



TSC ALERT

Edited by Vicky Holets Whittemore, PhD

March 2005

Welcome to the March 2005 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 April 2005 *TSC Alert* contact: Vicky.Whittemore@tsalliance.org

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IMPORTANT DEADLINES

TSC/LAM International Research Symposium – Call for Abstracts!

Deadline for submission of Late-breaking Abstracts: March 15, 2005

(See information below in Conferences)

Eppendorf & Science Prize for Neurobiology - \$25,000 Prize for Neurobiology

Now accepting entries for the \$25,000. Deadline is June 15, 2005.

Visit: <http://www.eppendorf.com/prize2005>

GRANT ANNOUNCEMENTS

REQUEST FOR PROPOSAL TRANSLATIONAL RESEARCH GRANT PROGRAM

Deadline: April 1, 2005

The Epilepsy Research Foundation, a partnership between The Epilepsy Project www.epilepsyproject.org and the Epilepsy Foundation www.efa.org is requesting proposals for its New Therapy Grants Program. The primary focus of this new program will be to bring new approaches and therapies to patients through translational research.

The Epilepsy Research Foundation is providing grants to scientific and clinical investigators who seek support for innovative, high impact projects that demonstrate a clear path from the lab to the patient. We anticipate awarding grants of \$100,000 on average although larger grants and multi-year grants will be considered. For examples of previously funded proposals please see: www.epilepsyproject.org/sec/funds_awarded

The Epilepsy Research Foundation's review board will evaluate all proposals.

For more information, please see our Web site, www.epilepsyproject.org/grants or contact us at EpilepsyCure@aol.com

Research Infrastructure Award Program Deadline March 15th

This program was established last year to provide an opportunity for scientists to obtain support for nationwide or international networks of clinical or basic science researchers focused on understanding the causes, consequences and treatment of epilepsy. This program is jointly funded by AES and the Epilepsy Foundation and is not limited to AES members. The application process has two steps. The Letter of Intent is due March 15th.

http://www.aesnet.org/Visitors/Research/awards/research_infrastructure.cfm.

Research Initiative Fund Award Program Deadline March 15th

This program is for AES members and provides seed support to encourage innovative collaborative research in all disciplines (clinical, social, basic science, etc.) associated with the epilepsy field. The application process has two steps. The Letter of Intent is due March 15th. For details go to http://www.aesnet.org/Visitors/Research/sponsoredgrants/research_init.cfm.

Research Funding from CURE

CURE, Citizens United for Research in Epilepsy, is requesting proposals for its 2006 Research Program. Deadline is June 30, 2005. Please visit www.CUREepilepsy.org.

Behavioral Research at NIMH: Reorganizing the Portfolio to Advance Public Health

http://www.nimh.nih.gov/about/dirupdate_behavioralresearch.cfm

Frequently Asked Questions about Funding Basic Research at NIMH

http://www.nimh.nih.gov/about/dirupdate_basicresearch_faq.cfm

NEW TSC PUBLICATIONS

Journal of Child Neurology September 2004 Issue Focused on TSC

The September 2004 issue of the Journal of Child Neurology, Vol. 19, Number 9, contains 15 articles on TSC that were presented at the 2003 Child Neurology Society meeting in the "Neurobiology of Disease in Children" Symposium organized by Bernard L. Maria, MD, MBA. E. Steve Roach, MD and David Gutmann, MD, PhD co-chaired the symposium. You may access the PDF of this issue on the Tuberous Sclerosis Alliance Web site at:

<http://www.tsalliance.org/pages.aspx?content=131>

Basic Science Spotlight: Rolfe M, McLeod LE, Pratt PF, Proud CG (2005) **Activation of protein synthesis in cardiomyocytes by the hypertrophic agent phenylephrine requires activation of ERK and involves phosphorylation of TSC2.** Biochem J 2005 Mar 10 [Epub ahead of print]

