



TSC ALERT

Edited by Vicky H Whittemore, PhD

September 2006

Welcome to the September 2006 edition of *TSC Alert* – an online research newsletter for individuals interested in Tuberous Sclerosis Complex (TSC) research and clinical care. This online newsletter contains information of interest to the TSC research and health care community. Please forward this newsletter to colleagues who are interested in TSC. To be added/deleted to/from the mailing list for *TSC Alert* and/or to submit information for the October 2006 *TSC Alert* contact: vwhittemore@tsalliance.org

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SAVE THE DATE

May 24-26, 2007

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

Venue: Grand Hotel Palazzo Carpegna, Rome, Italy

Information: curatolo@uniroma2.it

September 23-25, 2007

Tuberous Sclerosis Complex: From Genes to New Therapeutics

International TSC Conference organized by the Tuberous Sclerosis Alliance

Loews Annapolis Hotel, Annapolis, MD

More information coming soon!

September 11-14, 2008

International TSC Conference

Organized by the Tuberous Sclerosis Association, U.K.

Brighton, U.K.

More information coming soon!

REQUEST FOR INFORMATION

Request for Information (RFI): Proposed Policy for Sharing of Data obtained in NIH supported or conducted Genome-Wide Association Studies (GWAS)

Notice Number: NOT-OD-06-094

Key Dates

Release Date: August 30, 2006

Response Date: October 31, 2006

Issued by

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

The NIH is seeking comments regarding a proposed policy for NIH supported or conducted Genome-Wide Association Studies (GWAS). A genome-wide association study is currently defined as any study of genetic variation across the entire human genome that is designed to identify genetic associations with observable traits (such as blood pressure or weight), or the presence or absence of a disease or condition. The proposed policy addresses (1) data sharing procedures, (2) data access principles, (3) intellectual property and (4) issues regarding the protection of research participants through all phases of GWAS. Many of the principles contained in the policy reflect and extend existing NIH policies (e.g., the 2003 [data sharing policy](#)¹) and other recent NIH discussions.²

The goal of the proposed policy is to advance science for the benefit of the public through the creation of a centralized NIH GWAS data repository. Maximizing the availability of resources facilitates research and enables medical science to better address the health needs of people based on their individual genetic information. The NIH is seeking public input and advice on the overall concept of the proposed policy and specific feedback on the following questions:

1. What are the potential benefits and risks associated with wide sharing of phenotypic and genotypic data where identifying information has been removed?
2. In addition to removing personal identifying information, what protections are needed to minimize risks to research participants whose phenotypic and genotypic data are included in a centralized NIH data repository and shared with qualified investigators for research purposes?
3. What are the advantages and disadvantages of the proposed:
 - a. centralized NIH data repository?
 - b. approach to data submission?
 - c. approach to scientific publication?
 - d. approach to intellectual property?
4. What specific resources may investigators and institutions need to meet the goals of this proposed policy?

The NIH encourages comments concerning its proposed policy to enhance access to GWAS data as outlined in this notice. Persons, groups, and organizations interested in commenting on NIH's proposed policy should direct their comments to the following NIH Web site:

http://grants.nih.gov/grants/guide/rfi_files/NOT-OD-06-094_rfi_add.htm. As an alternative, comments may be submitted by e-mail to GWAS@nih.gov or sent by mail to the following address:

NIH GWAS RFI Comments, National Institutes of Health, Office of Extramural Research, 6705 Rockledge Drive, Room 350, Bethesda, MD 20892-7963.

For additional information regarding this Request for Information, please visit:

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-06-094.html>

Request for Information: Tuberous Sclerosis Complex Research Program, Department of Defense

The Department of Defense Tuberous Sclerosis Complex Research Program (TSCRCP) is launching a request for information (RFI) regarding TSC research and seeks your input.

The TSCRCP is nearing its 5-year anniversary! To achieve the goals of improving the detection, diagnosis, and treatment of TSC, funding has encompassed basic science, development of preclinical tools and reagents, and natural history studies.

Over the last 5 years, funding for the TSCRCP has increased from \$1M to \$4.3M. We are enthusiastic about expanding the program and want to accomplish this in the best way possible. Therefore, we welcome your ideas about where the research field is going and how the TSCRCP can best facilitate progress. We anticipate that responses to this RFI will help us identify gaps and barriers in TSC research, thereby enabling us to develop a strategy to target support to critical areas of research.

Please download and complete the attached RFI. When responding to the questions, please think as broadly as possible. We value your perspective as a member of the TSC research community. Outcomes of this RFI will help the TSCRCP launch new funding initiatives targeted to support critical areas of research.

