



TSC ALERT

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

September 2004

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

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GRANT ANNOUNCEMENTS:

TUBEROUS SCLEROSIS ALLIANCE

Deadline for Letters of Intent: November 12, 2004

The Tuberous Sclerosis Alliance has released a Request for Applications (RFA). Funding will be provided for postdoctoral fellows, junior and senior investigator awards, as well as for conference grants. A Letter of Intent (LOI) is required prior to submission of a grant application and the PI will be invited to submit a complete grant proposal by the January 28, 2005 deadline. These

grants are available to all clinical and basic researchers for proposals pertaining to TSC and are not restricted to grants in the U.S.A.

For more information, see the TS Alliance Web site at: <http://www.tsalliance.org>

TUBEROUS SCLEROSIS COMPLEX RESEARCH PROGRAM (TSCR) IN THE CDMRP

Deadline: February 22, 2005

The Fiscal Year 2005 (FY05) Defense Appropriations Act provides \$3.2 million to the Department of Defense Tuberous Sclerosis Complex Research Program (TSCR) to support innovative research directed toward improved prevention, diagnosis, and treatment of TSC. This program is administered by the US Army Medical Research and Materiel Command through the Office of the Congressionally Directed Medical Research Programs (CDMRP).

FY05 TSCR Program Announcements for the following mechanisms are expected to be released in early **November 2004**, with receipt of electronic submissions due **February 22, 2005 at 5:00 p.m. Eastern time:**

- **Natural History Study Awards - New**
- **Natural History Development Awards**
- **Concept Awards**
- **Idea Development Awards**

Detailed descriptions of each mechanism will be provided in the FY05 TSCR Program Announcements, which are expected to be posted on the CDMRP website in early November. Requests for e-mail notification of the Program Announcement release may be sent to prequest@constellagroup.com. For more information about the TSCR or other CDMRP-sponsored programs, please visit the CDMRP website at: <http://cdmrp.army.mil/pubs/press/05tsrpfundopps.htm>

TISSUE AVAILABILITY:

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

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

NEW TSC PUBLICATIONS:

TSC BASIC SCIENCE HIGHLIGHT: Bateman JM, McNeill H (2004) Temporal control of differentiation by the insulin receptor/tor pathway in *Drosophila*. *Cell* 119(1):87-96

Multicellular organisms must integrate growth and differentiation precisely to pattern complex tissues. Despite great progress in understanding how different cell fates are induced, it is poorly understood how differentiation decisions are temporally regulated. In a screen for patterning

mutants, Bateman and McNeill isolated alleles of *tsc1*, a component of the insulin receptor (InR) growth control pathway. They found that loss of *tsc1* disrupts patterning due to a loss of temporal control of differentiation. *tsc1* controls the timing of differentiation downstream or in parallel to the RAS/MAPK pathway. Examination of InR, PI3K, PTEN, Tor, Rheb, and S6 kinase mutants demonstrates that increased InR signaling leads to precocious differentiation while decreased signaling leads to delays in differentiation. Importantly, cell fates are unchanged, but tissue organization is lost upon loss of developmental timing controls. These data suggest that intricate developmental decisions are coordinated with nutritional status and tissue growth by the InR signaling pathway.

TSC CLINICAL SCIENCE HIGHLIGHT: Bolton PF (2004) Neuroepileptic correlates of autistic symptomatology in tuberous sclerosis. Ment Retard Dev Disabil Res Rev 10(2):126-31

Tuberous sclerosis is a genetic condition that is strongly associated with the development of an autism spectrum disorder. However, there is marked variability in expression, and only a subset of children with tuberous sclerosis develop autism spectrum disorder. Clarification of the mechanisms that underlie the association and variability in expression will potentially throw light on the biological processes involved in the etiology of idiopathic forms of autism spectrum disorder. Current evidence indicates that the likelihood of a child with tuberous sclerosis developing an autism spectrum disorder is greater if the child has a mutation in the *TSC2* gene, although autism can and does develop in children with *TSC1* mutations. The likelihood is also greater if the child has early-onset infantile spasms that are difficult to control, especially if there is an epileptiform focus in the temporal lobes. The emerging evidence is consistent with the notion that early onset electrophysiological disturbances within the temporal lobes (and perhaps other locations) has a deleterious effect on the development and establishment of key social cognitive representations concerned with processing social information, perhaps especially from faces. However, alternative mechanisms to account for the findings cannot yet be ruled out. Future research will have to employ prospective longitudinal designs and treatment trials to clarify the processes involved.

