News and Resources from the National Institutes of Health

Diabetes Dateline

National Diabetes Information Clearinghouse

Winter 2008

People with Diabetes and Sickle Cell Trait Should Have Reliable A1C Test

Campaign Informs Physicians and Patients

A new National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) information campaign highlights the importance of using accurate methods to test hemoglobin A1C in people with diabetes who have sickle cell trait or other inherited forms of variant hemoglobin.

The hemoglobin A1C blood test is an essential tool in diabetes care because it shows a person's average blood glucose level over the past 2 to 3 months. Physicians base their treatment decisions largely on A1C test results. Inaccurate A1C readings, whether falsely high or low, can lead to overtreatment or undertreatment of diabetes.

"In the United States, more than 3,000 labs rely on 20 different methods to measure A1C in people with diabetes," said Randie Little, Ph.D., who heads the National Glycohemoglobin Standardization Program (NGSP) at the University of Missouri School of Medicine. "However, six of these methods yield unreliable results in patients with sickle cell trait. Health care professionals caring for people with diabetes should know that specific A1C tests should be used in this group of patients."

The NGSP, supported by the NIDDK and the Centers for Disease Control and Prevention, is working to improve and standardize the measurement of A1C in laboratories around the world. The NGSP website, *www.NGSP.org*, lists the test methods that accurately measure A1C in patients with hemoglobin variant S, also known as sickle cell trait, and variant C, another common variant in the United States.

Hemoglobin is the oxygen-transporting protein in red blood cells. Mutations in the genes that code for the protein, which occur more frequently in people of African, Mediterranean, and Southeast Asian descent, cause variations in the structure or amount of hemoglobin. Researchers have identified hundreds of hemoglobin variants, affecting millions of people worldwide.

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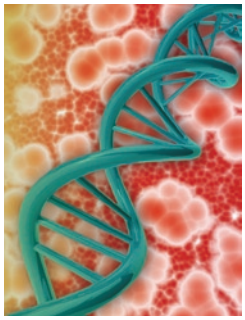
NIDDK
National Institute of Diabetes and Digestive and Kidney Diseases



The NGSP, supported by the NIDDK and the Centers for Disease Control and Prevention, is working to improve and standardize the measurement of A1C in laboratories around the world.

Hemoglobin Variants, from page 1

The most common variant is sickle cell trait, in which a person inherits a gene for hemoglobin S and a gene for hemoglobin A, the usual form of hemoglobin. Sickle cell trait affects about 8 percent of African Americans. Having sickle cell trait or another hemoglobin variant does not increase a person's risk for developing diabetes.

Many individuals are unaware they have a hemoglobin variant such as sickle cell trait because the condition usually causes no symptoms. In diabetes patients of African, Mediterranean, or Southeast Asian descent, the following situations may suggest the presence of a hemoglobin variant:

- an A1C result does not correlate with results of self blood glucose monitoring
- an A1C result is different than expected or radically differs from a previous test result after a change in laboratory A1C methods
- an A1C result is higher than 15 percent

"If you see a significant discrepancy between a patient's A1C reading and the results of routine blood glucose monitoring, consider the possibility that your patient may have a hemoglobin variant and find out if your lab is using a reliable method to measure A1C," advised NIDDK Director Griffin P. Rodgers, M.D. ■

The NIDDK's National Diabetes Information Clearinghouse has prepared two new publications to explain the specific needs for testing blood glucose control in people with diabetes and hemoglobin variants: *Sickle Cell Trait and Other Hemoglobinopathies and Diabetes: Important Information for Physicians* and *For People of African, Mediterranean, or Southeast Asian Heritage: Important Information about Diabetes Blood Tests*. For copies of the publications, go to *www.diabetes.niddk.nih.gov*.

Diabetes
Dateline

National Diabetes Information Clearinghouse
NDIC
www.diabetes.niddk.nih.gov
CELEBRATING 25 YEARS

Diabetes Dateline, an email newsletter, is sent to subscribers by the National Diabetes Information Clearinghouse (NDIC). The newsletter features news about diabetes, special events, patient and professional meetings, and new publications available from the NDIC and other organizations.