Please email your completed RFI to cdmrp.pa@amedd.army.mil or fax it to **301-619-7792** by **September 8, 2006**.

[Request for Information \(Down load\)](#)

FUNDING OPPORTUNITIES



PKD/TSC Collaborative Research Awards

Deadline for Letter of Intent: October 31, 2006

The PKD Foundation and the Tuberous Sclerosis Alliance (TS Alliance) endeavor to stimulate, support and coordinate research that will lead to a cure for polycystic kidney disease (PKD) and tuberous sclerosis complex (TSC), while improving the lives of those affected. This joint initiative is intended

to foster research that impacts both PKD and TSC by encouraging researchers to work collaboratively.

The PKD/TSC Collaborative Research Awards will focus support on:

- Research that reflects innovative approaches and techniques
- Research that will develop necessary pilot data for seeking larger awards from the NIH, DOD and other funding sources

PKD/TSC Collaborative Research Awards are designed to provide funding for a collaborative study on TSC and PKD on:

- Mechanisms of action and/or interaction of the genes for TSC and PKD
- Mechanisms of renal cyst formation in PKD and TSC
- Development and preclinical testing of candidate therapeutics for PKD and TSC
- Research on the overlapping clinical manifestations of PKD and TSC

This grant mechanism IS NOT designed to support:

- Clinical trial development and/or clinical trials
- Support for predoctoral students or post doctoral fellows

Amounts: Maximum annual budget of \$75,000 per year for one- or two-year awards; total not to exceed \$150,000

Indirect Costs: The PKD Foundation and the TS Alliance do not support any indirect costs on any of their grant awards

Requisites:

- Open to investigators at established academic and/or research institutions worldwide.
- The proposed project is focused on research relevant to both PKD and TSC and the overlapping areas of research.

Grant Review: A joint PKD Foundation/TS Alliance Grant Review Panel will review all applications submitted in response to this RFP. All grants recommended for funding will receive final approval by both the PKD Foundation and the TS Alliance Boards of Directors.

Deadlines:

Letter of Intent: October 31, 2006

Deadline for Receipt of Completed Application: January 15, 2007

Awards Announced: June 2007

Earliest Project Start Date: July 1, 2007

Additional information is available on the PKD Foundation at: <http://www.pkdcure.org> and the TS Alliance Website at: <http://www.tsalliance.org>

For any related inquiries, please contact us at:

Lorrie Rome, M.S.
National Director – Scientific Programs
PKD Foundation
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Kansas City, MO 64114-3367
USA
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USA
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E-mail: vwhittemore@tsalliance.org

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

National Institute of Neurological Disorders and Stroke
National Cancer Institute
National Institute of Arthritis and Musculoskeletal and Skin Diseases
National Institute of Diabetes and Digestive and Kidney Diseases

National Institute of Mental Health
Tuberous Sclerosis Alliance
Application Receipt/Submission Date(s): Multiple dates, see announcement.
<http://grants.nih.gov/grants/guide/pa-files/PAS-06-205.html>

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

National Institute of Neurological Disorders and Stroke
National Cancer Institute
National Institute of Arthritis and Musculoskeletal and Skin Diseases
National Institute of Diabetes and Digestive and Kidney Diseases
National Institute of Mental Health
Tuberous Sclerosis Alliance
Application Receipt/Submission Date(s): Multiple dates, see announcement.
<http://grants.nih.gov/grants/guide/pa-files/PAS-06-206.html>

National Research Service Award Postdoctoral Fellowships In Epidemiology, Clinical Trials, And Outcomes Research In Skin Diseases (F32) (PAR-06-536)

National Institute of Arthritis and Musculoskeletal and Skin Diseases
Application Receipt/Submission Date(s): Application Receipt Date(s): Oct. 23, 2006; Feb. 23, June 23, Oct. 23, 2007; and Feb. 23, June 23, 2008
<http://grants.nih.gov/grants/guide/pa-files/PAR-06-536.html>

**Medical Foundation Invites Applications for Research Program in Brain Circuitry
Deadline: September 12, 2006**

The Medical Foundation (<http://www.tmfnet.org/>) is a nonprofit, public health and medical research funding organization committed to helping people live healthier lives and creating healthy communities through prevention, health promotion, and research.

The Medical Foundation's Research Grants Division administers programs for clients who support innovative research in the biomedical sciences, clinical investigation, and community health.

As part of this program, Bank of America has announced the creation of the Robert Leet and Clara Guthrie Patterson Trust Postdoctoral Fellowship Program in Brain Circuitry. Research conducted by Patterson Trust Fellows will seek fundamental insights into the mechanisms by which neural circuits control behavior. Through these insights, it may become possible to clarify the root causes of diseases that affect millions, including schizophrenia, mood disorders, degenerative brain disorders, epilepsy, and neurodevelopmental disorders such as autism.