TSC PUBLICATIONS:

Babu KL, Rai K, Hegde AM (2004) Tuberous sclerosis: a case report. *J Clin Pediatr Dent* 28(4):347-9

Bateman JM, McNeill H (2004) Temporal control of differentiation by the insulin receptor/tor pathway in *Drosophila*. *Cell* 119(1):87-96

Baybis M, Yu J, Lee A, Golden JA, Weiner H, McKhann G 2nd, Aronica E, Crino PB (2004) mTOR cascade activation distinguishes tubers from focal cortical dysplasia. *Ann Neurol* 2004 Sep 28;56(4):478-487 [Epub ahead of print]

Billings B, Hamrick LC, Bueschen AJ, Kenney PJ (2004) Coexisting angiomyolipoma and renal cell carcinoma in a kidney of an elderly woman: case report and review of the literature. *ScientificWorldJournal*. 2004 Jun 7;4 Suppl 1:27-30.

Bolton PF (2004) Neuroepileptic correlates of autistic symptomatology in tuberous sclerosis. *Ment Retard Dev Disabil Res Rev* 10(2):126-31

Kawahara I, Tsutsumi K, Hirose M, Matsuo Y, Yokoyama H (2004) [Solitary subependymal giant cell astrocytoma: a forme fruste of tuberous sclerosis complex?] *No To Shinkei* 56(7):585-91

[Article in Japanese]

Lang CH, Frost RA (2004) Endotoxin disrupts the leucine-signaling pathway involving phosphorylation of mTOR, 4E-BP1, and S6K1 in skeletal muscle. *J Cell Physiol* 2004 Sep 10 [Epub ahead of print]

Li Y, Inoki K, Guan KL (2004) Biochemical and functional characterizations of small GTPase Rheb and TSC2 GAP activity. *Mol Cell Biol* 24(18):7965-75

Messori A, Salvolini U (2004) Hybrid phacomatosis: from initial CT observation to molecular studies. *AJNR Am J Neuroradiol* 25(7):1297-8

Miyata H, Chiang AC, Vinters HV (2004) Insulin signaling pathways in cortical dysplasia and TSC-tubers: Tissue microarray analysis. *Ann Neurol* 2004 Sep 28;56(4):510-519 [Epub ahead of print]

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Ryvlin P, Mauguier F (2004) [Functional neuroimaging in adults] *Rev Neurol (Paris)* 160 Spec no 1:117-30 [Article in French]

Sanghvi JP, Rajadhyaksha SB, Ursekar M (2004) Spectrum of congenital CNS malformations in pediatric epilepsy. *Indian Pediatr* 41(8):831-8

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preliminary structural characterization of the GTPase domain of human Rheb. *Acta Crystallogr D Biol Crystallogr* 60(Pt 10):1883-1887

TSC-RELATED PUBLICATIONS

[No authors listed] (2004) [Combination of pulmonary lymphangioliomyomatosis (LAM) with angiomyolipoma (AML) of the kidney and multilocular cystic nephroma.] *Arkh Patol* 66(4):39-41 [Article in Russian]

Amy D. Sinor and Laura Lillien (2004) Akt-1 Expression Level Regulates CNS Precursors. *J Neurosci* 24 8531-8541