<http://www.biochemj.org/bj/imps/refer.htm?MSID=BJ20041888.htm>

The pro-hypertrophic G q protein-coupled receptor agonist phenylephrine (PE) activates protein synthesis. Rolfe and coworkers (2005) showed previously that activation of protein synthesis by PE requires MEK and mammalian target of rapamycin (mTOR). However, it remained unclear whether ERK activation was required and which downstream components were involved in activating mTOR and protein synthesis. Using an adenovirus encoding the MAP kinase phosphatase MKP3 to inhibit ERK activity; they demonstrate that ERK is essential for activation of protein synthesis by PE. Activation and phosphorylation of ribosomal protein S6 kinase 1 and phosphorylation of eukaryotic initiation factor 4E-binding protein, both mTOR targets, were also inhibited by MKP3, suggesting that ERK is also required for activation of mTOR signalling. PE-stimulation of cardiomyocytes induced phosphorylation of tuberous sclerosis complex 2 (TSC2), a negative regulator of mTOR activity. TSC2 was phosphorylated only weakly at Thr1462, but phosphorylated at additional sites within the sequence RXRXX(S/T). This differs from the phosphorylation induced by insulin, indicating that MEK/ERK signalling targets distinct sites in TSC2. This phosphorylation may be mediated by p90 RSK, which is activated by ERK, and appears to involve phosphorylation at Ser1798. Activation of protein synthesis by PE is partially insensitive to the mTOR inhibitor, rapamycin. Inhibition of the MAP kinase-interacting kinases (Mnks) by CGP57380 reduces the phosphorylation of eukaryotic initiation factor 4E and PE-induced protein synthesis. Moreover, CGP57380 plus rapamycin inhibited protein synthesis to that same extent as blocking ERK activation, suggesting that Mnks and regulation of mTOR each contribute to the activation of protein synthesis by PE in cardiomyocytes.

Clinical Science Spotlight: King JA, Stamilio DM (2005) **Maternal and fetal tuberous sclerosis complicating pregnancy: a case report and overview of the literature.** Am J Perinatol 22(2):103-8

Tuberous sclerosis complex (TSC) is an autosomal-dominant phakomatosis that can result in cardiac and central nervous system lesions and may adversely impact fetal and maternal health. King and Stamilio (2005) report a case of a 19-year-old primigravida with TSC whose pregnancy was complicated by preeclampsia, preterm labor, and fetal demise. The fetus, also affected with TSC, was diagnosed with a cardiac rhabdomyoma on ultrasound at 24 gestational weeks and intracranial tubers on fetal magnetic resonance imaging at 26 gestational weeks. Hydrops fetalis developed in the 30th gestational week. Fetal demise occurred during induction of labor. A

systematic review of the medical literature was conducted. Their objective was to quantify maternal and fetal morbidity and mortality associated with TSC. They identified 36 additional cases of fetal TSC with cardiac rhabdomyoma diagnosed prenatally. Including this case, they also identified 23 pregnancies (17 mothers) complicated by maternal TSC. Rates of complications are calculated. The authors conclude that pregnancies complicated by maternal or fetal TSC deserve careful vigilance. Although benign histologically, cardiac rhabdomyomas can result in fetal morbidity and mortality.

New TSC Publications:

Artigas-Pallares J, Gabau-Vila E, Guitart-Feliubadalo M (2005) [Syndromic autism: II. Genetic syndromes associated with autism.] *Rev Neurol* 40 Suppl 1:S151-62 [Article in Spanish]

Atherton PJ, Babraj JA, Smith K, Singh J, Rennie MJ, Wackerhage H (2005) Selective activation of AMPK-PGC-1 α or PKB-TSC2-mTOR signaling can explain specific adaptive responses to endurance or resistance training-like electrical muscle stimulation. *FASEB J.* 2005 Feb 16; [Epub ahead of print] <http://www.fasebj.org/cgi/reprint/04-2179fjev1>

Cassetty CT (2004) Tuberous sclerosis complex (Bourneville disease). *Dermatol Online J* 10(3):17

Corso R, Carrafiello G, Rampoldi A, Leni D, Ticca C, Vercelli R, Vanzulli A (2005) Pseudoaneurysm After Spontaneous Rupture of Renal Angiomyolipoma in Tuberous Sclerosis: Successful Treatment with Percutaneous Thrombin Injection. *Cardiovasc Intervent Radiol.* 2005 Feb 16; [Epub ahead of print]