Awards will be made to investigators working in nonprofit research institutions in Connecticut, New Jersey, and New York.

Up to ten two-year awards will be made, with at least two designated for each of the three eligible states. Two-year stipends ranging from \$44,500 to \$54,000 per year will fund postdoctoral fellows whose research has direct relevance to the understanding of brain circuitry.

Application materials are available at the Medical Foundation Web site.

RFP Link:

<http://fconline.foundationcenter.org/pnd/10003586/tmfnet>

For additional RFPs in Medical Research, visit:

http://foundationcenter.org/pnd/rfp/cat_medical_research.jhtml

Parents Against Childhood Epilepsy, Inc. (PACE)

A Research and Education Fund

Deadline: September 18, 2006

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 PACE is interested in stimulating 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
- Neuroimmunological 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 18, 2006.

You can reach PACE online at: www.paceusa.org

E-mail: pacenyemail@aol.com

FAX: 212-327-3075

Phone: 212-665-PACE (7223)

Solicitation of Compounds for High Throughput Screening (HTS) in the Molecular Libraries Screening Centers Network (MLSCN) (NOT-RM-06-017)

National Institute of Mental Health

<http://grants.nih.gov/grants/guide/notice-files/NOT-RM-06-017.html>

Exploratory/Developmental Grant for Clinical Studies of Complementary and Alternative Medicine (R21) (PA-06-510)

National Center for Complementary and Alternative Medicine

National Cancer Institute

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

<http://grants.nih.gov/grants/guide/pa-files/PA-06-510.html>

Predocutorial Training at the Interface of the Behavioral and Biomedical Sciences (T32) (PAR-06-503)

National Institute of General Medical Sciences

Application Receipt/Submission Date(s): October 24, 2006; September 10, 2007; September 10, 2008

<http://grants.nih.gov/grants/guide/pa-files/PAR-06-503.html>

Development and Application of PET and SPECT Imaging Ligands as Biomarkers for Drug Discovery and for Pathophysiological Studies of CNS Disorders (R21) (PA-06-461)

National Institute of Mental Health

National Institute on Aging

National Institute on Alcohol Abuse and Alcoholism

National Institute of Biomedical Imaging and Engineering

National Institute on Drug Abuse

National Institute of Neurological Disorders and Stroke

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

<http://grants.nih.gov/grants/guide/pa-files/PA-06-461.html>

Development and Application of PET and SPECT Imaging Ligands as Biomarkers for Drug Discovery and for Pathophysiological Studies of CNS Disorders (R33) (PA-06-462)

National Institute of Mental Health

National Institute on Aging

National Institute on Alcohol Abuse and Alcoholism

National Institute on Drug Abuse
National Institute of Neurological Disorders and Stroke
Application Receipt/Submission Date(s): Multiple dates, see announcement.
<http://grants.nih.gov/grants/guide/pa-files/PA-06-462.html>

Development and Application of PET and SPECT Imaging Ligands as Biomarkers for Drug Discovery and for Pathophysiological Studies of CNS Disorders (Phased Innovation Award [R21/R33]) (PA-06-463)

National Institute of Mental Health
National Institute on Aging
National Institute on Alcohol Abuse and Alcoholism
National Institute on Drug Abuse
Application Receipt/Submission Date(s): Multiple dates, see announcement.
<http://grants.nih.gov/grants/guide/pa-files/PA-06-463.html>

Mentored Clinical Scientist Research Career Development Award (K08) (PA-06-512)

National Institute on Aging
National Center for Complementary and Alternative Medicine
National Cancer Institute
National Eye Institute
National Heart, Lung, and Blood Institute
National Institute on Alcohol Abuse and Alcoholism
National Institute of Allergy and Infectious Diseases
National Institute of Arthritis and Musculoskeletal and Skin Diseases
National Institute of Child Health and Human Development
National Institute on Drug Abuse
National Institute on Deafness and Other Communication Disorders
National Institute of Dental and Craniofacial Research
National Institute of Diabetes and Digestive and Kidney Diseases
National Institute of Environmental Health Sciences
National Institute of General Medical Sciences
National Institute of Mental Health
National Institute of Neurological Disorders and Stroke
Office of Dietary Supplements
Application Receipt/Submission Date(s): Multiple dates, see announcement.
<http://grants.nih.gov/grants/guide/pa-files/PA-06-512.html>

Chronic Lung Diseases Genetics and Genomics: Career Development Program (K12) (RFA HL-07-004)

