



TSC ALERT

November 2007

Table of Contents

[Clicking on one of the headings takes you directly to that section of TSC Alert]

IMPORTANT SUBMISSION DEADLINES	1
FUNDING OPPORTUNITIES	2
NEW TSC PUBLICATIONS	5
CONFERENCES AND SEMINARS	9
NEWS	10
TSC CLINICAL TRIALS AND STUDIES	11
TSC INFORMATION	12

IMPORTANT SUBMISSION DEADLINES

TS Alliance Announces New Requests for Applications:

The Tuberous Sclerosis Alliance announces Requests for Applications for the following grant mechanisms:

- Predoctoral, Postdoctoral and Clinical Fellowships
- TSC Innovator Awards
- TSC Supplemental Funding Awards
- TSC Workshop/Conference Awards (one year awards only)

Amounts: Up to \$60,000 per year for three-year awards; total not to exceed \$180,000

Indirect Costs: The TS Alliance will support up to an additional 10% indirect costs on research grant awards (maximum total request of \$66,000 per year)

Requisites: Open to investigators at established academic and/or research institutions worldwide

Letter of Intent: Before submitting an application for research support, an applicant must submit a Letter of Intent (LOI) briefly describing the project. If the research proposed in the LOI meets the TS Alliance's funding priorities in a given year, the investigator will be invited to submit a formal proposal. The TS Alliance Grant Review Committee carefully reviews all LOIs submitted for review.

Deadline for Receipt of Letter of Intent: December 17, 2007

Deadline for Receipt of Completed Application: March 3, 2008

Awards Announced: June 2008

Earliest Project Start Date: July 1, 2008

Additional information, including the Letter of Intent Form, is available on the TS Alliance Website at: <http://www.tsalliance.org>

Electronic submissions are mandatory using the online TS Alliance grant application forms. No paper grant applications sent via the mail or FAX will be accepted.

FUNDING OPPORTUNITIES

FEDERAL FUNDING AGENCIES

Understanding and Treating Tuberos Sclerosis Complex (R01) (PAS-07-190)

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

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

<http://grants.nih.gov/grants/guide/pa-files/PAS-07-190.html>

Multidisciplinary K12 Urologic Research (KURe) Career Development Program (RFA-DK-07-006)

National Institute of Diabetes and Digestive and Kidney Diseases

Application Receipt Date(s): March 18, 2008

<http://grants.nih.gov/grants/guide/rfa-files/RFA-DK-07-006.html>

NIDDK Limited Competition for Continuation of the Prospective Study of Chronic Kidney Disease in Children (U01) (RFA-DK-07-501)

National Institute of Diabetes and Digestive and Kidney Diseases

National Institute of Child Health and Human Development

Application Receipt Date(s): December 11, 2007

<http://grants.nih.gov/grants/guide/rfa-files/RFA-DK-07-501.html>

Enhancing Developmental Biology Research at Undergraduate Institutions (R15) (RFA-HD-07-021)

National Institute of Child Health and Human Development

Application Receipt Date(s): February 15, 2008

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HD-07-021.html>

High Throughput Tools for Brain and Behavior (SBIR [R43/R44]) (PA-08-001)

National Institute of Mental Health

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-08-001.html>

High Throughput Tools for Brain and Behavior (STTR [R41/R42]) (PA-08-002)

National Institute of Mental Health

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-08-002.html>

Network for Translational Research (NTR): Optical Imaging in Multimodal Platforms (U54) (RFA-CA-08-002)

National Cancer Institute

Application Receipt Date(s): January 24, 2008

<http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-08-002.html>

Data Coordinating Center for the HALT-Polycystic Kidney Disease Trials (U01) (RFA-DK-07-008)

National Institute of Diabetes and Digestive and Kidney Diseases

Application Receipt Date(s): December 13, 2007

<http://grants.nih.gov/grants/guide/rfa-files/RFA-DK-07-008.html>

NIH Partners in Research Program (R03) (RFA-OD-07-001)