Jansen FE, van Huffelen AC, Bourez-Swart M, van Nieuwenhuizen O (2005) Consistent Localization of Interictal Epileptiform Activity on EEGs of Patients with Tuberous Sclerosis Complex. *Epilepsia* 46(3):415-9

King JA, Stamilio DM (2005) Maternal and fetal tuberous sclerosis complicating pregnancy: a case report and overview of the literature. *Am J Perinatol* 22(2):103-8

Prando A (2003) Radiological classification of renal angiomyolipomas based on 127 tumors. *Int Braz J Urol* 29(3):208-16

Ristagno RL, Biddinger PW, Pina EM, Meyer CA (2005) Multifocal micronodular pneumocyte hyperplasia in tuberous sclerosis. *AJR Am J Roentgenol* 184(3 Suppl):S37-9

Rolfe M, McLeod LE, Pratt PF, Proud CG (2005) Activation of protein synthesis in cardiomyocytes by the hypertrophic agent phenylephrine requires activation of ERK and involves phosphorylation of TSC2. *Biochem J* 2005 Mar 10 [Epub ahead of print] <http://www.biochemj.org/bj/imps/refer.htm?MSID=BJ20041888.htm>

Shields JA, Eagle RC Jr, Shields CL, Marr BP (2004) Aggressive retinal astrocytomas in four patients with tuberous sclerosis complex. *Trans Am Ophthalmol Soc* 102:139-47; disc 147-8

Sun XF, Yan CL, Fang L, Shen FM, Liao KH (2005) Cutaneous lesions and visceral involvement of tuberous sclerosis. *Chin Med J (Engl)* 118(3):215-9

Yu Y, Li S, Xu X, Li Y, Guan K, Arnold E, Ding J (2005) Structural basis for the unique biological function of small GTPase human Rheb. *J Biol Chem.* 2005 Feb 23 [Epub ahead of print] <http://www.jbc.org/cgi/reprint/M501253200v1>

CONFERENCES

April 8-10, 2005

TSC/LAM Research Conference & TSC Adult Conference

The Hyatt Regency, Downtown Cincinnati, OH

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

The Tuberous Sclerosis Alliance and the LAM Foundation invite you to attend the first joint TSC/LAM conference in Cincinnati, Ohio in April 2005. Sessions will include:

- The TSC Genes in the Brain – What Do They Do?
- Signaling Pathways and Basic Biology of TSC1/TSC2
- TSC-LAM Translational Research
- What Causes Epilepsy in TSC?
- Behavioral Phenotypes in TSC
- Late-Breaking Science and Roadmap for a Cure for TSC

CALL FOR LATE-BREAKING SCIENCE ABSTRACTS

Platform and poster presentations will be selected from submitted abstracts based on scientific merit and thematic considerations. The application and instructions may be completed electronically or downloaded from the Tuberous Sclerosis Alliance Web site at

<http://www.tsalliance.org>

Deadline for submission of Late-Breaking TSC Abstracts: March 15, 2005

Deadline for Early Registration: February 18, 2005

For more information, Agenda and Registration information: <http://www.tsalliance.org>

May 5-7, 2005

The Young Child with Special Needs

Las Vegas Hilton, Las Vegas, NV

<http://www.contemporaryforums.com>

May 10-12, 2005

PharmaDiscovery

Washington, D.C. Convention Center

<http://www.pharmadiscovery2005.com>

May 20-25, 2005

International Conference of the American Thoracic Society

San Diego Convention Center

San Diego, CA

<http://www.thoracic.org>

June 21-22, 2005

National Summit on Preconception Care

The National Center on Birth Defects and Developmental Disabilities

Marriott Century Center, Atlanta, GA

Questions should be directed to Chris Parker via email at cparker@cdc.gov or telephone at (404)498-3098

Additional information and registration:

<http://www.signup4.net/Public/ap.aspx?EID=NATI14E>

July 21-23, 2005

XXVII Annual Meeting of the Cognitive Science Society

Stresa, Italy

<http://www.psych.unito.it/csc/cogsci05/home.html>

August 28 – September 1, 2005

26th International Epilepsy Congress

Le Palais des Congres de Paris

Paris, France

<http://www.epilepsycongress.org>

September 11-14, 2005

The Second International Conference on Birth Defects and Disabilities in the Developing World

Jiuhua Spa and Resort, Beijing, China

www.chinamed.com.cn/birthdefects

December 2-6, 2005

American Epilepsy Society & American Clinical Neurophysiology Society

Washington, DC Convention Center

Washington, DC

Deadline for submission of abstracts: May 6, 2005

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

May 4-5, 2006

TSC International Research Conference 2006

Berlin, Germany

More information coming soon!