National Heart Lung, and Blood Institute
Applications/Proposals Due: November 30, 2006
[RFA-HL-07-004: Career Development Program in the Genetics and Genomics of Lung Diseases \(K12\)](http://grants.nih.gov/grants/guide/pa-files/PA-06-512.html)

Lung Stem Cell Biology and Cell Based Therapy: Collaborative Studies (RFA HL-07-003)

Applications/Proposals Due: December 12, 2006
[RFA-HL-07-003: Collaborative Studies on Lung Stem Cell Biology and Cell Based Therapy \(R01\)](http://grants.nih.gov/grants/guide/pa-files/PA-06-512.html)

Extramural Pediatric Research Loan Repayment Program (LRP) (PA-06-516)

National Institutes of Health
Application Receipt/Submission Date(s): September 1, 2006 through December 1, 2006, 8 p.m. EST
<http://grants.nih.gov/grants/guide/pa-files/PA-06-516.html>

Extramural Loan Repayment Program for Clinical Researchers (LRP) (PA-06-517)

National Institutes of Health
Application Receipt/Submission Date(s): September 1, 2006 - December 1, 2006, 8 P.M. EST
<http://grants.nih.gov/grants/guide/pa-files/PA-06-517.html>

Networks and Pathways Collaborative Research Projects (R01) (PA-06-522)

National Center for Research Resources

National Cancer Institute

National Heart, Lung, and Blood Institute

National Institute on Aging

National Institute on Drug Abuse

National Institute of Diabetes and Digestive and Kidney Diseases

National Institute of Environmental Health Sciences

National Institute of General Medical Sciences

National Institute of Mental Health

National Institute of Neurological Disorders and Stroke

Office of Dietary Supplements

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

<http://grants.nih.gov/grants/guide/pa-files/PA-06-522.html>

Predocutorial Training Program from NIGMS

The National Institute of General Medical Sciences has announced a new predoctoral training program to prepare scientists to conduct research at the interface of the basic behavioral and biomedical sciences. For more information, go to <http://grants1.nih.gov/grants/guide/pa-files/PAR-06-503.html>.

NEW TSC PUBLICATIONS

[No authors listed] (2006) [Leiomyomatosis of the lung.] Probl Tuberk Bolezn Legk (7):47-50
[Article in Russian]

Area G, Pacheco E, Alfonso I, Duchowny MS, Melnick SJ (2006) Characteristic brain magnetic resonance imaging (MRI) findings in neonates with tuberous sclerosis complex. J Child Neurol 21(4):280-5

Astrinidis A, Henske EP (2006) Mutation detection in tumor suppressor genes using archival tissue specimens. Methods Mol Med 126:185-96

Binitha MP, Thomas D, Asha LK (2006) Tuberous sclerosis complex associated with dyschromatosis universalis hereditaria. Indian J Dermatol Venereol Leprol 72(4):300-2

Buoni S, Zannolli R, de Santi M, Macucci F, Havek J, Orsi A, Scarinci R, Buscalferri A, Cuccia A, Zappella M, Miracco C (2006) Neurocutaneous syndrome with mental delay, autism, blockage in intracellular vesicular trafficking and melanosome defects. Eur J Neurol 13(8):842-51

Cisse A, Cisse AF, Toure A, Souare IS, Bah H, Kourouma S, Cisse B, Koulibaly M, Morel Y, Diaby MM, Kone S, Ka ML, Doukoure M (2006) [Clinical and tomographic aspects of 29 cases of phakomatosis in Guinea.] Med Trop (Mars) 66(3):247-51 [Article in French]

Clements D, Mayer RJ, Johnson S (2006) Sub-cellular distribution of the TSC-2 gene product tuberin is driven by multiple localisation sequences and is cell cycle dependent. Am J Physiol Lung Cell Mol Physiol 2006 Aug 11 [Epub ahead of print]

Dash PK, Orsi SA, Moore AN (2006) Spatial memory formation and memory-enhancing effect of glucose involves activation of the tuberous sclerosis complex-Mammalian target of rapamycin pathway. J Neurosci 26(31):8048-56

