



TSC ALERT

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January 2005

Welcome to the January 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 February 2005 *TSC Alert* contact: Vicky.Whittemore@tsalliance.org

Table of Contents

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

IMPORTANT DEADLINES.....	1
GRANT ANNOUNCEMENTS.....	2
NEW TSC PUBLICATIONS.....	4
NEWS.....	8
TSC INFORMATION.....	11

IMPORTANT DEADLINES

TSC/LAM International Research Symposium – Call for Abstracts!

Deadline for submission of abstracts: January 28, 2005

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

Deadline for Registration: February 18, 2005

(See information below in Conferences)

SOLICITING NOMINATIONS FOR MANUEL R. GOMEZ AWARD

Deadline for submission of nominations: February 1, 2005

(See information below in News)

TUBEROUS SCLEROSIS COMPLEX RESEARCH PROGRAM (TSCRCP) IN THE CDRMP

Deadline: February 22, 2005

(See information below in Grant Announcements)

GRANT ANNOUNCEMENTS

TUBEROUS SCLEROSIS COMPLEX RESEARCH PROGRAM (TSCRCP) IN THE CDMRP

Deadline: February 22, 2005

The Fiscal Year 2005 (FY05) Defense Appropriations Act provides \$3.2 million to the Department of Defense Tuberos Sclerosis Complex Research Program (TSCRCP) 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). The deadline for the receipt of electronic submissions is February 22, 2005 at 5:00 p.m. Eastern time.

FY05 TSCRCP Program Announcements for the following mechanisms can be found on the DCMRP Web site.

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

Detailed descriptions of each mechanism are provided in the FY05 TSCRCP Program Announcements on the CDMRP Web site. For more information about the TSCRCP or other CDMRP-sponsored programs, please visit the CDMRP website at:
<http://cdmrp.army.mil/funding/05tscrp.htm>

James S. McDonnell Foundation: 21st Century Science Initiative - 2005

Research Award Application Deadline: 6:00 pm CST March 7, 2005

The James S. McDonnell Foundation (JSMF) announces updated program descriptions and application guidelines for its 21st Century Science Initiative Research Awards. The 21st Century Research Awards support investigator-initiated research. Funding is available for research projects in Brain Cancer; Bridging Brain, Mind, and Behavior; and Studying Complex Systems. Program information, application guidelines, and proposal preparation instructions are available at: <http://www.jsmf.org>. No geographic restrictions; international applications are encouraged. Information on the Foundation's 21st Century Collaborative Activity Awards is also available on the website.

NIH Earmarks \$1 Million for Research Into Therapies Using Genomic, Proteomic Technologies

By a GenomeWeb staff reporter

NEW YORK, Jan. 17 (GenomeWeb News) - The National Institutes of Health issued last week a request for applications for projects designed to support "the career development of translational researchers in genomics."

According to the NIH, it will award three-, four-, and five-year grants of between \$150,000 and \$230,000 to "clinicians who propose an integrated clinical research and bench research project that applies genomics and proteomics tools to the study of human patients whose disease has a genetic component." This includes "the application of increasing knowledge of the genome and the proteome to the development and implementation of novel therapeutic strategies as applied to genetic diseases and complex diseases with a genetic component," the NIH said.

According to the NIH, the funding will be awarded under the institute's K23 mechanism, which "requires an integrated clinical-laboratory research project that directly involves patients affected by the disease being studied so that awardees can develop skills in both clinical research and basic science; [and] emphasizes career development and a research program that focuses on developing effective therapeutic interventions." Additionally, this mechanism "requires significant utilization of genomic and proteomic tools and technologies in the research project," the NIH said.

The NIH said it anticipates awarding four to six grants under this RFA.

Letters of intent from applicants are due by May 16. Applications are due by June 15. Additional details about the RFA can be found [here](#) and below.

K 23 with Emphasis on Therapeutic Interventions Employing Genomic or Proteomic Technologies (RFA-HG-05-013)

National Human Genome Research Institute

National Institute on Drug Abuse

Office of Rare Diseases

Application Receipt Date(s): June 15, 2005

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-05-013.html>

2005 NIH DIRECTOR'S PIONEER AWARD PROGRAM OPENS The National Institutes of Health announce the 2005 NIH Director's Pioneer Award, a key component of the NIH Roadmap for Medical Research.