Office of the Director, NIH
National Institute of Child Health and Human Development
National Institute of Nursing Research
Application Receipt Date(s): January 11, 2008
<http://grants.nih.gov/grants/guide/rfa-files/RFA-OD-07-001.html>

Human Tissue and Organ Research Resource (Limited Competition U42) (RFA-RR-07-006)

National Center for Research Resources
National Eye Institute
National Heart, Lung, and Blood Institute
National Institute of Allergy and Infectious Diseases
National Institute of Arthritis and Musculoskeletal and Skin Diseases
National Institute of Diabetes and Digestive and Kidney Diseases
Office of Rare Diseases
Application Receipt Date(s): January 30, 2008
<http://grants.nih.gov/grants/guide/rfa-files/RFA-RR-07-006.html>

NIDDK Medical Student Research Training Program (MSRT) (NOT-DK-08-001)

National Institute of Diabetes and Digestive and Kidney Diseases
<http://grants.nih.gov/grants/guide/notice-files/NOT-DK-08-001.html>

Request for Information (RFI): Monoclonal Antibodies for Developmental Neuroscience - Request for Targets (NIH Neuroscience Blueprint) (NOT-NS-08-001)

National Institutes of Health
National Center for Complementary and Alternative Medicine
National Center for Research Resources
National Eye Institute
National Institute on Aging
National Institute on Alcohol Abuse and Alcoholism
National Institute of Biomedical Imaging and Engineering
National Institute of Child Health and Human Development
National Institute on Drug Abuse
National Institute on Deafness and Other Communication Disorders
National Institute of Dental and Craniofacial Research
National Institute of Environmental Health Sciences
National Institute of General Medical Sciences
National Institute of Mental Health
National Institute of Mental Health
National Institute of Neurological Disorders and Stroke
Office of Behavioral and Social Science Research
<http://grants.nih.gov/grants/guide/notice-files/NOT-NS-08-001.html>

Prefrontal Cortical Influences on Brain Systems Supporting Complex Mental Function (R01) (RFA-MH-08-110)

National Institute of Mental Health
Application Receipt Date(s): January 11, 2008
<http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-08-110.html>

Prefrontal Cortical Influences on Brain Systems Supporting Complex Mental Function (R21) (RFA-MH-08-111)

National Institute of Mental Health
Application Receipt Date(s): January 11, 2008
<http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-08-111.html>

Genetic Susceptibility & Variability of Human Structural Birth Defects (R01) (PA-08-011)

National Institute of Child Health and Human Development

National Institute of Dental and Craniofacial Research

National Institute of Environmental Health Sciences

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

<http://grants.nih.gov/grants/guide/pa-files/PA-08-011.html>

Continued Development and Maintenance of Software (R01) (PAR-08-010)

National Center for Research Resources

National Cancer Institute

National Human Genome Research Institute

National Heart, Lung, and Blood Institute

National Institute on Alcohol Abuse and Alcoholism

National Institute of Biomedical Imaging and Engineering

National Institute on Drug Abuse

National Institute of General Medical Sciences

National Institute of Mental Health

National Institute of Neurological Disorders and Stroke

Application Receipt/Submission Date(s): January 17, 2008; May 21, 2008; September 22, 2008;

January 22, 2009; May 22, 2009; September 22, 2009; January 22, 2010; May 21, 2010;

September 22, 2010

<http://grants.nih.gov/grants/guide/pa-files/PA-08-010.html>

NIAMS Building Interdisciplinary Research Team (BIRT) Revision Awards (R01) (RFA-AR-08-001)

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Application Receipt Date(s): March 18, 2008

<http://grants.nih.gov/grants/guide/rfa-files/RFA-AR-08-001.html>

Molecular Therapy Core Center (P30) (RFA-DK-07-010)