- Eto I (2006) Nutritional and chemopreventive anti-cancer agents up-regulate expression of p27Kip1, a cyclin-dependent kinase inhibitor, in mouse JB6 epidermal and human MCF7, MDA-MB-321 and AU565 breast cancer cells. *Cancer Cell Int* 2006 Aug 9 6(1):20 [Epub ahead of print]
- Gimeno Argente V, Bosquet Sanz M, Bonillo Garcia MA, Gomez Perez L, Pontones Moreno JL, Jimenez Cruz JF (2006) [Conservative surgery of bilateral renal angiomyolipoma during pregnancy.] *Actas Urol Esp* 30(6):633-7 [Article in Spanish]
- Jozwiak J, Jozwiak S (2006) Giant Cells: Contradiction to Two-Hit Model of Tuber Formation? *Cell Mol Neurobiol* 2006 Aug 9 [Epub ahead of print]
- Jozwiak S, Kotulska K (2006) Are all prenatally diagnosed multiple cardiac rhabdomyomas a sign of tuberous sclerosis? *Prenat Diagn* 26(9):867-869 [Epub ahead of print]
- Jozwiak S, Kotulska K, Kasprzyk-Obara J, Domanska-Pakiela D, Tomyń-Draik M, Roberts P, Kwiatkowski D (2006) Clinical and Genotype Studies of Cardiac Tumors in 154 Patients With Tuberous Sclerosis Complex. *Pediatrics* 2006 Aug 28 [Epub ahead of print]
- Krapp M, Axt-Flieđner R, Gopel W, Johannsen W (2006) Prenatal diagnosis of a renal tumor in tuberous sclerosis. *Ultrasound Obstet Gynecol* 2006 Aug 31 28(4):536 [Epub ahead of print]
- Liu S, An N, Yang H, Yang M, Hou Z, Liu L, Liu Y (2006) Pediatric intractable epilepsy syndromes: Reason for early surgical intervention. *Brain Dev* 2006 Aug 21 [Epub ahead of print]
- Matsumoto F, Fujii H, Abe M, Kajino K, Kobayashi T, Matsumoto T, Ikeda K, Hino O (2006) A novel tumor marker, Niban, is expressed in subsets of thyroid tumors and Hashimoto's thyroiditis. *Hum Pathol* 2006 Aug 31 [Epub ahead of print]
- McCormack, FX (2006) Lymphangioliomyomatosis. *MedGenMed* 18;8(1):15
- Orens JB, Estenne M, Arcasov S, Conte JV, Corris P, Egan JJ, Egan T, Keshavjee S, Knoop C, Kotloff R, Martinez FJ, Nathan S, Palmer S, Patterson A, Singer L, Snell G, Studer S, Vachiery JL, Glanville AR, Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation (2006) International guidelines for the selection of lung transplant candidates: 2006 update--a consensus report from the Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation. *J Heart Lung Transplant* 25(7):745-55
- Parfitt JR, Bella AJ, Izawa JI, Wehrli BM (2006) Malignant neoplasm of perivascular epithelioid cells of the liver. *Arch Pathol Lab Med* 130(8):1219-22
- Shah OJ, Hunter T (2006) Turnover of the Active Fraction of IRS1 Involves Raptor-mTOR- and S6K1-Dependent Serine Phosphorylation in Cell Culture Models of Tuberous Sclerosis. *Mol Cell Biol* 26(17):6425-34
- Shields CL, Benevides R, Materin MA, Shields JA (2006) Optical Coherence Tomography of Retinal Astrocytic Hamartoma in 15 Cases. *Ophthalmology* 113(9):1553-1557
- Sodhi A, Chaisuparat R, Hu J, Ramsdell AK, Manning BD, Sausville EA, Sawai ET, Molinolo A, Gutkind JS, Montaner S (2006) The TSC2/mTOR pathway drives endothelial cell transformation induced by the Kaposi's sarcoma-associated herpesvirus G protein-coupled receptor. *Cancer Cell* 10(2):133-43
- Sparagana SP (2006) Tuberous sclerosis complex: from basic science to clinical phenotypes: international review of child neurology series. *Neurology* 67(3):546

Steiger HJ (2006) Preventive neurosurgery: population-wide check-up examinations and correction of asymptomatic pathologies of the nervous system. *Acta Neurochir (Wien)* 2006 Sep 8 [Epub ahead of print]

Vary TC, Lynch CJ (2006) Meal feeding stimulates phosphorylation of multiple effector proteins regulating protein synthetic processes in rat hearts. *J Nutr* 136(9):2284-90

Weber RG, Hoischen A, Ehrler M, Zipper P, Kaulich K, Blaschke B, Becker AJ, Weber-Mangal S, Jauch A, Radlwimmer B (2006) Frequent loss of chromosome 9, homozygous CDKN2A/p14(ARF)/CDKN2B deletion and low TSC1 mRNA expression in pleomorphic xanthoastrocytomas. *Oncogene* 2006 Aug 7 [Epub ahead of print]

Wienecke R, Fackler I, Linsenmaier U, Mayer K, Licht T, Kretzler M (2006) Antitumoral activity of rapamycin in renal angiomyolipoma associated with tuberous sclerosis complex. *Am J Kidney Dis* 2006 Sep 48(3):e27-9