"The Pioneer Award supports scientists of exceptional creativity who take innovative approaches to major challenges in biomedical research," said NIH Director Elias A. Zerhouni, M.D. "We look forward to adding a new cohort of visionary thinkers to the outstanding group of scientists chosen in the first year of this program."

Unlike other NIH grants, which support research projects, the Pioneer Award supports individual scientists. The award gives recipients the intellectual freedom to pursue new research directions and highly innovative ideas that have the potential for unusually great impact.

The program is open to scientists at all career levels. The scientists may currently be engaged in any field of research provided they are interested in exploring biomedically relevant topics and willing to commit the major portion of their effort to Pioneer Award research. Awardees must be U.S. citizens, non-citizen nationals, or permanent residents.

In September 2005, NIH expects to make five to ten new Pioneer Awards of up to \$500,000 in direct costs per year for five years. The first nine Pioneer Awards were made in September 2004 and support scientists working on a variety of challenging scientific problems.

The self-nomination process includes a three- to five-page essay, a biographical sketch, a list of current research support and the names of three references. Nominations may be submitted between March 1 and April 1, 2005, on the Pioneer Award Web site, <<http://nihroadmap.nih.gov/pioneer>>

"To maximize the diversity of those considered for Pioneer Awards, we encourage nominations from women, members of groups that are underrepresented in biomedical research, individuals in the early to middle stages of their careers, and scientists working in fields that have not traditionally been supported by NIH," said Jeremy M. Berg, Ph.D., director of the National Institute of General Medical Sciences. Dr. Berg and Nora D. Volkow, M.D., director of the National Institute on Drug Abuse, are co-chairs of the NIH committee that oversees the Pioneer Award program.

The complete Pioneer Award announcement is posted at <<http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-05-021.html>>

The NIH, a part of the U.S. Department of Health and Human Services, is the primary Federal agency for conducting and supporting medical research. More information about the NIH can be found on its Web site: <<http://www.nih.gov>>.

The NIH Roadmap is a series of far-reaching initiatives designed to transform the nation's medical research capabilities and speed the movement of research discoveries from the bench to the bedside. It provides a framework of the priorities the NIH must address in order to optimize its entire research portfolio and lays out a vision for a more efficient and productive system of medical research. For more information about the NIH Roadmap, please visit the Web site at: <<http://www.nihroadmap.nih.gov>>

This NIH News Release is available online at: <http://www.nih.gov/news/pr/jan2005/od-10.htm>

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: Ballif BA, Roux PP, Gerber SA, Mackeigan JP, Blenis J, Gygi SP (2005) Quantitative phosphorylation profiling of the ERK/p90 ribosomal S6 kinase-signaling cassette and its targets, the tuberous sclerosis tumor suppressors. Proc Natl Acad Sci U S A 2005 Jan 12 [Epub ahead of print]

Reversible protein phosphorylation is an essential cellular regulatory mechanism. Many proteins integrate and are modulated by multiple phosphorylation events derived from complex signaling cues. Simultaneous detection and quantification of temporal changes in all of a protein's phosphorylation sites could provide not only an immediate assessment of a known biochemical activity but also important insights into molecular signaling mechanisms. Here Ballif and coworkers at Harvard Medical School show the use of stable isotope-based quantitative MS to globally monitor the kinetics of complex, ordered phosphorylation events on protein players in the canonical mitogen-activated protein kinase signaling pathway. In excellent agreement with activity assays and phosphospecific immunoblotting with the same samples, they quantified epidermal growth factor-induced changes in nine phosphorylation sites in the extracellular signal-regulated kinase (ERK)/p90 ribosomal S6 kinase-signaling cassette. Additionally, they monitored 14 previously uncharacterized and six known phosphorylation events after phorbol ester stimulation in the ERK/p90 ribosomal S6 kinase-signaling targets, the tuberous sclerosis complex (TSC) tumor suppressors TSC1 and TSC2. By using quantitative phosphorylation profiling in conjunction with pharmacological kinase inhibitors we uncovered a ERK-independent, protein kinase C-dependent pathway to TSC2 phosphorylation. These results establish quantitative phosphorylation profiling as a means to simultaneously identify, quantify, and delineate the kinetic changes of ordered phosphorylation events on a given protein and defines parameters for the rapid discovery of important in vivo phosphoregulatory mechanisms.