National Institute of Diabetes and Digestive and Kidney Diseases

Application Receipt Date(s): March 27, 2008

<http://grants.nih.gov/grants/guide/rfa-files/RFA-DK-07-010.html>

2008 NIH Director's Pioneer Award Program (DP1) (RFA-RM-08-013)

NIH Roadmap Initiatives

Application Receipt Date(s): January 16, 2008

<http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-013.html>

NHLBI Ruth L. Kirschstein National Research Service Awards for Individual Predoctoral MD/PhD Fellows (F30) (PA-08-021)

National Heart, Lung, and Blood Institute

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

<http://grants.nih.gov/grants/guide/pa-files/PA-08-021.html>

Specialized Programs of Research Excellence (SPOREs) in Human Cancer for the Year 2008 and 2009 (P50) (PAR-08-020)

National Cancer Institute

National Institute of Dental and Craniofacial Research

National Institute of Neurological Disorders and Stroke

Application Receipt/Submission Date(s): January 23, 2008; May 23, 2008; September 23, 2008;

January 23, 2009; May 22, 2009; September 22, 2009

<http://grants.nih.gov/grants/guide/pa-files/PA-08-020.html>

AHRQ Mentored Research Scientist Development Award (K01) (PAR-08-022)

Agency for Healthcare Research and Quality

Application Receipt/Submission Date(s): January 07, 2011

<http://grants.nih.gov/grants/guide/pa-files/PAR-08-022.html>

Anemia of Inflammation and of Chronic Diseases (R01) (PAS-08-019)

National Institute of Diabetes and Digestive and Kidney Diseases

National Cancer Institute

National Heart, Lung, and Blood Institute

National Institute on Aging

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

<http://grants.nih.gov/grants/guide/pa-files/PAS-08-019.html>

NEW TSC PUBLICATIONS

Aissat N, Le Tourneau C, Ghouil A, Serova M, Bieche I, Lokiec F, Raymond E, Faivre S (2007) Antiproliferative effects of rapamycin as a single agent and in combination with carboplatin and paclitaxel in head and neck cancer cell lines. *Cancer Chemother Pharmacol* 2007 Oct 2 [Epub ahead of print]

Auvichayapat N, Tassniyom S, Treerotphon S, Auvichayapat P (2007) Treatment of infantile spasms with sodium valproate followed by benzodiazepines. *J Med Assoc Thai* 90(9):1809-14

Brewer C, Yeager N, Di Cristofano A (2007) Thyroid-stimulating hormone initiated proliferative signals converge in vivo on the mTOR kinase without activating AKT. *Cancer Res* 67(17):8002-6

Brown NF, Stefanovic-Racic M, Sipula IJ, Perdomo G (2007) The mammalian target of rapamycin regulates lipid metabolism in primary cultures of rat hepatocytes. *Metabolism* 56(11):1500-7

Chen F, Aoyama A, Okamoto T, Takahashi A, Satoda N, Fujinaga T, Shoji T, Sakai H, Matsumoto I, Wada H, Bando T (2007) [Viral infection after lung transplantation] *Kyobu Geka* 60(11):982-7 [Article published in Japanese]

Chiang GG, Abraham RT (2007) Targeting the mTOR signaling network in cancer. *Trends Mol Med* 13(10):433-42 [Epub 2007 Oct 1]

Curtis JR, Hurst E, Lee M, Sheehan DJ (2007) A true molluscum pendulum. *Int J Dermatol* 46(8):853-4

Deutsch MA, Kaczmarek I, Huber S, Schmauss D, Beiras-Fernandez A, Schmoeckel M, Ochsenkuehn R, Meiser B, Mueller-Hoecker J, Bruno Reichart B (2007) Sirolimus-associated infertility: case report and literature review of possible mechanisms. *Am J Transplant* 7(10):2414-21

Devost D, Carrier ME, Zingg HH (2007) Oxytocin-induced activation of eukaryotic elongation factor eEF2 in myometrial cells is mediated by protein kinase C. *Endocrinology* 2007 Oct 18 [Epub ahead of print]