If you would like to subscribe, go to *http://catalog.niddk.nih.gov/newsletter.cfm*. You can read or download a PDF version of the newsletter at *www.diabetes.niddk.nih.gov/about/newsletter.htm*.

Executive Editor: Judith Fradkin, M.D.

Dr. Fradkin is the director of the Division of Diabetes, Endocrinology, and Metabolic Diseases for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), part of the National Institutes of Health in Bethesda, MD. Dr. Fradkin earned her M.D. from the University of California at San Francisco and completed an internship and residency at Harvard's Beth Israel Hospital in Boston. Dr. Fradkin came to the NIDDK as a clinical associate in 1979 after an endocrinology fellowship at Yale University. She has overseen NIDDK-supported research in various roles, directing the Institute's research programs in diabetes, cystic fibrosis, endocrinology, and metabolic diseases. A practicing endocrinologist, Dr. Fradkin continues to treat patients at the National Naval Medical Center in Bethesda, where she worked as a staff endocrinologist in the early 1980s.

NIH Recruits Participants for Islet Transplantation Trials

The National Institutes of Health (NIH) is recruiting participants for several islet transplantation studies to improve the safety and long-term success of transplanting islets in people with type 1 diabetes whose islets have been destroyed.

For more information about the islet transplantation studies, call 1–877–isletstudy (475–3878) or visit *www.citisletstudy.org*.

Islets contain the insulin-producing cells of the pancreas. In islet transplantation, thousands of islets are isolated from a donor pancreas and injected into the portal vein feeding a recipient's liver. In a successful transplant, the islets become embedded in the liver and begin producing insulin.

One of the studies, a pivotal phase 3 trial, plans to enroll 130 participants who have received a kidney transplant to compare the success of islet transplantation versus intensive insulin treatment, according to Thomas L. Eggerman, M.D., Ph.D., director of the Islet Transplantation Clinical Trials Program at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The NIDDK is conducting the studies with the National Institute of Allergy and Infectious Diseases.

Another pivotal phase 3 trial plans to study the success of islet transplantation in 48 subjects with very hard-to-control type 1 diabetes. Experimental islet transplantation procedures are currently limited to participants who have had a kidney transplant or who have very hard-to-control type 1 diabetes.

Other islet transplantation studies are aimed at improving transplant approaches, said Eggerman. Through the Clinical Islet Transplantation Consortium (CITC), these studies will focus on

- improving the number of islets that survive transplantation
- reducing the side effects of immunosuppression
- achieving good blood glucose control without hypoglycemia
- following the fate of islets after transplantation and determining why donor islets sometimes fail
- evaluating new ways to safely prevent immune rejection of donor tissues

The Clinical Islet Transplantation Consortium (CITC) includes the following sites and principal investigators:

- University of Minnesota
  Bernhard J. Hering, M.D.
- Northwestern University
  Dixon B. Kaufman, M.D., Ph.D.
- Uppsala University
  Olle Korsgren, M.D., Ph.D.
- Emory University
  Christian Larsen, M.D., Ph.D.
- University of Pennsylvania
  Ali Naji, M.D., Ph.D.
- University of Miami
  Camillo Ricordi, M.D.
- University of Alberta
  James Shapiro, M.D., Ph.D., F.R.C.S.C.

The data management center is located at the University of Iowa. The project director is William R. Clarke, Ph.D.

For more information about the islet transplantation studies, call 1–877–isletstudy (475–3878) or visit *www.citisletstudy.org*. For a copy of an NIDDK fact sheet about islet transplantation, go to *www.diabetes.niddk.nih.gov/dm/pubs/pancreaticislet*. ■

NIDDK Announces Pathfinder Award for Type 1 Diabetes Research

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is seeking applications from exceptionally creative new investigators with innovative proposals for type 1 diabetes research under a new grants program.