July 2-6, 2006

7th European Congress of Epileptology

Helsinki Fair Centre, Helsinki, Finland

<http://www.epilepsyhelsinki2006.org>

NEWS

TSC RESEARCH FEATURED BY ASCO, MEDSCAPE AND eMEDICINE TSC researcher, Sandra Dabora, M.D., Ph.D., from Brigham & Women's Hospital, Boston, was interviewed by a writer for Reuters Health who reviewed the TSC preclinical paper that was published this month (Lee et al., 2005). The story was posted by ASCO, Medscape and eMedicine. Here is the link to the story:

NCI CREATES GENE EXPRESSION DATABASE OF NORMAL HUMAN ORGAN TISSUE

Researchers at the National Cancer Institute (NCI), part of the National Institutes of Health (NIH), have built the largest open-source database for normal tissue from human organs. Scientists searching for genes that go awry and cause disease can use the NCI database as a crucial point of reference because it pinpoints which genes are expressed in many of the body's major organs under normal conditions (without known disease). Scientists can compare the genes from their own biological samples to this dictionary of normal expression. "Genes identified by the database as abnormally active in a particular disease could become potential targets, guiding researchers to better candidates for new drug therapies, immune-based vaccine treatments, and potential biomarkers to help with diagnosis," explained Javed Khan, M.D., chief

of the Oncogenomics Section of NCI's Pediatric Oncology Branch. A study validating the database appears in the March 2005 issue of "Genome Research".*

"The NCI database is an important addition to the growing body of knowledge about gene expression in normal human tissues," added James Jacobson, Ph.D., acting branch chief of the Diagnostics Research Branch in NCI's Division of Cancer Treatment and Diagnosis. "These data give investigators a baseline against which to compare gene expression data obtained from tumor or other disease specimens, and should be a valuable resource for the research community."

The normal organ database uses a technology known as gene expression microarrays, more commonly known as gene chips, to provide a kind of fingerprint that researchers and clinicians can use to compare cells and tissue they suspect may have cancerous or other malfunctioning genes. To create these fingerprints, Khan and his team assembled a complementary DNA (cDNA) microarray, using a pair of glass slides on which thousands of known genes have been printed in tiny spots. Cells can be tested by manipulating them so that genes activated in the cell will match up with the known gene samples, like two pieces of Velcro attaching to each other. The cellular genes are treated with fluorescence and literally light up the gene dots on the chip. The light pattern is then measured with a special type of microscope and the results are fed into a computer for analysis.

Gene expression microarrays have been used in numerous applications, including identifying novel genes associated with certain cancers, classifying tumors, and predicting patient outcome. Another NCI-funded study recently demonstrated that microarray analysis of identical tissue samples at geographically separate laboratories can produce the same quality of results as those done within a single lab**. The normal organ database takes that one step further, enabling scientists and clinicians to compare the gene expression results for their own tissue or genes of interest to a baseline standard that represents a generic picture of normal gene activity, organ by organ, in the human body. Users of the array on the new NCI web site (<http://home.ccr.cancer.gov/oncology/oncogenomics/>) will find expression profiles for 18,927 genes, which include most of the genes that are known to help direct basic activities of the human body.

Recently the Human Genome Project revealed a surprisingly low number of human genes (20,000-25,000), and Khan said it had been previously reported that "only a fraction of that, perhaps 10,000 genes, are actively transcribed in normal cell processes." Thus it becomes strategically useful to characterize this essential backdrop. "The normal organ database provides a platform that may help scientists find new targets in the cells of previously incurable cancers. The driving force of research in our section is to translate genomic information to the clinic. The goal is to save lives and improve the quality of life for children with high-risk cancer."