Diekmann F, Rovira J, Carreras J, Arellano EM, Banon-Maneus E, Ramirez-Bajo MJ, Gutierrez-Dalmau A, Brunet M, Campistol JM (2007) Mammalian target of rapamycin inhibition halts the progression of proteinuria in a rat model of reduced renal mass. *J Am Soc Nephrol* 18(10):2653-60 [Epub 2007 Sep 5]

- Endo H, Murata K, Mukai M, Ishikawa O, Inoue M (2007) Activation of insulin-like growth factor signaling induces apoptotic cell death under prolonged hypoxia by enhancing endoplasmic reticulum stress response. *Cancer Res* 67(17):8095-103
- Farrell CJ, Plotkin SR (2007) Genetic causes of brain tumors: neurofibromatosis, tuberous sclerosis, von hippel-lindau, and other syndromes. *Neurol Clin* 25(4):925-46
- Finlay GA, Malhowski AJ, Liu Y, Fanburg BL, Kwiatkowski DJ, Toksoz D (2007) Selective Inhibition of Growth of Tuberous Sclerosis Complex 2 Null Cells by Atorvastatin Is Associated with Impaired Rheb and Rho GTPase Function and Reduced mTOR/S6 Kinase Activity. *Cancer Res* 67(20):9878-86
- Floto RA, Sarkar S, Perlstein EO, Kampmann B, Schreiber SL, Rubinsztein DC (2007) Small Molecule Enhancers of Rapamycin-Induced TOR Inhibition Promote Autophagy, Reduce Toxicity in Huntington's Disease Models and Enhance Killing of Mycobacteria by Macrophages. *Autophagy* 3(6):620-2 [Epub 2007 Aug 16]
- Fouladi M, Laningham F, Wu J, O'Shaughnessy MA, Molina K, Broniscer A, Spunt SL, Lockett I, Stewart CF, Houghton PJ, Gilbertson RJ, Furman WL (2007) Phase I study of everolimus in pediatric patients with refractory solid tumors. *J Clin Oncol* 25(30):4806-12
- Freilinger A, Rosner M, Hanneder M, Hengstschlager M (2007) Ras mediates cell survival by regulating tuberlin. *Oncogene* 2007 Oct 8 [Epub ahead of print]
- Fujiwara K, Iwado E, Mills GB, Sawaya R, Kondo S, Kondo Y (2007) Akt inhibitor shows anticancer and radiosensitizing effects in malignant glioma cells by inducing autophagy. *Int J Oncol* 31(4):753-60
- Grden M, Podgorska M, Kocbuch K, Rzepko R, Szutowicz A, Pawelczyk T (2007) High glucose suppresses expression of equilibrative nucleoside transporter 1 (ENT1) in rat cardiac fibroblasts through a mechanism dependent on PKC-zeta and MAP kinases. *J Cell Physiol* 2007 Oct 16 [Epub ahead of print]
- Habib SL, Danial E, Nath S, Schneider J, Jenkinson CP, Duggirala R, Abboud HE, Thameem F (2007) Genetic polymorphisms in OGG1 and their association with angiomyolipoma, a benign kidney tumor in patients with tuberous sclerosis. *Cancer Biol Ther* 7(1) [Epub ahead of print]
- Hartford CM, Ratain MJ (2007) Rapamycin: something old, something new, sometimes borrowed and now renewed. *Clin Pharmacol Ther* 82(4):381-8 [Epub 2007 Aug 29]
- Holman JD, Dyer JA (2007) Genodermatoses with malignant potential. *Curr Opin Pediatr* 19(4):446-54
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- Kameyama S, Kakita A (2007) [Magnetic resonance imaging and pathology in epilepsy. (4) Tuberous sclerosis] *No Shinkei Geka* 35(10):1027-35 [Article published in Japanese]
- Karbowiczek M, Spittle CS, Morrison T, Wu H, Henske EP (2007) mTOR Is Activated in the Majority of Malignant Melanomas. *J Invest Dermatol* 2007 Oct 4 [Epub ahead of print]

