
National Institute of Arthritis and Musculoskeletal and Skin Diseases
INDEX: ARTHRITIS, MUSCULOSKELETAL, SKIN DISEASES
<http://grants.nih.gov/grants/guide/pa-files/PA-04-003.html>

INTERDISCIPLINARY BEHAVIORAL SCIENCE CENTERS FOR MENTAL HEALTH
National Institute of Mental Health
INDEX: MENTAL HEALTH
<http://grants.nih.gov/grants/guide/pa-files/PA-04-004.html>

NIH ROADMAP RELEASED

The purpose of the NIH Roadmap is to identify major opportunities and gaps in biomedical research that no single institute at NIH could tackle alone but that the agency as a whole must address to make the biggest impact on the progress of medical research. The NIH Roadmap provides a framework of the priorities the NIH as a whole must address in order to optimize its entire research portfolio. It lays out a vision for a more efficient and productive system of medical research. It identifies the most compelling opportunities in three main areas: new pathways to discovery, research teams of the future, and re-engineering the clinical research enterprise. (For further information on the NIH Roadmap see: <http://nihroadmap.nih.gov/index.asp>.)

Listed below are the RFAs that have been published as part of the NIH Roadmap Initiative.

[DK-04-001 METABOLOMICS TECHNOLOGY DEVELOPMENT](#)

[RR-04-001 NATIONAL CENTERS FOR BIOMEDICAL COMPUTING](#)

[RR-04-002 EXPLORATORY CENTERS \(P20\) FOR INTERDISCIPLINARY RESEARCH](#)

TSC TISSUE AVAILABILITY:

Please contact the Brain and Tissue Bank if you are interested in obtaining donated tissue from individuals with TSC for your research. You may contact them by phone at: 1-800-847-1539 or via e-mail at btbumab@umaryland.edu Additional information can be found on their Web site at: <http://som1.umaryland.edu/BTBank/main.html>

RESOURCES:

TSC ANIMAL MODELS AVAILABLE

Several animal models for TSC are currently available from Jackson Laboratories, the National Cancer Institute and/or individual researchers. A list of these models can be found on The Rothberg Institute Web site at: <http://www.childhooddiseases.org/rsc.html#>

If you have additional animal models or other resources that you would like to have listed, please send that information to: data@childhooddiseases.org

NEWS:

NATIONAL POSTDOCTORAL ASSOCIATION

The National Postdoctoral Association (NPA) was established in 2003 to address issues relevant to postdoctoral scholars. NPA works closely with individuals, postdoctoral associations and postdoctoral offices, and with national professional societies and funding agencies to achieve positive changes for postdoctoral researchers. If you are interested in learning more or becoming a member, please visit NPA's Web site (<http://www.nationalpostdoc.org>) or contact NPA at feedback@nationalpostdoc.org.

TS ALLIANCE AWARDS MANUEL R. GOMEZ AWARD TO HOPE NORTHRUP

The Manuel R. Gomez Award was established by the Tuberous Sclerosis Alliance to recognize individuals who have made significant and major contributions to TSC research. The TS Alliance announces that Hope Northrup, M.D. from the University of Texas – Houston is the recipient of the 4th Manuel R. Gomez Award. This award was given to Dr. Northrup in recognition of her research on the genetics of TSC, including the significant contributions she and her colleagues made in the development of the diagnostic genetic test for TSC that is now commercially available through Athena Diagnostics. Dr. Northrup has been involved in TSC research since the 1980's, and is a member of the TS Alliance Professional Advisory Board, currently serving as Co-Chair, and the TS Alliance Board of Directors. Everyone who knows Hope knows that she is an incredible clinician, researcher and friend to everyone with TSC and their families. Congratulations, Hope!

CALL FOR NOMINATIONS FOR 2004 MANUEL R. GOMEZ AWARD

The Tuberous Sclerosis Alliance invites nominations for the fifth Manuel R. Gomez Award. Any individual or group may submit a nomination to the TS Alliance by no later than November 15, 2003. Mail all nominations to Holly Knorr at the TS Alliance at 801 Roeder Road, Suite 750, Silver Spring, MD 20910 or send by e-mail to holly.knorr@tsalliance.org.