Andres M, Andre VM, Nguyen S, Salamon N, Cepeda C, Levine MS, Leite JP, Neder L, Vinters HV, Mathern GW (2004) Human Cortical Dysplasia and Epilepsy: An Ontogenetic Hypothesis Based on Volumetric MRI and NeuN Neuronal Density and Size Measurements. *Cereb Cortex* 2004 Aug 5 [Epub ahead of print]

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Chang SM, Kuhn J, Wen P, Greenberg H, Schiff D, Conrad C, Fink K, Robins HI, Cloughesy T, De Angelis L, Razier J, Hess K, Dancey J, Prados MD; North American Brain Tumor Consortium And The National Cancer Institute (2004) Phase I/pharmacokinetic study of CCI-779 in patients with recurrent malignant glioma on enzyme-inducing antiepileptic drugs. *Invest New Drugs* 22(4):427-35

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Ferri N, Carragher NO, Raines EW (2004) Role of discoidin domain receptors 1 and 2 in human smooth muscle cell-mediated collagen remodeling: potential implications in atherosclerosis and lymphangioliomyomatosis. *Am J Pathol* 164(5):1575-85

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Hovland A, Bjornstad H (2004) Pericardial effusion in a patient with lymphangioliomyomatosis. *Scand J Infect Dis* 36(6-7):521-2

Johnson SR, Whale CI, Hubbard RB, Lewis SA, Tattersfield AE (2004) Survival and disease progression in UK patients with lymphangioliomyomatosis. *Thorax* 59(9):800-3

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Ruggieri VL (2004) [Epilepsy beginning in the neonatal period and early infancy.] *Rev Neurol* 39(3):251-62 [Article in Spanish]

Shields WD (2004) Diagnosis of infantile spasms, Lennox-Gastaut syndrome, and progressive myoclonic epilepsy. *Epilepsia* 45 Suppl 5:2-4

Snoeckx A, Van de Perre S, Op de Beeck B, De Schepper A (2004) Pulmonary lymphangioliomyomatosis and rounded atelectasis. *JBR-BTR* 87(3):152-3

Wheless JW (2004) Nonpharmacologic treatment of the catastrophic epilepsies of childhood. *Epilepsia* 45 Suppl 5:17-22.

Xiong HQ (2004) Molecular targeting therapy for pancreatic cancer. *Cancer Chemother Pharmacol* 2004 Aug 13 [Epub ahead of print]

CONFERENCES:

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

October 18-19, 2004

Fifth Meeting of the Secretary's Advisory Committee on Genetics, Health, and Society
Bethesda Marriott, Bethesda, MD

Agenda: <http://www4.od.nih.gov/oba/SACGHS/meetings/October2004/SACGHSOct2004.htm>

The meeting is open to the public, and pre-registration is not required. Seating will be available on a first-come-first-serve basis. For directions and to make online lodging reservations, please visit: <http://marriott.com/property/propertyPage/WASBT>

Webcast: The meeting will also be webcast. Information on how to gain access to the webcast will be available on the day of the meeting at:

<http://www4.od.nih.gov/oba/SACGHS/meetings/October2004/SACGHSOct2004.htm>

November 6-7, 2004

New England Regional TSC Conference

Holiday Inn, Boston Logan, Boston, MA

Sponsored and organized by the NE Community Alliance of the Tuberous Sclerosis Alliance

For more information and registration: <http://www.tsalliance.org/NEconf.asp>

January 27-28, 2005

National Coalition for Health Professional Education in Genetics (NCHPEG) & Genetics Resources on the Web (GROW) 8th Annual Meeting: Focus on Family History

Hyatt Regency Bethesda, Bethesda, MD

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

February 19-20, 2005

West Coast Regional TSC Conference

Mission Inn, Riverside, CA

Sponsored and organized by the Community Alliance of the Tuberous Sclerosis Alliance

For more information, contact April Cooper at ACoope@ardenrealty.com

Save the date!