Lavin Castejon I, Mut Oltra J, Trillo Balizon C, Maldonado Barrionuevo A (2007) [Lhermitte-Duclos disease associated to Cowden disease: A case report.] *An Med Interna* 24(5):239-41 [Article published in Spanish]

Lee CH, Inoki K, Karbowiczek M, Petroulakis E, Sonenberg N, Henske EP, Guan KL (2007) Constitutive mTOR activation in TSC mutants sensitizes cells to energy starvation and genomic damage via p53. *EMBO J* 2007 Oct 25 [Epub ahead of print]

Lee CL, Frost JD Jr, Swann JW, Hrachovy RA (2007) A new animal model of infantile spasms with unprovoked persistent seizures. *Epilepsia* 2007 Oct 18 [Epub ahead of print]

Lefrou L, d'Alteroche L, Harchaoui Y, Franco D, Metman EH (2007) Peritoneovenous shunt after failure of octreotide treatment for chylous ascites in lymphangioleiomyomatosis. *Dig Dis Sci* 52(11):3188-90

Levine AJ, Hu W, Feng Z, Gil G (2007) Reconstructing Signal Transduction Pathways: Challenges and Opportunities. *Ann N Y Acad Sci* 2007 Oct 12 [Epub ahead of print]

Li Y, Wang Y, Kim E, Beemiller P, Wang CY, Swanson J, You M, Guan KL (2007) Bnip3 mediates the hypoxia-induced inhibition on mTOR by interacting with Rheb. *J Biol Chem* 2007 Oct 10 [Epub ahead of print]

Martin KA, Merenick BL, Ding M, Fetalvero KM, Rzucidlo EM, Kozul CD, Brown DJ, Chiu HY, Shyu M, Drapeau BL, Wagner RJ, Powell RJ (2007) Rapamycin promotes vascular smooth muscle cell differentiation through IRS-1/PI 3-Kinase/Akt2 feedback signaling. *J Biol Chem* 2007 Sep 30 [Epub ahead of print]

Mori N, Kyo S, Sakaguchi J, Mizumoto Y, Ohno S, Maida Y, Hashimoto M, Takakura M, Inoue M (2007) Concomitant activation of AKT with extracellular-regulated kinase 1/2 occurs independently of PTEN or PIK3CA mutations in endometrial cancer and may be associated with favorable prognosis. *Cancer Sci* 2007 Oct 9 [Epub ahead of print]

Murai N, Kaneko T (2007) [A case of jugular foramen schwannoma associated with tuberous sclerosis] *No Shinkei Geka* 35(10):1007-11 [Article published in Japanese]

Muzykewicz DA, Newberry P, Danforth N, Halpern EF, Thiele EA (2007) Psychiatric comorbid conditions in a clinic population of 241 patients with tuberous sclerosis complex. *Epilepsy Behav* 2007 Oct 11 [Epub ahead of print]

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Pacheco-Rodriguez G, Steagall WK, Crooks DM, Stevens LA, Hashimoto H, Li S, Wang JA, Darling TN, Moss J (2007) TSC2 Loss in Lymphangioleiomyomatosis Cells Correlated with Expression of CD44v6, a Molecular Determinant of Metastasis. *Cancer Res* 67(21):10573-10581

Panaretakis T, Hjortsberg L, Tamm KP, Bjorklund AC, Joseph B, Grander D (2007) IFN α Induces Nucleus-independent Apoptosis by Activating ERK1/2 and JNK Downstream of PI3K and mTOR. *Mol Biol Cell*. 2007 Oct 17 [Epub ahead of print]

Pantelis A, Bootz F, Kuhnel T (2007) [Laser skin resurfacing and fibrin sealing as successful treatment for facial angiofibromas in tuberous sclerosis.] *HNO* 2007 Oct 3 [Epub ahead of print] [Article published in German]