Award recipients will be selected on the basis of two principal criteria:

- Achievement for either a single significant breakthrough, or for going above and beyond the call of duty in caring for individuals with TSC during their career;
- Achievement of national or international scope.

Information about additional selection criteria and what materials need to be included with your nominations can be found on the TS Alliance Web site – <http://www.tsalliance.org>

This award is made possible by a generous donation from Mr. and Mrs. Harold Aronson in honor of their son, Peter Aronson, M.D. Peter is currently a member of the TS Alliance Professional Advisory Board and has also served as a member of the TS Alliance Board of Directors in the past. The organization will present the award in December 2003. Previous Manuel R. Gomez Award recipients are:

- 2000 – Vicky Holets Whittemore, Ph.D.
- 2001 – David Kwiatkowski, M.D., Ph.D.
- 2002 – E. Steve Roach, M.D.
- 2003 – Hope Northrup, M.D.

TS ALLIANCE RECEIVES AWARD FROM THE CHILD NEUROLOGY FOUNDATION

The Child Neurology Foundation has selected the Tuberous Sclerosis Alliance (TS Alliance) as recipient of the second annual Child Neurology Foundation Advocacy Award of Merit. Recipient organizations are nominated by members of the Child Neurology Society and selected by the Board of Directors of the Child Neurology Foundation. The 2003 award was presented in Miami on October 2nd at the 32nd Annual Meeting of the Child Neurology Society.

The TS Alliance was selected and recognized for its outstanding achievements on behalf of patients and families, with a special emphasis placed upon the TS Alliance's efforts to create increased public awareness of the specific neurological condition, tuberous sclerosis complex (TSC). TS Alliance President and CEO, Michael J. Coburn, was present to receive the award on behalf of the organization.

The TS Alliance, in conjunction with the Child Neurology Society and the National Institutes of Health also presented a special day-long symposium on TSC as part of the Child Neurology Society's annual meeting next week. The Child Neurology Society is the preeminent non-profit professional association of pediatric neurologists in the United States, Canada, and worldwide devoted to fostering the discipline of child neurology and promoting the optimal care and welfare of children with neurological and neurodevelopmental disorders.

CLINICAL TRIALS/STUDIES:

TS ALLIANCE AND LAM FOUNDTION: RAPAMYCIN CLINICAL TRIAL FOR RENAL AND LUNG INVOLVEMENT IN TSC AND LAM

Patients with TSC and/or LAM are being enrolled in a clinical trial to study the effect of rapamycin on tumor growth in these two diseases. **Contact:** Dr. Frank McCormack at frank.mccormack@uc.edu; or 513-558-4831, Dr. John Bissler at john.bissler@chmcc.org, or Dr. David Franz at david.franz@chmcc.org.

NHLBI: LYMPHANGIOLEIOMYOMATOSIS (LAM) PROTOCOL

The Tuberous Sclerosis Alliance encourages women with TSC and physicians who have patients with TSC, whether or not they have been diagnosed with LAM, to participate in this worthwhile study. Studies such as this are the first step in understanding this devastating disease and we are fortunate that the NHLBI has initiated a protocol aimed at understanding the pathogenesis of LAM. If you are interested in further information or have any questions, you may contact NHLBI at 1-877-NIH-LUNG (1-877-644-5864). Choose # 3 from the menu items after dialing. This is a toll free number.

NEW TSC PUBLICATIONS:

TSC RESEARCH SPOTLIGHT:

Sparagana SP, Delgado MR, Batchelor LL, Roach ES (2003) Seizure remission and antiepileptic drug discontinuation in children with tuberous sclerosis complex. Arch Neurol 60(9):1286-9