April 8-10, 2005

CNS Manifestations of TSC, held in conjunction with LAMposium 2005 and the Rare Lung Disease Consortium Conference

Hyatt Downtown, Cincinnati, OH

Sponsored and organized by the Tuberous Sclerosis Alliance, LAM Foundation, and Rare Lung Disease Consortium

More information coming soon!

Save the date! May 4-5, 2006

TSC International Research Conference 2006

Berlin, Germany

More information coming soon!

NEWS:

Physician Perspectives on Communications Barriers A focus group study has been published by the Hablamos Juntos project entitled, *Physician Perspectives on Communications Barriers*. The 40-page report details common hurdles experienced with non-English proficient (NEP) and limited-English proficient (LEP) patients such as information accuracy, patient confidentiality and the associated burden on physician practice resources.

The report has been posted as a brief and executive summary at:

<http://foundation.acponline.org/news/hablamos.htm> The full text is available by following a link from this page to the Hablamos Juntos website at

<http://www.hablamosjuntos.org/physicians>

You are urged to review the report and disseminate it to interested parties. Your input regarding the opportunities and barriers to patient communications as presented in the report is welcome.

CONVULSIONS IN WORMS MIMIC EPILEPTIC SEIZURES Researchers at the University of Alabama have found a way to mimic epileptic seizures in the tiny roundworm *C. elegans*. The finding could make the worm a powerful model for unraveling the molecular regulation of epilepsy, a condition that affects two percent of the population. This research was published in the August 31, 2004, issue of Human Molecular Genetics. For the full story, go to <http://www.hhmi.org//news/caldwell2.html>

RARE DEFICIT MAPS THINKING CIRCUITRY Using brain imaging, neuroscientists at the NIH's National Institute of Mental Health (NIMH) have pinpointed the site of a defect in a brain circuit associated with a specific thinking deficit. Their study demonstrates how a rare genetic disorder, Williams Syndrome, can offer clues as to how genetic flaws may translate into cognitive symptoms in more common and complex major mental disorders. Andreas Meyer-Lindenberg, M.D., Karen Berman, M.D., and colleagues, traced the thinking deficit to a circuit at the back of the brain that processes locations of objects in the visual field. The researchers report on their Magnetic Resonance Imaging (MRI) study in the September 2, 2004 "Neuron".

The study focused on the inability to visualize an object as a set of parts and then construct a replica, as in assembling a puzzle -- a key cognitive deficit experienced by people with Williams Syndrome. In addition to this visuospatial construction deficit, people with Williams Syndrome also tend to be overly friendly and anxious and often have mental retardation and learning disabilities. Compared to most mental disorders, which are thought to involve complex interactions between multiple genes and environmental triggers, the genetic basis of Williams Syndrome is remarkably well understood. People with the disorder lack about 21 genes in a particular part of chromosome 7.

"Williams Syndrome yields a unique opportunity to study how genes influence our ability to construct our social and spatial worlds," said NIMH Director Thomas Insel, M.D. "By studying people with this disorder, we can discover how genetic mutations change not only molecular and cellular processes, but lead to differences in the brain circuitry for complex aspects of cognition."

To identify where in the brain things go awry in the visuospatial construction deficit, Meyer-Lindenberg and Berman recruited 13 "high functioning" Williams Syndrome patients with normal intelligence. Even though they were missing the same genes as their mentally retarded peers, they were able to perform complex cognitive tasks during functional MRI (fMRI) experiments, and their brain structure and activity could be compared with matched healthy controls of similar IQ.

The researchers suspected that the visuospatial construction deficit would be found in a visual processing circuit that courses forward and upward from the back of the brain. This "where" circuit processes information about locations of objects and spatial relationships, whereas a parallel "what" circuit, running downward from the back of the brain, handles information about content of objects.

In the fMRI phase of the study, participants were scanned while performing spatial tasks -- matching geometric objects, assembling puzzle-like pieces into a square, and attending to the location of faces and houses. In each case, only those with Williams Syndrome failed to activate the "where" circuit, while the controls showed increased activation in that circuit. The patients' brains showed no difference from controls on tasks that activated the "what" circuit.