Until now, no publicly available, normal human organ database has used so many tissue samples (158), or included samples of tissue from different parts of the same organs from multiple donors. Tissue samples were harvested an average of 11 hours after death, from males and females of different ethnic groups, ranging from ages 3 months to 39 years old.

The very large cDNA microarray they constructed has more than 42,000 detectors built into two chips using verified cDNA libraries upon which many other researchers currently rely. Analyzing the organ tissue with this tool allowed Khan and his team to identify 18,927 genes that constitute their database. "We found that each organ had a unique expression level profile," said Khan, "and, remarkably, any truly random subset of 1,000 genes could distinguish one organ from another."

Each organ revealed a very distinct profile of active genes, different from all others. However, the gene profiles from different organs that share similar biological functions also showed patterns of expression. For example, though the cerebrum and the cerebellum are two distinct parts of the brain, located apart from each other and doing very different jobs, their gene expression profiles reflected their commonality as part of the nervous system. Similarly, "muscle contraction" genes were found in skeletal muscle, smooth muscle tissue, and the heart -- all organs that share a common way of functioning.

To illustrate the kind of useful data that can emerge from using this tool, Khan's team analyzed 100 samples of the most common pediatric solid tumor cancer, neuroblastoma (NB), which accounts for 7 percent to 10 percent of all childhood cancers. Even though the tumor samples were taken from a variety of patients with different stages of cancer, the database kicked out a list of 19 genes that were consistently overexpressed compared to normal brain tissue.

"All of these genes are involved in one way or another with the kinds of activities associated with the development of cancer -- processes such as apoptosis, growth, proliferation and transcription," said Khan. These results provide scientists studying and treating NB with a focused set of genes to explore.

For more information about cancer, please visit the NCI home page at <http://www.cancer.gov> or call NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237).

* Son, C.G., Bilke, S., Davis, S., Greer, B.T., Wei, J.S., Whiteford, C.C., Chen, Q.-R., Cenacchi, N., Khan, J. 2005. Database of mRNA gene expression of multiple human organs. "Genome Research" 15: 443-450. (<http://www.genome.org/>).

** Dobbin, K.K., et. al., 2005. "Clinical Cancer Research" 11:565-572.

NHGRI TARGETS 12 MORE ORGANISMS FOR GENOME SEQUENCING: Strategic Mix Includes Marmoset, Skate and the Vector of Chagas' Disease The National Human Genome Research Institute (NHGRI), one of the National Institutes of Health (NIH), announced that the Large-Scale Sequencing Research Network will begin sequencing 12 more strategically selected organisms, including the marmoset, a skate and several important insects, as part of its ongoing effort to expand understanding of the human genome.

The National Advisory Council for Human Genome Research, which is a federally chartered committee that advises NHGRI on program priorities and goals, recently approved a comprehensive plan that identified two groups of new sequencing targets on the basis of their collective scientific merits.

"Our sequencing strategy continues to focus on identifying the sets of organisms with the greatest potential to fill crucial gaps in biomedical knowledge," said Mark S. Guyer, Ph.D., director of NHGRI's Division of Extramural Research. "The most effective approach we currently have to identify the essential functional and structural components of the human genome is to compare it with the genomes of other organisms."

Two of the sequencing projects are aimed at gaining new insights into model organisms utilized in research on drug development and disease susceptibility. They are: sequencing the genome of a fellow primate, the marmoset ("Callithrix jacchus"); and identification of genetic variations (in the form of single nucleotide polymorphisms) in eight strains of rats.

The marmoset is a key model organism used in neurobiological studies of multiple sclerosis, Parkinson's disease and Huntington's disease. The marmoset is also an important model for research into infectious disease and pharmacology.

The marmoset was chosen also because of its unique position on the evolutionary tree, one step further removed from humans than other non-human primates already being sequenced, such as the chimpanzee ("Pan troglodytes"), the rhesus macaque ("Macaca mulatta") and orangutan ("Pongo pygmaeus"). Obtaining the marmoset genome sequence will provide a powerful tool to illuminate the similarities and differences among these primate genomes.