Abstract: BACKGROUND: Epilepsy is a common neurologic complication of tuberous sclerosis complex (TSC) and it is often refractory to treatment. Therefore, treating physicians are often reluctant to discontinue antiepileptic drugs (AEDs) in individuals with TSC who have attained seizure remission. To our knowledge, seizure remission and AED discontinuation in children with TSC has not been studied. OBJECTIVE: To characterize seizure remission and AED discontinuation in children with TSC. METHODS: Retrospective medical record and neuroimaging analysis of 15 children with TSC and epilepsy who had seizure remission, with a subsequent trial of discontinuation of AED treatment. RESULTS: The seizure remission rate for the group of patients with TSC and epilepsy was 14.2%. From the group of 15 patients who had a remission, the absolute relapse rate was 26.7% after a mean follow-up of 5 years 7 months. Patients with sustained remission were more likely to have normal intelligence and only a few cortical or subcortical lesions on neuroimaging. CONCLUSIONS: The proportion of children with TSC and epilepsy who achieve seizure remission is small. Nevertheless, some do attain seizure remission, and AEDs may be successfully discontinued. Mild cerebral involvement is a general clinical marker for seizure remission. The relapse rate in those who have undergone a trial of discontinuation of AED therapy is comparable with the rate in the general pediatric population with epilepsy.

Walker CL, Hunter D, Everitt JI (2003) Uterine leiomyoma in the Eker rat: A unique model for important diseases of women. Genes Chromosomes Cancer 38(4):349-56

Abstract: Eker rats carry a defect in the Tsc-2 tumor suppressor gene and female Eker rats develop uterine leiomyoma with a high frequency. The presentation, response to hormones and molecular alterations in these mesenchymal smooth muscle tumors, closely resembles their cognate human disease. Female rats and tumor-derived cell lines from Eker rat leiomyomas (ELT

lines) have been developed as an in vivo/in vitro model system for preclinical studies to identify novel therapeutic agents for this disease and for studying disease pathogenesis. In addition to serving as a model for uterine leiomyoma, Eker rats have proven valuable for studying lymphangi leiomyomatosis, a related proliferative smooth muscle disease of women.

NEW PUBLICATIONS:

[No authors listed] (2003) Giant shagreen patch associated with spina bifida occulta in tuberous sclerosis. *Pediatr Dermatol* 20(5):453-454

Antel SB, Collins DL, Bernasconi N, Andermann F, Shinghal R, Kearney RE, Arnold DL, Bernasconi A (2003) Automated detection of focal cortical dysplasia lesions using computational models of their MRI characteristics and texture analysis. *Neuroimage* 19(4):1748-59

Astrinidis A, Senapedis W, Coleman TR, Henske EP (2003) Cell cycle-regulated phosphorylation of hamartin, the product of the tuberous sclerosis complex 1 gene, by CDK1/cyclin B. *J Biol Chem* Oct 9 [Epub ahead of print] <http://www.jbc.org/cgi/reprint/M303956200v1>

Aviles Izquierdo JA, Huerta Brogeras M, Martinez Sanchez D, Recarte Garci-Andrade C (2003) [Adult's Scholein-Henonch purple and tuberous sclerosis in adults.] *An Med Interna* 20(8):440-1 [Article in Spanish]

Bonham L, Leung DW, White T, Hollenback D, Klein P, Tulinsky J, Coon M, De Vries P, Singer JW (2003) Lysophosphatidic acid acyltransferase-beta: a novel target for induction of tumour cell apoptosis. *Expert Opin Ther Targets* 7(5):643-61

Castro AF, Rebhun JF, Clark GJ, Quilliam LA (2003) Rheb binds tuberous sclerosis complex 2 (TSC2) and promotes S6 kinase activation in a rapamycin- and farnesylation-dependent manner. *J Biol Chem* 278(35):32493-6

Colombani J, Raisin S, Pantalacci S, Radimerski T, Montagne J, Leopold P (2003) A nutrient sensor mechanism controls Drosophila growth. *Cell* 114(6):739-49

Dauriat G, Brugiere O, Mal H, Camuset J, Castier Y, Leseche G, Fournier M (2003) Refractory chylothorax after lung transplantation for lymphangi leiomyomatosis successfully cured with instillation of povidone. *J Thorac Cardiovasc Surg* 126(3):875-7