Using structural MRI, the researchers found a small region early in the "where" circuit that lacked gray matter (neuron bodies) in the Williams Syndrome participants. Its location -- conspicuously just before the functionally abnormal areas -- raised suspicions; and a path analysis confirmed that the functional abnormalities could be accounted for by defective input from this structurally abnormal area. The researchers hypothesize that it is likely the primary site of the visuospatial construction deficit.

They are now attempting to trace the deficit to individual genes in this structurally abnormal area. "The location of the abnormality also suggests a strategy for improving visual-spatial-construction function," noted Meyer-Lindenberg. "It is like a roadblock, but it should mainly affect stimuli that don't move. Incorporating motion into stimuli might provide an alternate route and circumvent the problem by engaging temporal lobe circuitry."

In addition to the NIMH Intramural Research Program, the research was also funded by a grant from the National Institute on Neurological Disorders and Stroke (NINDS) to Dr. Carolyn Mervis, University of Louisville. Also participating in the study were Philip Kohn, Dr. Shane Kippenhan, Rosanna Olsen, NIMH, and Dr. Colleen Morris, University of Nevada.

Graphics: <http://www.nih.gov/news/pr/sep2004/nimh-01.htm#brainscans>

NIMH and NINDS are part of the National Institutes of Health (NIH), the Federal Government's primary agency for biomedical and behavioral research. NIH is a component of the U.S. Department of Health and Human Services.

NIH ANNOUNCEMENTS:

NIH OFFERS \$35,000 IN ANNUAL STUDENT LOAN REPAYMENT

In brief: NIH's application cycle for Loan Repayment Programs opens September 1, 2004, and closes December 15, 2004. The NIH awards up to \$35,000 annually in student loan repayments to health professionals engaged in qualifying research. Details and the online application are available at <http://www.lrp.nih.gov>

Starting Wednesday, September 1, 2004, the National Institutes of Health will accept applications to its five Loan Repayment Programs. December 15, 2004, is the application deadline.

The NIH Loan Repayment Programs can repay up to \$35,000 of qualified educational debt for health professionals pursuing careers in clinical, pediatric, contraception and infertility, or health disparities research. The programs also provide coverage for Federal and state tax liabilities.

Participants must possess a doctoral-level degree, devote 50% or more of their time to research funded by a non-profit organization or government entity (federal, state, or local), and have educational loan debt equal to or exceeding 20% of their institutional base salary. U.S. citizens, permanent residents, or U.S. nationals may apply. The five NIH Loan Repayment Programs are the Clinical Research LRP, Clinical Research for Individuals from Disadvantaged Backgrounds LRP, Contraception and Infertility Research LRP, Health Disparities LRP, and Pediatric Research LRP.

"The NIH Loan Repayment Programs is one of our nation's most significant efforts to ensure a solid foundation of clinical, pediatric, contraception and infertility, and health disparities research professionals for the next generation," says Ruth Kirschstein, M.D., Senior Advisor to the Director, NIH. "These programs provide a means for health professionals to launch their research careers unfettered by the burden of student loan debt."

All applications for 2005 awards must be completed by 5 p.m., December 15, 2004. Visit <http://www.lrp.nih.gov> to apply.

NHGRI LAUNCHES CENTERS FOR EXCELLENCE IN ETHICAL, LEGAL AND SOCIAL IMPLICATIONS RESEARCH: Four Sites Selected to Pioneer Interdisciplinary Initiative

The National Human Genome Research Institute (NHGRI), part of the National Institutes of Health (NIH), announced today the funding of four interdisciplinary centers as part of a new initiative to address some of the most pressing ethical, legal and social questions raised by recent advances in genetic and genomic research.