The second project chosen for its considerable medical relevance to humans will identify 280,000 single nucleotide polymorphisms, known as "SNPs," in the genomes of eight different strains of laboratory rats. SNPs can be used as markers to zero in on genetic variations that may affect an individual's risk of developing common, complex illnesses such as heart diseases, diabetes and cancer. Building a catalog of rat SNPs will assist researchers trying to find genetic variations associated with common, complex diseases in rats, which can then be used to help identify similar genetic variations that may be involved in human disease.

The eight rat strains selected are the PVG strain, commonly used as a healthy control in studies; the F344 strain, used in toxicological and pharmacological studies; the SS strain, used for cardiovascular disease studies; the LEW strain, often used in studies of transplants and immune response; the BB strain, used in studies of diabetes; the FHH strain, also used for cardiovascular studies; the DA strain, used for studies of arthritis and cancer; and the SHR strain, used in studies of hypertension.

"The overriding goal of sequencing the genomes of a diverse set of organisms is to understand the biological processes at work in human health and illness," said NHGRI Director Francis S. Collins, M.D., Ph.D. "It is also gratifying to know that these tools, freely available to the entire biomedical research community, can be used in other scientific fields to further improve animal and human welfare."

Another set of 11 non-mammalian organisms were strategically chosen, each representing a position on the evolutionary timeline marked by important innovations in animal anatomy, physiology, development or behavior. The organisms are: a skate ("Raja erinacea"); a sea slug ("Aplysia californica"); a disease-carrying insect ("Rhodnius prolixus"); a pea aphid ("Acyrtosiphon pisum"); a wasp ("Nasonia vitripennis") and two related insect species ("Nasonia giraulti" and "Nasonia longicornis"); a free-living soil amoeba ("Acanthamoeba castellanii"); and three fungi ("Schizosaccharomyces octosporus", "Schizosaccharomyces japonicus", "Batrachochytridium dendrobatidis").

It has been shown that most sequences of the human genome originated long before humans themselves. Consequently, scientists will use the genome sequences of the 11 non-mammalian animals to learn more about how, when and why the human genome came to be composed of certain DNA sequences, as well as to gain new insights into organization of genomes. In addition, many of the organisms can shed light on human disease.

For instance, the skate (related to many species of shark and cartilaginous fish) was chosen because it belongs to the first group of primitive vertebrates that developed jaws, an important step in vertebrate evolution. Other innovations in this group of animals include an adaptive immune system similar to that of humans, a closed and pressurized circulatory system, and myelination of the nervous system. Understanding these systems of the skate at a genetic level will help scientists identify the minimum set of genes that create a nervous system or develop a

jaw, possibly illustrating how these systems have evolved in humans, and how they sometimes go wrong.

Aplysia ("*Aplysia californica*") is a sea slug that has been a very useful model in studying learning and memory in humans. *Aplysia* have very large neurons which can be manipulated and studied easily by researchers. In 2000, Eric Kandel, M.D., of Columbia University in New York, shared the Nobel Prize in Physiology or Medicine for his work elucidating how memories are formed in the human brain using *Aplysia* as a model.

The disease-carrying insect, "*Rhodnius prolixus*", spreads Chagas' disease, caused by the parasite "*Trypanosoma cruzi*", which is carried by the insect. Chagas' disease is prominent in Latin America, affecting about 20 million people in South America alone and killing 50,000 of them a year. Having the genome sequence of "*Rhodnius prolixus*" presents an opportunity for experts from the United States, Canada and Latin America to collaborate on understanding this widespread infectious disease.

The pea aphid ("*Acyrtosiphon pisum*") is an insect which causes hundreds of millions of dollars of crop damage each year. The pea aphid is a model for studying rapid adaptation because this species is exceptionally able at adapting to and resisting many pesticides. Understanding this resistance at a molecular level can lead to safer and more effective pesticides and improve human nutrition. The genome of the pea aphid, used extensively as an experimental model, will be a valuable comparison with other insects, such as the closely related insect, "*Rhodnius prolixus*".

Another insect, the parasitoid wasp "*Nasonia vitripennis*", is a natural enemy of houseflies, and its relatives are natural enemies of ticks, mites, roaches and other arthropods. It is the genetic model for parasitoids, which lay their eggs on and kill arthropods, thus controlling pest populations. In the United States, the use of parasitoid wasps in agriculture as a biological control of crop damaging insects saves approximately \$20 billion annually. The wasp will serve as a good comparison for the honey bee genome, which has been sequenced already. Two related wasp species, "*Nasonia giraulti*" and "*Nasonia longicornis*", will be sequenced at less dense coverage to aid in the comparative studies.