Through the new Type 1 Diabetes Pathfinder Award Program, the NIDDK is soliciting proposals in any scientific area relevant to type 1 diabetes research, but not limited to a conventional biomedical or behavioral discipline. The program aims to provide a foundation for investigators to develop innovative approaches to addressing major obstacles to curing, preventing, and treating people with type 1 diabetes. The NIDDK encourages applications proposing hypothesis-driven research and new tools and technology development.

"This is an excellent opportunity for talented new investigators to apply their skills to benefit people with type 1 diabetes."

Judith Fradkin, M.D.
Director of the NIDDK's Division of Diabetes, Endocrinology, and Metabolic Diseases

The NIDDK also welcomes applications from investigators who have not previously studied diabetes but would like to apply their expertise to type 1 diabetes research, such as those with experience in vascular biology, immunology, or neuroscience.

These applicants are strongly encouraged to collaborate with co-investigators who have a strong background in diabetes research. However, applications must have a single principal investigator who has not previously held an R01 or equivalent National Institutes of Health (NIH) grant. Compelling opportunities that might be pursued with the awards are described in a strategic plan for type 1 diabetes research available at *www2.niddk.nih.gov/AboutNIDDK/ResearchAndPlanning/Type1Diabetes*.

"This is an excellent opportunity for talented new investigators to apply their skills to benefit people with type 1 diabetes," said Judith Fradkin, M.D., director of the NIDDK's Division of Diabetes, Endocrinology, and Metabolic Diseases. "We hope these awards will be the start of long and fruitful careers in type 1 diabetes research that will contribute to preventing, reversing, and curing the disease."

Complementary Programs

The Pathfinder Award Program complements ongoing efforts by the NIH and its Institutes and Centers to fund new investigators through other grant programs. Because Pathfinder awards cannot be renewed, awardees are expected to seek support to continue their research through traditional routes, such as applying for an R01 grant.

The Pathfinder Award Program expects to award eight grants in fiscal year 2008. Applicants may request up to $1.5 million in direct costs for the 5-year budget project period.

The NIDDK has answers to many questions about the program at *www2.niddk.nih.gov/Funding/FundingOpportunities/RFA/RFA_T1D_Pathfinder_Award.htm*. For a copy of the Pathfinder Award announcement, visit *www.grants.nih.gov/grants/guide/rfa-files/RFA-DK-08-001.html*.

Dates to Remember

- **March 10, 2008:** Earliest date for submitting a Pathfinder Award application
- **March 13, 2008:** Letter of Intent receipt date
- **April 10, 2008:** Application submission receipt date
- **June/July 2008:** Peer review date(s)
- **August 2008:** Council review date
- **September 30, 2008:** Earliest anticipated start date

Study Finds Increased Risk of Fetal Health Problems at Lower Maternal Blood Glucose Levels

Women with gestational diabetes mellitus (GDM) and their unborn babies may be at greater risk for health problems at lower maternal blood glucose levels than previously thought, according to results of the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study. The results of the study, which was supported by the National Institutes of Health and the American Diabetes Association (ADA), were announced at the ADA's 67th Annual Scientific Sessions in Chicago.

The National Diabetes Education Program has materials designed to help women with a history of gestational diabetes prevent or delay type 2 diabetes. For information, visit *www.ndep.nih.gov/campaigns/campaigns_index.htm.*

"We found that the risk of having a large baby, a first-time Cesarean delivery, low blood glucose levels in the newborn requiring treatment, and high blood insulin levels in the baby that may signal problems ahead all increased as the mother's blood glucose level during pregnancy increased," said Boyd E. Metzger, M.D., principal investigator of the study and professor of medicine in the division of endocrinology at Northwestern University's Feinberg School of Medicine. "These relationships were continuous over the entire range of blood glucose levels found in over 23,000 pregnancies, even in ranges previously considered to be within the normal range for pregnant women."