The initiative, the Centers for Excellence in Ethical, Legal and Social Implications Research, is being led by NHGRI, with significant contributions from the U.S. Department of Energy (DOE) and the National Institute of Child Health and Human Development (NICHD). About \$20 million in grants will be awarded over the next five years with DOE contributing \$500,000 and NICHD, \$450,000. The first four Centers are being established at Case Western Reserve University, Cleveland; Duke University, Durham, N.C.; Stanford University, Palo Alto, Calif.; and the University of Washington, Seattle.

"The NHGRI's pioneering program supporting research in the ethical, legal and social implications of genomic knowledge provides the basis for this exciting new initiative," said NHGRI Director Francis S. Collins, M.D., Ph.D. "We will now build upon this foundation by establishing interdisciplinary research centers that can take an even more dynamic and broad-based approach to identifying and addressing some of the most pressing issues facing individuals, families and communities in the genome era."

Each of the new centers will assemble a team of experts in several disciplines, such as bioethics, law, behavioral and social sciences, clinical research, theology, public policy, and genetic and genomic research. The interdisciplinary nature of these teams will allow the centers to develop innovative research approaches focused on specific sets of issues that relate to the numerous applications of genomic research, including the scientific goals and challenges identified by NHGRI in "A Vision for the Future of Genomics Research," which was published in April 2003 in the journal "Nature". The centers' output will be critical in formulating and implementing effective and equitable health and social policies related to genomic research. In addition, the centers will create new environments to support the growth of the next generation of researchers on the ethical, legal and social implications of genomic research. Special efforts will be made to recruit potential researchers from under-represented groups.

Elizabeth Thomson, M.S., R.N., of NHGRI's Ethical, Legal and Social Implications (ELSI) Research Program, said, "The breadth and depth of knowledge and skills that these centers have pulled together is impressive. These centers truly are excellent in every sense of the word. We look forward to the many ways in which their research and other activities will serve to shape discussions and inform future policy decisions related to genetics and genomics."

"Providing funding assistance, in concert with the NHGRI, to two of these centers (Duke and Stanford) reflects the importance that we continue to place on ethical, legal and social implication activities, especially issues of commercialization and of genetic contributions to complex characteristics," said Aristides Patrinos, Ph.D., associate director of DOE's Office of Biological and Environmental Research in the Office of Science.

The new Centers for Excellence in ELSI Research, their principal investigators and their total funding levels over five years are:

-- Case Western Reserve University's Center for Genetic Research Ethics and Law; Eric Juengst, Ph.D., \$5.3 million

This center will study the ethical issues in the design and conduct of human genetic research, including issues regarding the protection of human subjects in research. After first surveying existing ethical, legal and social implications research, and current genetic research regulations and guidelines to determine how adequately they address present and emerging ethical

concerns, the center will conduct research and develop resources that will contribute to stronger policies and guidelines in genetic research.

-- The Duke Center for the Study of Public Genomics; Robert Cook-Deegan, M.D., \$4.8 million

This center will assemble a team to gather and analyze information about the role of publication, data and materials sharing, patenting, database protection and other practices that may affect the flow of information in genomics research. Research pertaining to these topics will make a much-needed contribution to the understanding of how information flow influences development, commercialization and use of genomic products and services that may benefit human health.

-- Stanford University School of Medicine's Center for Integration of Research on Genetics and Ethics, Mildred Cho, Ph.D., \$3.8 million

This center will focus on the ethical, legal and social consequences of uncovering the genomic contributions that may contribute to behavioral and neurological conditions. Research that examines attributes and traits that are possibly found more frequently in certain populations has the potential to stigmatize both individuals and groups. The Stanford center will work to identify and understand the issues related to this genetic research, provide consultation and guidance to genetic researchers on these issues, and develop training and education materials that can be integrated into the design and implementation of neurological and behavioral genetic studies.