Sequencing efforts will be carried out by the five centers in the NHGRI-supported Large-Scale Sequencing Research Network: Agencourt Bioscience Corp., Beverly, Mass.; Baylor College of Medicine, Houston; the Broad Institute of MIT and Harvard, Cambridge, Mass.; The J. Craig Venter Science Institute, Rockville, Md.; and Washington University School of Medicine, St. Louis. Assignment of each organism to a specific center or centers will be determined at a later date.

NHGRI's selection process begins with two working groups comprised of experts from across the research community. Each of the working groups is responsible for developing a proposal for a set of genomes to sequence that would advance knowledge in one of two important scientific areas: understanding the human genome and understanding the evolutionary biology of genomes. A coordinating committee then reviews the working groups' proposals, helping to fine-tune the suggestions and integrate them into an overarching set of scientific priorities. The recommendations of the coordinating committee are then reviewed and approved by NHGRI's advisory council, which in turn forwards its recommendations regarding sequencing strategy to NHGRI leadership.

The genomes of a number of organisms have been or are being sequenced by the large-scale sequencing capacity developed by the Human Genome Project. These include the dog, the mouse, the rat, the chicken, the honey bee, two fruit flies, the sea urchin, two puffer fish, two sea squirts, two roundworms, several fungi, baker's yeast and many prokaryotes (bacteria and

archaea) including "Escherichia coli". Additional organisms already in the NHGRI sequencing pipeline are: the macaque, the orangutan, the kangaroo, the cow, the gray short-tailed opossum, the platypus, the red flour beetle, the domestic cat, the flatworm "Schmidtea mediterranea", more species of fruit fly and several species of fungi.

To learn more about the rapidly growing field of comparative genomic analysis, go to: www.genome.gov/1005835. For the white papers on other organisms currently in NHGRI's sequencing pipeline, go to: www.genome.gov/10002154 For more on NHGRI's selection process for large-scale sequencing projects, go to: www.genome.gov/Sequencing/OrganismSelection

High-resolution photos of the marmoset, skate, aplysia, and "Rhodnius prolixus" and many other organisms are available at: www.genome.gov/10005141

NHGRI is one of the 27 institutes and centers at NIH, an agency of the Department of Health and Human Services. The NHGRI Division of Extramural Research supports grants for research and for training and career development at sites nationwide. Additional information about NHGRI can be found at its Web site, www.genome.gov.

TeleConsults in Epilepsy – New Program

The Allied Health Education Subcommittee is proud to announce a spring audio conference on **Sleep and Epilepsy in Children**. This marks the tenth year of this program, which is geared to Allied Health or Epilepsy Care Professionals and others who do not normally attend the AES Annual Meeting. This spring's live audio conference program features Dr. Lawrence Brown and is scheduled for Tuesday, May 17th at 3pm Eastern and Friday, May 20th at Noon Eastern. For more information or to register, go to

<http://www.aesnet.org/Visitors/ProfessionalDevelopment/Educational/teleconsults05.cfm>

Programs from the past several years are also available on the website in text, audio and/or PowerPoint formats.

A REWARDING DISCOVERY SHOWS HOW DOPAMINE ACTIVATES BRAIN CIRCUITRY

Researchers funded by the Howard Hughes Medical Institute (HHMI) have discovered how dopamine – a molecule important for communication between neurons in the brain – stimulates the synthesis of proteins in neuronal processes. The new findings add to the understanding of dopamine's influence on the brain's reward circuitry that appears to be altered by addictive drugs. This research was published in the March 3, 2005, issues of Neuron by Eric M. Schuman, Ph.D., from the California Institute of Technology. For the full story, go to

<http://www.hhmi.org//nes/schuman3.html>

TSC INFORMATION

For information about TSC, visit the TS Alliance Web site at: <http://www.tsalliance.org> or call the Tuberous Sclerosis Alliance at 1-800-225-6872 or 301-562-9890.