EI-Hashemite N, Walker V, Zhang H, Kwiatkowski DJ (2003) Loss of Tsc1 or Tsc2 Induces Vascular Endothelial Growth Factor Production through Mammalian Target of Rapamycin. *Cancer Res* 63(17):5173-7

Elsinghorst TA (2003) First cases of animal diseases published since 2000. 1. Dogs. *Vet Q* 25(3):112-23

Francalanci P, Diomedi-Camassei F, Purificato C, Santorelli FM, Giannotti A, Dominici C, Inserra A, Boldrini R (2003) Malignant pancreatic endocrine tumor in a child with tuberous sclerosis. *Am J Surg Pathol* 27(10):1386-9

Glantschnig H, Fisher JE, Wesolowski G, Rodan GA, Reszka AA (2003) M-CSF, TNFalpha and RANK ligand promote osteoclast survival by signaling through mTOR/S6 kinase. *Cell Death Differ* 10(10):1165-77

- Guerreiro MM, Quesney LF, Salanova V, Snipes GJ (2003) Continuous electrocorticogram epileptiform discharges due to brain gliosis. *J Clin Neurophysiol* 20(4):239-42
- Henske EP (2003) Metastasis of benign tumor cells in tuberous sclerosis complex. *Genes Chromosomes Cancer* 38(4):376-81
- Hino O (2003) Hereditary renal carcinogenesis fitting Knudson's two-hit model: Genotype, environment, and phenotype. *Genes Chromosomes Cancer* 38(4):357-67
- Kawaguchi S, Harada K, Supriatno, Yoshida H, Sato M (2003) Overexpression of tuberous sclerosis complex 2 exerts antitumor effect on oral cancer cell lines. *Oral Oncol* 39(8):836-41
- Kivelitz DE, Muhler M, Rake A, Scheer I, Chaoui R (2003) MRI of cardiac rhabdomyoma in the fetus. *Eur Radiol* Oct 9 [Epub ahead of print]
<http://www.springerlink.com/app/home/contribution.asp?wasp=af8awnqyqj1wdc2glftx&referrer=parent&backto=issue,11,143;journal,1,91;linkingpublicationresults,id:100472,1>
- Krishnan B, Lechago J, Ayala G, Truong L (2003) Intraoperative consultation for renal lesions. Implications and diagnostic pitfalls in 324 cases. *Am J Clin Pathol* 120(4):528-35
- Kwong KL, Sung WY, Wong SN, So KT (2003) Early predictors of medical intractability in childhood epilepsy. *Pediatr Neurol* 29(1):46-52
- Leclerc J, Marchal F, Stines J, Regent D (2003) [Epithelioid renal angiomyolipoma: benign or malignant tumor?] *J Radiol* 84(7-8-C1):851-854 [Article in French]
- Long X, Muller F, Avruch J (2004) TOR action in mammalian cells and in *Caenorhabditis elegans*. *Curr Top Microbiol Immunol* 279:115-38
- Maldonado M, Baybis M, Newman D, Kolson DL, Chen W, McKhann G, Gutmann DH, Crino PB (2003) Expression of ICAM-1, TNF-alpha, NFkappaB, and MAP kinase in tubers of the tuberous sclerosis complex. *Neurobiol Dis* 14(2):279-90
- Mita MM, Mita A, Rowinsky EK (2003) The Molecular Target of Rapamycin (mTOR) as a Therapeutic Target Against Cancer. *Cancer Biol Ther* 2(4 Suppl 1):S169-77
- Miyata H, Chute DJ, Fink J, Villablanca P, Vinters HV (2003) Lissencephaly with agenesis of corpus callosum and rudimentary dysplastic cerebellum: a subtype of lissencephaly with cerebellar hypoplasia. *Acta Neuropathol (Berl)*. Oct 18 [Epub ahead of print].
- Mizuguchi M, Mori M, Nozaki Y, Momoi MY, Itoh M, Takashima S, Hino O (2003) Absence of allelic loss in cytomegalic neurons of cortical tuber in the Eker rat model of tuberous sclerosis. *Acta Neuropathol (Berl)*. 2003 Oct 18 [Epub ahead of print].
- Murthy V, Han S, Beauchamp RL, Smith N, Haddad LA, Ito N, Ramesh V (2003) Pam and its ortholog highwire interact with and may negatively regulate the TSC1-TSC2 complex. *J Biol Chem* Oct 14 [Epub ahead of print]. <http://www.jbc.org/cgi/reprint/M310208200v1>
- Neeli I, Yellaturu CR, Rao GN (2003) Arachidonic acid activation of translation initiation signaling in vascular smooth muscle cells. *Biochem Biophys Res Commun* 309(4):755-61
- Pascual Castroviejo I, Pascual Pascual SI, Via o J, Martinez V, Palencia R (2003) [Malformations of cortical development and their clinical repercussions in a series of 144 cases] *Rev Neurol*