-- University of Washington's Center for Genomic Health Care and the Medically Underserved; Wylie Burke, M.D., Ph.D., \$4.7 million

This center will conduct research on the ethical, legal and social factors that influence the translation of genetic information to improved human health. It will be dedicated to addressing two overarching themes resulting from the clinical integration of genomics: the need to define criteria for clinical integration that lead to clinically and socially appropriate applications of genomic health care, and the need for a translational pathway that incorporates the goal of reducing health and health care disparities among the medically underserved. A major outcome will be the development of methods to inform all segments of society about technological advances, and to improve the mechanisms for obtaining input from diverse populations to help to identify and assess policy options for addressing these challenges.

In addition to funding these four centers of excellence, NHGRI announced the award of three exploratory grants that provide two to three years of support to investigators for planning and developing potential new centers at their institutions. Exploratory grants were awarded to:

-- Alexandra Shields, Ph.D., Georgetown University, Washington, \$560,000 over three years. Dr. Shields plans to develop a center dedicated to examining the intersection of genetics, vulnerable populations and health disparities in tobacco dependence, asthma and diabetes.

-- Charmaine Royal, Ph.D., Howard University, Washington, \$700,000 over three years. Dr. Royal plans to develop a center to analyze social and cultural identities of individuals and communities of African descent and how those identities influence attitudes about genomics and health care as well as health behaviors.

-- Donald Bailey, Ph.D., University of North Carolina at Chapel Hill. \$430,000 over two years. Dr. Bailey will plan a center to examine how information from large-sample genetic studies is used and disclosed in biomedical research. During the exploratory phase, the researchers will focus on issues related to newborn screening, adolescent health research and centralized DNA banking.

NHGRI's ELSI Research Program was established in 1990 as an integral part of the Human Genome Project to foster basic and applied research and to support education and outreach activities. The program, which is part of NHGRI's Division of Extramural Research, funds and manages studies related to the ethical, legal and social implications of genetic and genomic research, and also supports workshops, research consortia and policy conferences related to such topics. The ELSI Research Program is the largest sponsor of research on the ethical, legal and social aspects of biomedicine in the world.

NHGRI is one of the 27 institutes and centers at NIH, an agency of the Department of Health and Human Services. For more information about NHGRI's ELSI Research Program, see

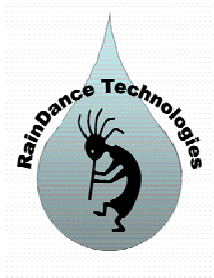
<http://www.genome.gov/1000161>

For more information about NHGRI, see <http://www.genome.gov>

EMPLOYMENT OPPORTUNITIES:

POSITION WANTED Sybille Swanson worked as a psychologist in the UK for approximately the past 11 years and for one year (2002 to 2003) she was coordinator of the Tuberous Sclerosis Clinic at the Great Ormond Street Hospital in London and worked together with Professor Brian Neville. The clinic was also taking part in the TS 2000 Cohort Study, a natural history study of TSC. She is looking for a similar job here in the U.S. She may be contacted at:

sybille@swansons.us



RainDance Technologies (RDT) is a new startup company devoted to discovering, developing and commercializing the precise manipulation of minute amounts of fluids in microfluidic devices for a variety of downstream applications. We offer the successful candidate the opportunity to be part of a dynamic team at the inception of a fluidics company. The candidate must be able to work well in the environment of a small group of energetic employees focused on rapid progress. RainDance Technologies offers a competitive salary and benefits package. We are located on the picturesque Connecticut shoreline in Guilford, CT.

RainDance Technologies has the following positions open. Please send your resume, indicating Job code to: Human Resources at jobs@raindancetechnologies.com

They offer a highly competitive compensation and benefits package. An equal opportunity employer. Visit their website @ www.raindancetechnologies.com

Engineer; Systems interface (2)

The primary job responsibilities include the design and implementation of a computer interface between electronic, optical, and fluidic devices. You will be asked to interact with a team of scientists and engineers to solve device problems, design and build control circuitry, develop solutions for timing control, and electronic detection and control circuitry. The successful candidate must have a BS or MS degree in electrical or optical engineering or equivalent experience, experience with computer interface and device control, programming skills, and 3 to 5 years of industrial experience. **Job code: RDT04-01**