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

Wilson C, Bonnet C, Guy C, Idziaszczyk S, Colley J, Humphreys V, Maynard J, Sampson JR, Cheadle JP (2006) Tsc1 Haploinsufficiency without Mammalian Target of Rapamycin Activation Is Sufficient for Renal Cyst Formation in Tsc1+/- Mice. *Cancer Res* 66(16):7934-8

Witzig TE, Kaufmann SH (2006) Inhibition of the phosphatidylinositol 3-kinase/ mammalian target of rapamycin pathway in hematologic malignancies. *Curr Treat Options Oncol* 7(4):285-94

Wong R, Rajendram R, Poole TR (2006) Keratoconus in tuberous sclerosis. *Eye* 2006 Sep 1 [Epub ahead of print]

Wong V (2006) Study of the Relationship Between Tuberous Sclerosis Complex and Autistic Disorder. *J Child Neurol* 21(3):199-204

Xu Y, Chen SY, Ross KN, Balk SP (2006) Androgens Induce Prostate Cancer Cell Proliferation through Mammalian Target of Rapamycin Activation and Post-transcriptional Increases in Cyclin D Proteins. *Cancer Res* 66(15):7783-92

Zaroff CM, Barr WB, Carlson C, Lajoie J, Madhavan D, Miles DK, Nass R, Devinsky O (2006) Mental retardation and relation to seizure and tuber burden in tuberous sclerosis complex. *Seizure* 2006 Aug 25 [Epub ahead of print]

Zhang M, Fang X, Liu H, Wang S, Yang D (2006) Blockade of AKT activation in prostate cancer cells with a small molecule inhibitor, 9-chloro-2-methylellipticine acetate (CMEP). *Biochem Pharmacol* 2006 Aug 31 [Epub ahead of print]

CONFERENCES & SEMINARS

September 15-16, 2006 in Philadelphia

September 29-30, 2006 in Seattle

October 13-14, 2006 in Scottsdale, AZ

November 10-11, 2006 in Chicago, IL

Roadmap for Research

Many clinicians have a desire to include research in their professional lives. However, training in how to conduct high quality research is difficult to find, so the research experience can be

unsatisfying for all involved. In fact, 80% of first time investigators never participate in another trial. The Roadmap to Research symposia address this national need not just by providing participants with a working knowledge of the research process, but also by providing the tools necessary to establish and manage a successful research practice.

For more information, contact: 1-877-224-3278 or register on the web at:

<http://www.heartgallerypress.com/venues.php>

September 19, 2006

The second annual NIH Director's Pioneer Award Symposium will be held on Tuesday, September 19, 2006, in Masur Auditorium of the Clinical Center (Building 10) on the NIH campus in Bethesda, MD. The symposium will begin at 8:15 a.m. with remarks by NIH Director Elias A. Zerhouni, M.D. The symposium also feature research talks by the 2005 Pioneer Award recipients, a poster session by 2004 and 2005 awardees and members of their labs, and an announcement of the awardees for 2006. Talks continue until the poster session, which runs from 3:40 p.m. to 5:30 p.m. Attendance is free and no registration is required. The symposium agenda is at

<http://nihroadmap.nih.gov/pioneer/symposium2006>.

September 28 – October 1, 2006

NORD Annual Conference: *Road Map for Rare Disease Research*

Hyatt Regency Bethesda, Bethesda, MD

www.rarediseases.org

October 3, 2006

5:00 pm PT/8:00 pm ET (Teleconference Series)

Coping with Cancer at School: Finding Support at College When Your Parent Has Cancer (for all cancer types)

Presenter: Heather Servaty-Seib, Ph.D., Purdue University Faculty, Counseling and Development Program

Co-Sponsors: Students of Ailing Mothers and Fathers, Georgetown University; National Brain Tumor Foundation

To register, visit www.braintumor.org and fill out the online form or call 1-800-934-2873

October 12-16, 2006

55th Annual Montagna Symposium on the Biology of Skin: *Signaling to Structures: Skin Appendages, Development and Diseases*

Salishan Spa & Golf Resort, Oregon

E-mail: nowinasa@ohsu.edu

www.montagnasymposium.org

October 24, 2006

1 pm PT/4 pm ET (Teleconference Series)

New Advances in Chemotherapy for Brain Tumor Patients

Presenter: Howard Fine, M.D., Chair of the Neuro-oncology Branch of the National Cancer Institute

Sponsors: National Brain Tumor Foundation

To register, visit www.braintumor.org and fill out the online form or call 1-800-934-2873