- Proud CG (2007) Amino acids and mTOR signalling in anabolic function. *Biochem Soc Trans* 35(Pt 5):1187-90
- Que J, Lian Q, El Oakley RM, Lim B, Lim SK (2007) PI3 K/Akt/mTOR-mediated translational control regulates proliferation and differentiation of lineage-restricted RoSH stem cell lines. *J Mol Signal* 2(1):9 [Epub ahead of print]
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- Schick V, Majores M, Koch A, Elger CE, Schramm J, Urbach H, Becker AJ (2007) Alterations of Phosphatidylinositol 3-Kinase Pathway Components in Epilepsy-associated Glioneuronal Lesions. *Epilepsia* 48(s5):65-73
- Serra AL, Kistler AD, Poster D, Strucker M, Wuthrich RP, Weishaupt D, Tschirch F (2007) Clinical proof-of-concept trial to assess the therapeutic effect of sirolimus in patients with autosomal dominant polycystic kidney disease: SUISSE ADPKD study. *BMC Nephrol* 8(1):13 [Epub ahead of print]
- Sugiura C, Maegaki Y, Kure H, Inoue T, Ohno K (2007) Spontaneous remission of infantile spasms and hypsarrhythmia following acute infection with high-grade fever. *Epilepsy Res.* 2007 Oct 25 [Epub ahead of print]
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- Tamburini J, Chapuis N, Bardet V, Park S, Sujobert P, Willems L, Ifrah N, Dreyfus F, Mayeux P, Lacombe C, Bouscary D (2007) mTORC1 inhibition activates PI3K/Akt by up-regulating IGF-1R signaling in acute myeloid leukemia: rational for therapeutic inhibition of both pathways. *Blood* 2007 Sep 18 [Epub ahead of print]
- Widjaja E, Wilkinson ID, Griffiths PD (2007) Magnetic resonance perfusion imaging in malformations of cortical development. *Acta Radiol* 48(8):907-17
- Wu EH, Wu KK, Wong YH (2006-2007) Tuberin: a stimulus-regulated tumor suppressor protein controlled by a diverse array of receptor tyrosine kinases and G protein-coupled receptors. *Neurosignals* 15(5):217-27 [Epub 2007 Mar 28]
- Yadaden T, Molinie V, Ples R, Lazure T, Benoit G, Yonneau L, Ferlicot S (2007) [TSC2/PKD1 contiguous gene syndrome. Report of two cases.] *Ann Pathol* 27(2):136-40 [Article published in French]
- You SJ, Jung DE, Kim HD, Lee HS, Kang HC (2007) Efficacy and prognosis of a short course of prednisolone therapy for pediatric epilepsy. *Eur J Paediatr Neurol* 2007 Oct 19 [Epub ahead of print]
- Zdychova J, Vesela J, Kazdova L, Komers R (2007) Renal activity of Akt kinase in experimental Type 1 diabetes. *Physiol Res* 2007 Oct 11 [Epub ahead of print]

CONFERENCES AND SEMINARS

November 7-8, 2007 in Columbus, OH

November 15-16, 2007 in Denver, CO

EDUCATIONAL CARE FOR ALL KINDS OF MINDS is a day-and-a-half *exploratory* seminar for school leaders and others charged with creating a successful learning experience for students. Visit online for more information or to register

www.allkindsofminds.org/educationalcare/venue.aspx

November 27–29, 2007

2007 National Prevention and Health Promotion Summit

Hyatt Regency Capitol Hill

Washington D.C.

Conference Contact Information: <http://www.cdc.gov/cochp/conference/index.htm>

November 29, 2007

The Carolyn Frye-Halloran Symposium on Neuro-Oncology

“Tumor Suppressor Syndromes – The Path to Clinical Trials”

Massachusetts General Hospital, Boston, MA

To register: <http://fh2007.neurosurg.info>

November 30 – December 4, 2007

American Epilepsy Society

Philadelphia Convention Center, Philadelphia, PA

For more information go to: www.AESNET.org

TSC SIG will be held on Friday, November 30 at 1:00 pm, and stop by the TS Alliance exhibit in the Exhibit Hall!