Engineer; Surfactant and interface

The primary job responsibilities include solving materials related problems specific to fluids, interfaces, and surfactants, test and design fluid mixtures, assist in device micro fabrication, design new encapsulation strategies, develop charging technologies for fluid systems, and solve problems in emulsion stability and interfacial control of emulsions. The successful candidate must have an advanced degree in science or engineering, experience with fluids, surfactants, emulsion technology, encapsulation technology, electrochemistry, interfacial science, colloid science and +5 years of experience in a startup company environment. Additional desirable qualifications include; experience with microfluidic devices, CAD, and device integration and engineering experience. **Job code; RDT04-02**

Materials Engineer (2)

The primary job responsibilities include solving materials related problems specific to fluids, interfaces, and surfactants, test and design fluid mixtures, assist in device micro-fabrication, design new encapsulation strategies, develop charging technologies for fluid systems, and solve problems in emulsion stability and interfacial control of emulsions. The successful candidate must have a BS or MS degree in science or engineering, experience with fluids, surfactants, emulsion technology, encapsulation technology, electrochemistry, interfacial science, colloid science, excellent communication and leadership skills, and +2 years of industrial experience. Additional desirable qualifications include experience with microfluidic devices, CAD, device integration and engineering experience, and optics and electronics experience. **Job code; RDT04-03**

Engineer; Optical and electrical

The primary job responsibilities include solving problems in optical detection of fluorescent signal, interface optical and microfluidic components, solve problems in application of electrical fields, integrate detection and electronics for control of fluidics, integrate electrical control with fluidic devices, device micro-fabrication, and implement charging technologies for fluid systems. The successful candidate must have a BS, MS or PhD in science or engineering, experience with optical detection, electronics, optical design, excellent communication skills, and +2 years of industrial experience. Additional desirable qualifications include: experience with microfluidic devices, CAD, device integration and engineering experience, and optics and electronics experience, and fiber optics and waveguide experience. **Job code; RDT04-04**

Engineer; Senior Materials

The primary job responsibilities include; solve materials-related problems specific to fluids, interfaces, and surfactants, test and design fluid mixtures, device micro- fabrication, design new encapsulation strategies, develop charging technologies for fluid systems, play a leadership role in system development and integration, solve problems in emulsion stability and interfacial control of emulsions and contribute to development of business strategies. In addition, the successful candidate must have: an advanced degree in science or engineering, experience with fluids, surfactants, emulsion technology, encapsulation technology, electrochemistry, interfacial science, colloid science, +5 years of experience in a startup company environment, and excellent communication and leadership skills. Additional desirable qualifications include: experience with microfluidic devices, CAD, device integration and engineering experience. **Job code; RDT04-05**

Research Scientist -Molecular Biology

Ph.D. (or equivalent) with experience in DNA cloning, vector construction, DNA sequencing, mutagenesis, library construction, and PCR. Experience with mammalian cell culture and protein chemistry such as Western blots and protein expression and purification desired. Experience with directed evolution, microfluidics, materials sciences, liquid handling robotics and automation a big plus. Must be hands on, be exceptionally well organized and possess a track record of exceptional productivity as demonstrated in a publication record. The successful candidate will have project

leadership experience in an entrepreneurial environment. Be part of a team at the intersection of biology and engineering. **Job code RDT04-06**

Research Associate-Molecular Biology

BS or MS with experience in DNA cloning, vector construction, DNA sequencing, library construction, and PCR. Experience with mammalian cell culture and basic protein chemistry such as Western blots desired. Experience with directed evolution, microfluidics, materials sciences, liquid handling robotics and automation a big plus. Must love to be at the bench and be hands on, be exceptionally well organized (as demonstrated by lab notebooks) and possess a track record of exceptional productivity. The successful candidate will have had some experience in an entrepreneurial environment. Be part of a team at the intersection of biology and engineering.

Job code RDT04-07

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