GDM, defined as high blood glucose levels first discovered during pregnancy, affects about 135,000, or 4 percent, of pregnancies annually in the United States. Women with GDM receive treatment—meal planning, physical activity, and, if needed, insulin injections—to keep blood glucose levels on target during pregnancy.

GDM usually disappears after pregnancy, but women who have had it are at high risk for developing it in subsequent pregnancies—along with type 2 diabetes later in life. In addition, children of mothers with GDM may be at increased risk for obesity during childhood and type 2 diabetes in adulthood.

The HAPO study, conducted in nine countries over 7 years, examined the relationship in 23,325 women between blood glucose levels during the third trimester of pregnancy and the risk of adverse outcomes in the mother and fetus. At about week 28 of the pregnancy, each woman in the study provided three blood samples: a morning fasting blood glucose and, in the oral glucose tolerance test, one sample an hour after drinking a beverage containing 75 grams of glucose and another sample a second hour later. Outcomes were analyzed following delivery.

"We found major independent effects of the mother's blood glucose level on each of the outcomes—the size of the baby, the need for a first Cesarean delivery, low blood glucose requiring treatment, and high insulin levels in the newborn," said Metzger.

The study findings leave several questions open for discussion and resolution, including which blood glucose levels should be considered above normal and which type of blood glucose test is best for diagnosis. A conference involving health care providers, patients, and third-party payers to translate study results into clinical recommendations is planned for June 11 to 13, 2008, in Pasadena, CA, immediately following the ADA meeting in San Francisco.

The National Diabetes Information Clearinghouse has easy-to-read booklets in English and Spanish about gestational diabetes. The booklets are available at *www.diabetes.niddk.nih.gov/dm/pubs/gestational.* ■

NIDDK Scientists Receive Presidential Award

Two scientists from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) were honored at a White House ceremony in November for their outstanding scientific leadership in diabetes and kidney disease research.

The PECASE awards support the continued professional development of awardees, promote careers and foster innovation in science and technology, and recognize the scientific missions of participating agencies.

The presidential award, known as the Presidential Early Career Award for Scientists and Engineers (PECASE), was bestowed upon Alexandra C. McPherron, Ph.D., an NIDDK intramural scientist, and Michelle P. Winn, M.D., an NIDDK grantee, along with 10 other grantees from the National Institutes of Health (NIH). PECASE is the most prestigious award given to young scientists in the United States.

Myostatin and Metabolism

McPherron, a tenure-track investigator with the NIDDK's Genetics of Development and Disease Branch, was chosen for research in which she discovered myostatin, a secreted protein produced by skeletal muscle that inhibits muscle growth. Inhibiting myostatin might be therapeutically useful for treating muscle wasting diseases, diabetes, or obesity, according to McPherron.

From left, NIDDK Director Griffin P. Rodgers, M.D., M.A.C.P.; Alexandra C. McPherron, Ph.D.; and NIH Director Elias A. Zerhouni, M.D.

Through NIDDK research, McPherron is trying to understand the role of myostatin in adult metabolism. "The myostatin protein circulates in the bloodstream so it might act on other tissues, such as adipose, in addition to skeletal muscle," said McPherron. "We don't know whether the improvement in glucose metabolism is due purely to the increase in skeletal muscle mass, the loss of circulating myostatin acting on other tissues, or metabolic changes in skeletal muscle, such as becoming more sensitive to insulin.

We are also trying to understand how myostatin regulates the proliferation and differentiation of muscle precursor cells and their incorporation into muscle fibers."

Familial Kidney Disease

Winn, an assistant professor in the division of nephrology in Duke University's department of medicine, was recognized for the discovery of *TRPC6* as a cause of familial kidney disease. NIDDK-supported genetic studies aim to determine why focal segmental glomerulosclerosis (FSGS), which causes kidney failure, sometimes runs in families.

From left, NIDDK Director Griffin P. Rodgers, M.D., M.A.C.P.; NIDDK Hematology Training and Careers Program Director Terry R. Bishop, Ph.D.; Michelle P. Winn, M.D.; and NIH Director Elias A. Zerhouni, M.D.