April 4-6, 2008

LAM Foundation 2008 International Research Conference (LAMposium)

Westin Hotel, Cincinnati, OH

For more information: www.thelamfoundation.org

May 15-17, 2008

Conference on Diagnosis and Treatment in Pediatric Neurology

Warsaw, Poland

For more information: www.neuroped2008.pl

June 22-25, 2008

1st International Epilepsy Colloquium on the Mesial Temporal Lobe Epilepsies

Marburg, Germany

This colloquium is part of a series to be continued in Lyon, France in 2009 and Cleveland, Ohio, USA in 2010.

For more information:

AKM Congress Service GmbH

Hauptstr. 18

D-79576 Weil am Rhein

Phone: +49 (7621) 983345

Fax: +49 (7621) 78714

E-mail: laubscher.s@akmcongress.com

www.akmcongress.com

July 27-Aug 1, 2008

PKD Meeting Sponsored by FASEB

Snowmass, CO

More information coming soon!

September 11-13, 2008

TSC International Research Conference 2008

University of Sussex, Brighton, UK

Organized by the Tuberous Sclerosis Association, U.K.

For more information: www.tuberous-sclerosis.org

NEWS

TS Alliance Presents Manuel R. Gomez Award to Ann Hunt

The Tuberous Sclerosis Alliance awarded Ann Hunt from Oxfordshire, U.K. with the 2007 Manuel R. Gomez Award in recognition of the significant impact she made on TSC research, specifically research related to cognitive development and mental health issues in TSC. Ann's son, James, had TSC and was the inspiration of Ann's work to shed light on the often devastating and difficult mental health challenges and issues related cognitive development for individuals with TSC. Ann was one of the founders of the Tuberous Sclerosis Association in the U.K., and she worked tirelessly for the organization for many years as the Head of Research to coordinate numerous research conferences, professional study days, and impacted the lives of thousands of individuals with TSC worldwide. The TS Alliance was honored to present this award to Ann in memory of Manuel R. Gomez, and in honor of Peter Aronson, M.D. whose parents make this award possible.

Presidential Medal of Freedom Awarded to Francis Collins, M.D., Ph.D.

President George W. Bush has awarded the Presidential Medal of Freedom, the nation's highest civil award, to NHGRI Director Francis S. Collins, M.D., Ph.D. for revolutionizing genetic research. "Under his leadership, the Human Genome Project mapped and sequenced the full human genome and greatly expanded our understanding of human DNA." For more information:

<http://www.genome.gov>

Evolution Transforms "Junk" DNA into Genetic Machinery

Scientists have traced the 170 million-year evolution of a piece of "junk" DNA to its modern incarnation as an important regulator of energy balance in mammals. This research was published in the October 05, 2007, issue of PLoS Genetics by Marcelo Rubinstein, Ph.D., HHMI international scholar, Institute for Research on Genetic Engineering and Molecular Biology, CONICET. For the full story, go to: <http://www.hhmi.org/news/rubinstein20071004.html>

New Approach Builds Better Proteins Inside a Computer

With the aid of more than 70,000 home computer users throughout the world, Howard Hughes Medical Institute (HHMI) researchers have, for the first time, accurately predicted the three-dimensional structure of a small, naturally occurring globular protein using only its amino acid sequence. The accomplishment was achieved with a newly refined computational method for predicting protein structure, which the researchers say can also improve the detail and accuracy of protein structures generated with experimental techniques. This research was published in the October 17, 2007, issue of Nature by David Baker, Ph.D., HHMI investigator at the University of Washington School of Medicine. For the full story, go to:

<http://www.hhmi.org/news/baker20071017.html>

Eleven institutions selected in second round of Specialized Centers of Research on Sex and Gender Factors Affecting Women's Health

<http://www.nih.gov/news/pr/sep2007/od-24a.htm>

NIH announces addition of 22 new study centers in National Children's Study

<http://www.nih.gov/news/pr/oct2007/nichd-04.htm>

NIH launches extensive open-access dataset of genetic and clinical data

<http://www.nih.gov/news/pr/oct2007/nhlbi-01.htm>

NHGRI funds new Centers for Excellence in ethical, legal and social implications research
<http://www.nih.gov/news/pr/oct2007/nhgri-10.htm>