Clinical Science Spotlight: Kothary N, Soulen MC, Clark TW, Wein AJ, Shlansky-Goldberg RD, Crino PB, Stavropoulos SW (2005) Renal Angiomyolipoma: Long-term Results after Arterial Embolization. J Vasc Interv Radiol 16(1):45-50

Selective arterial embolization of renal angiomyolipomas (AMLs) was performed to prevent hemorrhage in patients with AMLs larger than 4 cm. This study was conducted to evaluate the long-term efficacy of AML embolization. Nineteen patients underwent embolization for 30 renal AMLs between July 1991 and June 2002. Of these, 10 patients had tuberous sclerosis (TS) with multiple AMLs and nine patients had a solitary sporadic AML. Embolization was performed with use of ethanol mixed with iodized oil (Ethiodol) in 29 tumors; coils were used in addition to the ethanol/Ethiodol mixture in one case. All tumors were completely embolized according to angiographic criteria including vascular stasis and absence of arterial feeders. The efficacy of embolization was determined over a mean follow-up period of 51.5 months (range, 6-132 months). Recurrence was defined as an increase in tumor size of greater than 2 cm on follow-up imaging and/or recurrent symptoms that required repeat embolization. An institutional review board exemption was obtained to perform this retrospective study. Embolization of the renal AMLs was technically successful in all 19 patients and for all 30 lesions. AML recurrence was noted in 31.6% of patients (n = 19) and for 30% of lesions overall (n = 9). Six of 10 patients in the TS group had AML recurrences. No recurrences occurred in the patients with sporadic AML. In the TS group of 10 patients, there was a total of 21 AMLs and the overall tumor recurrence rate was 42.9% (nine of 21). Six lesions in four patients had to be reembolized because of recurrent symptoms, including one hemorrhage, and three lesions in two patients required repeat embolization because of a greater than 2 cm increase in size. The median time interval from embolization to recurrence was 78.7 months (range, 13-132 months). Statistical testing with use of the Fisher exact test demonstrated that patients with TS were significantly more likely to develop recurrence than those without TS (P = .01). Transarterial embolization is effective in preventing hemorrhage in patients with renal AMLs. However, long-term follow-up revealed a high AML recurrence rate in patients with TS. Lifelong surveillance for recurrence after AML embolization is essential in patients with TS.

New TSC Publications:

Ballif BA, Roux PP, Gerber SA, Mackeigan JP, Blenis J, Gygi SP (2005) Quantitative phosphorylation profiling of the ERK/p90 ribosomal S6 kinase-signaling cassette and its targets, the tuberous sclerosis tumor suppressors. *Proc Natl Acad Sci U S A* 2005 Jan 12 [Epub ahead of print]

Chan JA, Zhang H, Roberts PS, Jozwiak S, Wieslawa G, Lewin-Kowalik J, Kotulska K, Kwiatkowski DJ (2004) Pathogenesis of tuberous sclerosis subependymal giant cell astrocytomas: biallelic inactivation of TSC1 or TSC2 leads to mTOR activation. *J Neuropathol Exp Neurol* 63(12):1236-42

Chugh SN, Atri S, Mittal P, Navdeep (2004) Tuberous sclerosis in a family with varied and rare manifestations. *J Assoc Physicians India* 52:511-2

Corradetti MN, Inoki K, Guan KL (2005) The stress-induced proteins RTP801 and RTP801L are negative regulators of the mammalian target of rapamycin pathway. *J Biol Chem.* 2005 Jan 4 [Epub ahead of print]

Hafen E (2004) Cancer, type 2 diabetes, and ageing: news from flies and worms. *Swiss Med Wkly* 134(49-50):711-9

Harrington LS, Findlay GM, Lamb RF (2005) Restraining PI3K: mTOR signalling goes back to the mem *Trends Biochem Sci* 30(1):35-42

Inoki K, Corradetti MN, Guan K (2005) Dysregulation of the TSC-mTOR pathway in human disease. *Nat Genet* 37(1):19-24

Jaff A, Molinie V, Mellot F, Guth A, Leuret T, Scherrer A (2004) Evaluation of imaging-guided fine-needle percutaneous biopsy of renal masses. *Eur Radiol* 2004 Dec 31 [Epub ahead of print]