"Dr. Winn's research is important because it has opened a new angle to understanding a disease that we have understood very poorly—and which disproportionately affects African Americans," said Rebekah Rasooly, NIDDK deputy director for the Division of Kidney, Urologic, and Hematologic Diseases.

FSGS is a common, irreversible process that can result in steroid-resistant nephrotic syndrome, a condition marked by very high protein levels in the urine; low protein levels in the blood; swelling, especially around the eyes, feet, and hands; and high cholesterol. FSGS often appears as a primary condition, with a propensity to progress to end-stage renal disease. The peak incidence

Presidential Award, continued on page 7

Featured in the NIDDK Reference Collection

Insulin Regimens and Type 2 Diabetes

This section about matching insulin regimens to individual needs in people with type 2 diabetes is from a special, continuing education supplement to *Diabetes Educator* that helps readers understand some of the barriers to insulin use among clients. Nearly 60 percent of individuals diagnosed with type 2 diabetes maintain A1C levels higher than the recommended 7 percent target. Insulin therapy is associated with the most substantial A1C reductions of any diabetes treatment available. The author focuses on frequently encountered barriers to insulin use and suggests strategies to ease the transition to insulin therapy.

Topics covered include the physiological benefits of insulin therapy, the psychological resistance of some patients to starting insulin, clinical inertia, and the establishment of appropriate dosing guidelines for patients with type 2 diabetes. The author concludes it is the role of diabetes educators to identify patients' management problems before glucose levels get too high for too long. "Tying It All Together: Matching Insulin Regimens to Individual Patient Needs" is available in *Diabetes Educator*. 33(Supl 4):S91–S95. April 2007.

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Reference Collection is a free, online database that helps health care professionals, health educators, patients, and the general public find educational materials not typically referenced in most databases. The NIDDK does not control or endorse the information contained in this collection—it is provided as a convenience to visitors.

Visit the Reference Collection at *www.catalog.niddk.nih.gov/resources* to find more diabetes resources.

Presidental Award, from page 6

is in adolescence and young adulthood. The familial forms appear more often in younger children. The worst prognosis is observed in African Americans.

"I can't even begin to say how grateful I am to the NIH and, specifically, to the NIDDK for all they've done," said Winn. "They have fostered my career and been very supportive."

Winn, who had an NIH K08 award, which provides physicians with up to 5 years of support to pursue research careers, is now in the second year of an R01 grant and will apply for another R01 in February. The R01 research project grant is awarded to eligible institutions on behalf of a principal investigator to support a discrete project related to the investigator's area of interest and competence.

The NIH has funded 129 PECASE recipients since the program's inception.

The PECASE awards, commissioned by President Clinton in 1996, support the continued professional development of awardees, promote careers and foster innovation in science and technology, and recognize the scientific missions of participating agencies. The NIH has funded 129 PECASE recipients since the program's inception. A list of previous NIH recipients of this prestigious award is available at *www.grants.nih.gov/grants/policy/pecase.htm*. ■

Additional Resources

The Awareness and Prevention Series fact sheets are written in English on one side and Spanish on the other.

Awareness and Prevention Series

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) has created a new health information series to raise awareness about diabetes, digestive diseases, and kidney and urologic diseases among people not yet diagnosed with these illnesses.

The Awareness and Prevention Series, which the NIDDK developed for community health fairs, workplace health forums, family reunions, and similar events, features two-page fact sheets on a wide range of health topics. Each fact sheet gives readers a snapshot of an illness, highlighting risk factors, symptoms, prevention tips, and where to go for more information. The fact sheets are written in English on one side and Spanish on the other. Diabetes fact sheets address type 2 diabetes, prevention of diabetes problems, diabetes and risk for heart disease and stroke, and gestational diabetes.

"The series is designed to encourage readers to ask 'Could this be me or someone I care for?'" said Kathy Kranzfelder, director of the NIDDK Information Clearinghouses. "Raising awareness of these illnesses, we hope, will help people learn to prevent them or see a doctor if they have symptoms."