37(4):327-44 [Article in Spanish]

Porras A, Zuluaga S, Valladares A, Alvarez AM, Herrera B, Fabregat I, Benito M (2003) Long-term treatment with insulin induces apoptosis in brown adipocytes: role of oxidative stress. *Endocrinology* 2003 Sep 18 [Epub ahead of print]
<http://endo.endojournals.org/cgi/rapidpdf/en.2003-0622v1>

Pruijm MT, Falke TH, Peltenburg HG (2003) [Sporadic renal angiomyolipoma.] *Ned Tijdschr Geneeskd* 147(35):1696-9 [Article in Dutch]

Saito M, Kakinuma H, Iinuma M, Tsuchiya N, Shimoda N, Ohyama C, Satoh S, Sato K, Kato T (2003) [A case of renal cell carcinoma in tuberous sclerosis.] *Nippon Hinyokika Gakkai Zasshi* 94(6):634-8 [Article in Japanese]

Shamji AF, Nghiem P, Schreiber SL (2003) Integration of growth factor and nutrient signaling. Implications for cancer biology. *Mol Cell* 12(2):271-80

Siegel C (2003) CT differentiation of large exophytic renal angiomyolipomas and perirenal liposarcomas. *J Urol* 170(1):321

Sparagana SP, Delgado MR, Batchelor LL, Roach ES (2003) Seizure remission and antiepileptic drug discontinuation in children with tuberous sclerosis complex. *Arch Neurol* 60(9):1286-9

Tabancay AP Jr, Gau CL, Machado IM, Uhlmann EJ, Gutmann DH, Guo L, Tamanoi F (2003) Identification of dominant negative mutants of Rheb GTPase and their use to implicate the involvement of human Rheb in the activation of p70S6K. *J Biol Chem* Oct 10 278(41):39921-30

Walker CL, Hunter D, Everitt JI (2003) Uterine leiomyoma in the Eker rat: A unique model for important diseases of women. *Genes Chromosomes Cancer* 38(4):349-56

Xie YC, Liu WP, Jiang YM, Zhao Y, Tang QL, Liang CY, Liu YH (2003) [A pathologic analysis on 9,666 cases of tumors of nose, pharynx and throat] *Zhonghua Er Bi Yan Hou Ke Za Zhi* 38(3):217-20 [Article in Chinese]

Yeung RS (2003) Multiple roles of the tuberous sclerosis complex genes. *Genes Chromosomes Cancer* 38(4):368-75

Yoshida Y, Matsushita T, Nakajima S, Kita T, Hirai H, Ozono K (2003) Rapid deterioration of renal artery dysplasia in tuberous sclerosis. *J Pediatr*. 143(3):406.

Zhang H, Cicchetti G, Onda H, Koon HB, Asrican K, Bajraszewski N, Vazquez F, Carpenter CL, Kwiatkowski DJ (2003) Loss of Tsc1/Tsc2 activates mTOR and disrupts PI3K-Akt signaling through downregulation of PDGFR. *J Clin Invest* 112(8):1223-33
<http://www.jci.org/cgi/content/full/112/8/1223>

CONFERENCES:

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

Save the date!!! September 16-18, 2004

Tuberous Sclerosis Association International Research Conference
Queens College, Cambridge UK
(More information coming soon!)

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%20Alertdefault.asp>

August 2003 TSC Alert

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

September 2003 TSC Alert – Coming Soon!