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Kitano Y, Honna T, Nihei K, Miyauchi J, Matsuoka K, Kuroda T, Tanaka K, Morikawa N, Fuchimoto Y (2004) Renal angiomyolipoma in Japanese tuberous sclerosis patients. *J Pediatr Surg* 39(12):1784-6

Kojima M, Nakamura S, Ohno Y, Sugihara S, Sakata N, Masawa N (2004) Hepatic angiomyolipoma resembling an inflammatory pseudotumor of the liver. A case report. *Pathol Res Pract* 200(10):713-6

Kothary N, Soulen MC, Clark TW, Wein AJ, Shlansky-Goldberg RD, Crino PB, Stavropoulos SW (2005) Renal Angiomyolipoma: Long-term Results after Arterial Embolization. *J Vasc Interv Radiol* 16(1):45-50

Padma MV, Simkins R, White P, Satter M, Christian BT, Dunigan K, Lee C, Jacobs M, Mukherjee J, Mantil JC (2004) Clinical utility of 11C-flumazenil positron emission tomography in intractable temporal lobe epilepsy. *Neurol India* 52(4):457-462
<http://www.neurologyindia.com/article.asp?issn=0028-3886;year=2004;volume=52;issue=4;spage=457;epage=462;aulast=Padma>

Restrepo CS, Largoza A, Lemos DF, Diethelm L, Koshy P, Castillo P, Gomez R, Moncada R, Pandit M (2005) CT and MR imaging findings of benign cardiac tumors. *Curr Probl Diagn Radiol* 34(1):12-21

Shah OJ, Hunter T (2005) Tuberous Sclerosis and Insulin Resistance: Unlikely Bedfellows Reveal A TORrid Affair. *Cell Cycle*. 2005 Jan 03 4(1) [Epub ahead of print]

Sharma MC, Ralte AM, Gaekwad S, Santosh V, Shankar SK, Sarkar C (2004) Subependymal giant cell astrocytoma - a clinicopathological study of 23 cases with special emphasis on histogenesis. *Pathol Oncol Res* 10(4):219-24 Epub 2004 Dec 27

Taveira-DaSilva AM, Stylianou MP, Hedin CJ, Hathaway O, Moss J (2004) Decline in lung function in patients with lymphangioleiomyomatosis treated with or without progesterone. *Chest* 126(6):1867-74

Tunali N, Gumurdulu D, Zorludemir S (2004) Splenic involvement in a stillborn fetus with tuberous sclerosis and multiple cardiac rhabdomyomas. *Turk J Pediatr* 46(4):357-61

Vargas Gonzalez R, San Martin-Brieke W, Gil-Orduna C, Lara-Hernandez F (2004) Desmoplastic fibroma-like tumor of maxillofacial region associated with tuberous sclerosis. *Pathol Oncol Res* 10(4):237-9 Epub 2004 Dec 27

Wheeler PG, Sadeghi-Nejad A (2005) Simultaneous occurrence of neurofibromatosis type 1 and tuberous sclerosis in a young girl. *Am J Med Genet A* 2005 Jan 6 [Epub ahead of print]

Wu EH, Wong YH (2004) Involvement of Gi/o proteins in nerve growth factor-stimulated phosphorylation and degradation of tuberin in PC12 cells and cortical neurons. *Mol Pharmacol* 2004 Dec 30 [Epub ahead of print]

CONFERENCES

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 and to register, visit the TS Alliance Web site at: <http://www.tsalliance.org>

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 ABSTRACTS

Platform and poster presentations will be selected from submitted abstracts based on scientific merit and thematic considerations. The application and instructions are enclosed and may also be completed electronically or downloaded from the Tuberous Sclerosis Alliance Web site at <http://www.tsalliance.org> or The LAM Foundation website at <http://lam.uc.edu>

Deadline for submission of abstracts: January 28, 2005

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

Deadline for Registration: February 18, 2005

For more information, Call for Abstracts, Agenda and Registration information:

<http://www.tsalliance.org>

Save the date! May 4-5, 2006

TSC International Research Conference 2006

Berlin, Germany

More information coming soon!

NEWS

THINK NEUROLOGY NOW This month the AAN and its Foundation are launching Think Neurology Now in Boston. Think Neurology Now is a public education campaign to raise awareness of neurology and the impact of neurological disorders. For more information about Think Neurology Now and events in Boston, visit www.thinkneurologynow.org. An online press kit will be available soon.