November 12-15, 2006

Fifth Annual AACR International Conference

Frontiers in Cancer Prevention Research

Hynes Convention Center, Boston, MA

www.aacr.org

December 1-5, 2006

2006 AES Annual Meeting/North American Regional Epilepsy Congress

San Diego Convention Center

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

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

December 5, 2006

1 pm PT/4 pm ET (Teleconference Series)

Understanding your MRI Report: A Guide for Brain Tumor Patients

Presenter: Philip Gutin, M.D., Chief, Neurosurgical Service and Fred Lebow, Chair in Neuro-oncology, Memorial Sloan-Kettering Cancer Center

Sponsors: National Brain Tumor Foundation

To register, visit www.brainumor.org and fill out the online form or call 1-800-934-2873

February 1-2, 2007

National Coalition for Health Professional Education in Genetics (NCHPEG) and Genetics Resources on the Web (GROW) 10th Annual Meeting: Pharmacogenomics

Hyatt Regency Bethesda, Bethesda, MD

Abstract deadline: October 6, 2006

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

March 29-30, 2007

Curing Epilepsy 2007: Translating Discoveries into Therapies

Natcher Conference Center, Bethesda, MD

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

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

April 19-22, 2007

2007 LAM International Research Conference

The LAM Foundation

Cincinnati, OH

<http://www.thelamfoundation.org>

May 9-12, 2007

68th Annual Meeting of the Society for Investigative Dermatology

The Century Plaza Hotel, Los Angeles, CA

E-mail: kimble@sidnet.org

www.sidnet.org

May 24-26, 2007

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

Venue: Grand Hotel Palazzo Carpegna, Rome, Italy

Information: curatolo@uniroma2.it

September 23-25, 2007

Tuberous Sclerosis Complex: From Genes to New Therapeutics

International TSC Research Symposium organized by the Tuberous Sclerosis Alliance

Loews Annapolis Hotel, Annapolis, MD

More information coming soon on the TS Alliance website at www.tsalliance.org

September 11-14, 2008

International TSC Conference

Organized by the Tuberous Sclerosis Association, U.K.

Brighton, U.K.

More information coming soon!

NEWS

Fly Genetics Reveal Key Workings Of Atkins Diet

Metabolic syndrome, an aging-associated group of disorders that includes [insulin resistance](#), heart disease and high lipid levels, may be treatable thanks to a newly discovered role for a regulatory gene, according to a team of scientists at the Burnham Institute for [Medical Research](#). In addition, the scientists found that this single gene may contribute to the body's responses to caloric restriction and may explain some aspects of the [Atkins Diet](#).

The gene's new function was discovered in Drosophila fruit flies; previously it was associated solely with the control of growth. Until now, how the gene regulates insulin, as well as other symptoms of metabolic syndrome, was largely unknown. The study was conducted by Sean Oldham, Ph.D., assistant professor, and his colleagues at the Burnham and the National Institute on Alcoholism and [Alcohol Abuse](#). Oldham's findings appear in the journal *Cell Metabolism* to be released on August 8th.

Using fruit flies bred with a newly created mutant form of the gene TOR (short for target of rapamycin), Oldham and his colleagues were able to determine how the TOR pathway interacted with other important regulators of insulin, glucose and [lipid](#) metabolism. TOR is an ancient gene, found in nearly all animal and plant cells. The researchers discovered that their new mutant fly reduced TOR function, allowing them to observe what happens when TOR's influence is removed.

Reductions in TOR function lowered glucose and lipid levels in the body. They also blocked the function of another important insulin regulator, a factor called FOXO, which is known to be a critical mediator of insulin signals and therefore glucose and lipid metabolism. In addition, flies with the mutated form of TOR had longer life spans than control flies.

"It has been unclear how TOR signaling affects the insulin pathway," said Oldham. "Our study adds another dimension to TOR's activity by revealing unexpected and novel levels of beneficial regulation of insulin metabolism, by reducing insulin resistance. This study provides the first details of how TOR may regulate energy homeostasis and responses to aging, in particular the coordination of weight reduction effects caused by caloric restriction and, in humans, it may explain the effects of the Atkins diet. It suggests that reducing TOR function could lead to a possible treatment for any or all symptoms of metabolic syndrome and insulin resistance."

Oldham's group, in collaboration with Dr. Rolf Bodmer at Burnham, showed that reducing TOR function also blocks the age-dependent decline of heart function, providing a partial explanation for why excess calories from overeating can lead to resistance to insulin's ability to process sugars and may contribute to reduced heart function.