Implementation of the Revised American Veterinary Medical Association Guidelines on Euthanasia (NOT-OD-08-005)
<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-005.html>

Availability of Data from the 2002 and 2007 National Health Interview Survey: Public Use of Complementary and Alternative Medicine (NOT-AT-08-001)
<http://grants.nih.gov/grants/guide/notice-files/NOT-AT-08-001.html>

TSC CLINICAL TRIALS AND STUDIES

1. Early Screening for Autism in the Tuberous Sclerosis Complex (TSC)

Purpose:

Up to 60% of children with TSC develop autism, but often the diagnosis is not made until much later in childhood. Early detection leads to earlier interventions and, hopefully, better behavioral outcomes. At Children's Hospital Boston (CHB), we are investigating early signs of autism in children with TSC.

Methods:

We are using a behavioral tests as well as measure of the brain's electrical response to faces to screen children for autism. We will follow infants with TSC from age three months through age two, at which time they will be definitively tested for autism. We then will determine if any early abnormalities in behavior and face processing can predict autism in these infants. We also are testing all children with TSC under the age of 4 to gather data at different age groups on behavior and electrophysiologic characteristics.

During the testing, if we detect any abnormalities that may warrant further interventions, we will notify you and your pediatrician.

Eligibility: Any child with TSC under the age of 4 years.

Location and Contact Information:

Dr. Mustafa Sahin or Dr. Shafali Jeste

Multi-disciplinary Tuberous Sclerosis Clinic

Children's Hospital, Boston

300 Longwood Avenue Fegan 11

Boston, MA 02115

Phone: 617-919-4518

Email: Mustafa.sahin@childrens.harvard.edu or shafali.jeste@childrens.harvard.edu

2. Research Study: Allelic Expression Imbalance (AEI) in Tuberous Sclerosis Complex (TSC)

This research project has been approved by the St. Joseph's Hospital and Medical Center IRB.

Principal Investigator:

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Co-Investigator:

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Description of the Research Study:

The goal of this research is to understand the basis of variability in clinical severity among patients with TSC. There can be a considerable variation in severity even within a single family, where all affected individuals have the same gene mutation. It is not rare that a child will be evaluated by a neurologist for seizures, and a parent not even be aware of the fact that he/she might carry the same disorder, but milder. Several factors may contribute to this phenotypic variability including the specific gene mutation, random occurrence of "second-hit" somatic mutations, influence of other "modifying genes", and environmental factors.

We hypothesize that allele-specific gene expression of the TSC genes plays an important role in modifying disease severity. In other words, a patient who expresses more of the normal gene (than the mutant gene) will have milder symptoms than a patient who expresses more of the mutant gene.

We have already done some preliminary studies in normal individuals showing that the expression from the two alleles (gene copies) of the TSC genes is not 50:50.

We are now recruiting families with more than one affected individual, especially those with a known genetic mutation. By this strategy, we hope to determine if the variation in severity correlates with the ratio of mutant:normal gene expression, in each family. We hope that this will lead to a method for predicting clinical severity in newly diagnosed patients.

What is involved in the study?

- 1) Explanation of the research study, and review of the informed consent documents.
- 2) Interview (either in person or by telephone) to review the family history, and the clinical features in affected individuals; this will enable us to assign a "clinical severity score".
- 3) Obtain a blood sample from enrolled individuals – affected and unaffected - (about 10 cc or 2 teaspoons) for RNA and DNA analysis, to measure the ratio of mutant:normal gene expression.

TSC Clinical Trials

A list of clinical trials that are currently enrolling study participants can be viewed on the TS Alliance web site at: <http://tsalliance.easycgi.com/pages.aspx?content=370>

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.

This is the November 2007 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 December 2007 *TSC Alert* contact: vwhitemore@tsalliance.org

Archived issues of the TSC Alert can be found at: <http://www.tsalliance.org/pages.aspx?content=25>