Research News from the Howard Hughes Medical Institute: Human Brain Evolution Was a 'Special Event' Genes that control the size and complexity of the brain have undergone much more rapid evolution in humans than in non-human primates or other mammals, according to a new study by HHMI researcher Bruce T. Lahn, Ph.D. at the University of Chicago and published in the December 29, 2004, issue of Cell.

The accelerated evolution of these genes in the human lineage was apparently driven by strong selection. In the ancestors of humans, having bigger and more complex brains appears to have carried a particularly large advantage, much more so than for other mammals. As a result, genetic mutations that produced bigger and more complex brains spread in the population very quickly. This led ultimately to a dramatic "speeding up" of evolution in genes controlling brain size and complexity.

For the full story, go to <http://www.hhmi.org/news/lahn3.html>

INTERNATIONAL COALITION TO FUND AUTISM GENETICS RESEARCH An international public/private partnership of government health agencies and private advocacy organizations has

committed more than \$21 million for research to identify the genes associated with autism spectrum disorders, a range of developmental disorders that impair communication and other mental abilities. The National Institutes of Health (NIH) is spearheading the coalition, whose members include the Canadian and Irish governments and three private autism foundations.

The coalition recently issued a Request for Applications (RFA), "Identifying Autism Susceptibility Genes," which has an application receipt date of April 15, 2005. Applications will undergo peer review during July 2005. The coalition will award funding for the research project in the fall of 2005 and expects to fund two to three organizations to participate in the 5-year project.

"NIMH appreciates the challenge of leading this impressive team," said Thomas R. Insel, M.D., director of the NIMH, the lead organization in the effort. "This remarkable partnership shows what can be accomplished when public/private efforts join forces. This international approach can advance the autism field by leaps and bounds."

With three to six new cases per 1,000 children, autism is more common than several other disabling but better-understood diseases of childhood, such as type 1 diabetes and cystic fibrosis. Symptoms of autism, a complex neuropsychiatric syndrome, include varying degrees of impairment in communication and social skills, and restricted, repetitive, and stereotyped patterns of behavior. While heredity, in the form of multiple genes, appears to be a major determinant of whether a particular individual develops autism, experts believe that environmental influences also play a significant role.

Researchers have already reported progress on the genetic underpinnings of autism. There are reports of several chromosomal regions associated with the disorder, but few specific genes have been identified. The RFA is intended to advance knowledge of the relation between genetics and autism by examining existing data for genes and gene variants that confer susceptibility to autism. The RFA also requires researchers to assess the functional significance of autism-associated genetic variants. This research may provide a means to subdivide autism spectrum disorders into identifiable, distinct disorders, with different molecular mechanisms.

The organizations participating in the project are the National Institute of Mental Health (NIMH), National Institute for Neurological Disorders and Stroke (NINDS), the National Institute on Deafness and Other Communications Disorders (NIDCD), the National Institute of Child Health and Human Development (NICHD), and the National Institute of Environmental Health Sciences (NIEHS), all from the NIH; the Canadian Institutes of Health Research; the Health Research Board, Ireland; and the Southwest Autism Research and Resource Center, Cure Autism Now, and the National Alliance for Autism Research, all private organizations.

For more information please visit:

Autism on the NIMH website

<http://www.nimh.nih.gov/healthinformation/autismmenu.cfm>

To go to the RFA

<http://grants1.nih.gov/grants/guide/rfa-files/RFA-MH-05-007.html>

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

NIDCD <<http://www.nidcd.nih.gov>>

NICHD <<http://www.nichd.nih.gov>>

NIEHS <<http://www.niehs.nih.gov>>

This NIH News Release is available online at:
<http://www.nih.gov/news/pr/dec2004/nimh-28.htm>

FEDERAL/PRIVATE PARTNERS LAUNCH RESOURCE FOR DIABETIC KIDNEY DISEASE GENE STUDIES The National Institutes of Health (NIH), Juvenile Diabetes Research Foundation (JDRF), and Centers for Disease Control and Prevention (CDC) announced the availability of the largest single collection of biosamples and data for research on the genetic causes of kidney disease in type 1 diabetes.

The Genetics of Kidneys in Diabetes (GoKinD) collection has nearly 10,000 DNA, serum, plasma and urine samples, plus genetic and clinical data, from more than 1,700 adults with type 1 diabetes in the United States and Canada. Of those, 818 have had diabetes at least 10 years and have developed kidney disease, a common complication of diabetes. The other 893 have had diabetes at least 15 years but do not have kidney disease. Also in the collection are data and samples from 1,096 parents (548 sets).