Dr. Oldham and his colleagues are continuing their search to understand how TOR mediates caloric restriction, aging and other effects on insulin signaling and metabolism. They want to understand TOR's role in the relationship between growth, metabolism and aging, both in healthy individuals and individuals with metabolic diseases. The researchers also are screening possible drugs that could treat metabolic syndrome by reducing TOR function.

"This study provides the first direct evidence that reducing TOR function could be clinically beneficial to counter insulin resistance, metabolic syndrome and diabetes," said Oldham. "We believe further studies on fruit flies are invaluable to discovering more details about this pathway, and will give us indispensable insight into pathological aspects of aging and senescence."

This study was supported by a grant from the National Heart Lung and Blood Institute of the National Institutes of Health, and with support from The Fishman Fund.

Researchers Identify Human DNA on the Fast Track

Since completing the sequencing of the chimpanzee genome last year, geneticists have spent many hours comparing human DNA sequences to those of our closest evolutionary relative, looking for the differences that distinguish the two species. Now a team of HHMI researchers, David Haussler, Ph.D. and their colleagues at the University of California, Santa Cruz, have found the human DNA sequence with the most dramatically increased rate of change. This research was published in the August 16, 2006, issue of Nature. For the full story, go to: <http://www.hhmi.org//news/haussler20060816.html>

Experimental Medication Kicks Depression in Hours Instead of Weeks

<http://www.nimh.nih.gov/press/ketamine.cfm>

Shy Temperament: More than Just Fearful

<http://www.nimh.nih.gov/press/me-striatuminhib-kids.cfm>

Receptor Knockout Yields an Adventurous Mouse

<http://www.nimh.nih.gov/press/conflictanxiety.cfm>

Males with Autism Have Fewer Cells in Brain's Emotional Memory Hub

<http://www.nimh.nih.gov/press/schumannautism.cfm>

TSC CLINICAL TRIALS AND STUDIES

1. Sirolimus in Treating Patients with Angiomyolipoma of the Kidney

Official Title: Phase II Study of Sirolimus in Patients with Angiomyolipoma of the Kidney Secondary to Tuberous Sclerosis or Lymphangioleiomyomatosis

Study Purpose:

Rationale: Drugs used in chemotherapy, such as sirolimus, work in different ways to stop the growth of tumor cells, either by killing the cells or by stopping them from dividing.

Purpose: This phase II trial is studying how well sirolimus works in treating individuals with angiomyolipoma of the kidney.

Eligibility:

Ages Eligible for Study: 18 Years - 65 Years

Genders Eligible for Study: Both

Location and Contact Information:

Please refer to this study by ClinicalTrials.gov identifier NCT00126672

Connecticut

Connecticut Children's Medical Center, Hartford, Connecticut, 06106, United States; Recruiting Francis J. DiMario, MD 860-545-9460

Massachusetts

Massachusetts General Hospital, Boston, Massachusetts, 02114, United States; Recruiting Elizabeth Thiele, MD, PhD 617-726-6540

New York

New York University Medical Center, New York, New York, 10016, United States; Recruiting

Daniel K. Miles, MD 212-263-8318

Ohio

Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, 45229-3039, United States; Recruiting
David Franz, MD 513-636-4222 david.franz@chmcc.org

Pennsylvania

University of Pennsylvania Medical Center, Philadelphia, Pennsylvania, 19104-4283, United States; Recruiting
Peter Crino, MD, PhD 215-349-5312

Texas

University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, 75390, United States; Recruiting
Arthur I. Sagalowsky, MD 214-645-8797 arthur.sagalowsky@utsouthwestern.edu

Study chairs or principal investigators: Sandra Dabora, MD, PhD, Study Chair, Brigham and Women's Hospital

For more information about this clinical trial, visit:
<http://www.cancer.gov/clinicaltrials/DFCI-04298>

2. Siblings Wanted for a Modifier Gene Research Study



The Herscot Center for Tuberous Sclerosis Complex and the Center for Human Genetic Research at the Massachusetts General Hospital are trying to identify additional genes that play a role in neurological problems in TSC.

We would like to enroll TSC siblings over 2 years of age that differ in their expression of
autism or infantile spasms or uncontrollable seizures

Participants will have:

- clinical evaluation by a neurologist specialized in TSC (Dr. Elizabeth Thiele)
- blood drawn
- brain MRI
- EEG
- neuropsychological testing (only for siblings differing in autism)

The whole study will take about 2 days to complete. There is no direct cost to the participants.

Travel and lodging will be reimbursed for participants who live more than 2 hours away from Boston.

For more information contact Susana Camposano 617-726 0240 (M-F, 8-5),
scamposano@partners.org

TSC INFORMATION

For information about TSC and the Tuberous Sclerosis Alliance, 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.