"GoKinD is a tremendous resource. We're thrilled about the promise it represents," said Rebekah Rasooly, Ph.D., who oversees the project for NIH and directs genetics and genomics programs at NIH's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). "We fund research all the time, but this kind of project reflects a new way of thinking. GoKinD is a gift that will keep on giving, and we are deeply indebted to the individuals and families who made this invaluable resource possible."

Researchers can apply for DNA, extensive clinical data and some genetic data from GoKinD at www.gokind.org/access; serum, plasma and urine samples will be made available later. Methods of treatment, insulin doses, complications, smoking history and other data have been documented for all GoKinD participants. Also, DNA has been genotyped for genes well-known to predispose to type 1 diabetes. To protect the privacy of patients and families, researchers do not have access to names and other identifying information.

"This study is of exceptional quality and offers a unique opportunity for genetic research," said Patricia Mueller, Ph.D., chief of CDC's diabetes and molecular risk assessment laboratory.

Gathering information and samples of the kind, quality and quantity that individual researchers alone would be unable to collect, GoKinD provides a rich means for learning about the genetics of both kidney disease and type 1 diabetes.

"GoKinD will help us tease out genes linked to kidney disease versus those that are primarily important causes of diabetes itself," said Concepcion R. Nierras, Ph.D., director of research for JDRF.

Both NIH and JDRF will separately consider requests to fund research on GoKinD data and samples. NIH grant applications are at <http://grants.nih.gov>, and resources for type 1 diabetes research are listed at www.niddk.nih.gov/fund/diabetesspecialfunds/funding.htm. JDRF grant applications are under the research tab at www.jdrf.org.

Once found, genes for susceptibility to kidney disease can be studied to find out what they do, how they do it and how researchers might intervene to prevent the disease or improve

treatment. Studies have already linked several genes to susceptibility to type 1 diabetes, but scientists are confident that more genes exist and that other, as yet unknown, genes increase susceptibility to complications such as kidney disease. (Learn more about genetic factors in diabetes at www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=diabetes.chapter.987.)

"These genes alone don't explain the complete genetic risk for diabetes, and little is known about genes for kidney disease or other complications. Yet, there is clearly a genetic risk for complications, because they run in families and among certain populations," said Paul L. Kimmel, M.D., F.A.C.P., a nephrologist working part-time with Rasooly and NIDDK on GoKinD. Kimmel also directs the renal disease and hypertension division at George Washington University Medical Center in Washington, D.C.

Diabetes is the leading cause of kidney failure in the United States. In 2002, treatment of kidney failure cost Medicare and private insurers \$25 billion for more than 400,000 people, 40 percent of whom had diabetes. Twenty to 40 percent of people with type 1 diabetes will develop kidney failure by the age of 50, but some develop it before the age of 30.

Type 1 diabetes accounts for up to 10 percent of people diagnosed with diabetes in the United States (up to 1 million people). This form of diabetes usually strikes children and young adults, who need several insulin injections a day or an insulin pump to survive. Insulin, though critical for controlling blood glucose, is no cure. Most people with the disease eventually develop one or more complications, including damage to the heart and blood vessels, eyes, nerves, and kidneys.

NIH, JDRF and CDC collaborated on GoKinD. NIH supported the study through a special fund for type 1 diabetes research established by Congress in 1997 and coordinated by NIDDK. In all, the fund will provide \$1.14 billion between fiscal years 1998 and 2008, supplementing funds available for type 1 diabetes research through regular NIH appropriations.

Under JDRF, the Joslin Diabetes Center and the George Washington University (GWU) Biostatistics Center (and its associated clinical centers) each recruited about half the patients and their parents. GWU will also distribute GoKinD data. CDC provided genotyping data for the major type 1 diabetes risk factors, HLA DRB1, DQA1, and DQB1 and the -23 insulin gene single nucleotide polymorphism (SNP). In addition, CDC will distribute samples and conduct research on the collection. Biochemical clinical data were provided by the University of Minnesota.

Investigators and centers that recruited participants and provided clinical and genetic data can be seen at: <http://www.nih.gov/news/pr/dec2004/niddk-28.htm>

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.