The copyright-free Awareness and Prevention Series publications can be downloaded or ordered through the National Diabetes Information Clearinghouse website at *www.diabetes.niddk.nih.gov/dm/ap.htm*. The website also has fact sheets and booklets with more complete information about these topics and many others related to diabetes. ■

New Interactive Tools

New to the Interactive Health Education Tools section of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) website are

Podcasts

- NIDDK to Launch New Information Campaign: Important Information about Diabetes Blood Tests
- Interview with Dr. Francine Kaufman: World Diabetes Day

Vodcasts

- Information about World Diabetes Day

The NIDDK interactive tools section consolidates all the tools and resources about diabetes from the National Institutes of Health and the National Library of Medicine. To access these resources, visit *www.diabetes.niddk.nih.gov/resources/HealthTools*. ■

NDEP Introduces Resources to Help Teens Manage Diabetes

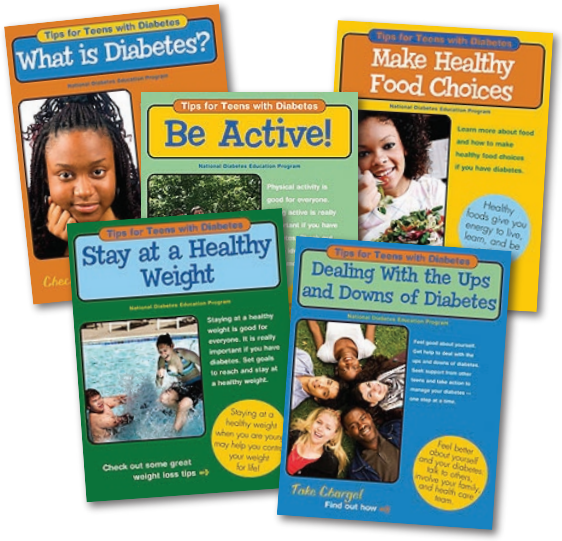
The National Diabetes Education Program (NDEP) has introduced a series of tip sheets and an online quiz to help teens manage their diabetes and reduce their risk for complications.

The Tips for Teens with Diabetes Series includes

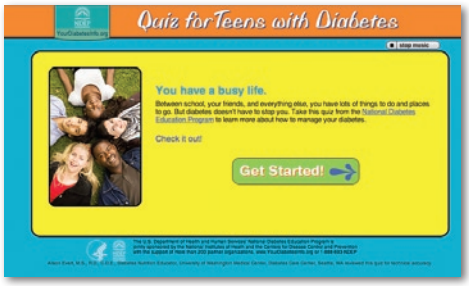
- *What is Diabetes?*
- *Be Active*
- *Make Healthy Food Choices*
- *Stay at a Healthy Weight*
- *Dealing With the Ups and Downs of Diabetes*

The interactive quiz is based on information in the tip sheets and links directly to them. The NDEP also created a tip sheet for teens at risk for type 2 diabetes. The new tools support the 2007 World Diabetes Day campaign theme "Diabetes in Children and Adolescents," which raises awareness of the rising prevalence of both type 1 and type 2 diabetes among youth worldwide.

While type 1 diabetes remains the most common form of diabetes among children and young adults, soaring obesity rates among young people are making type 2 diabetes more common, particularly in Hispanic, African American, and American Indian teens. One in 523 people younger than age 20—about 176,500 young people—has diabetes, according to the U.S. Centers for Disease Control and Prevention. ■



To download or order copies of the tip sheets, visit *www.ndep.nih.gov/diabetes/youth/youth.htm#TSKidsType2.*

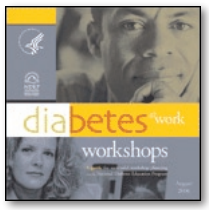


To access the quiz for teens with diabetes, go to *www.ndep.nih.gov/diabetes/youth/quiz.*

NATIONAL DIABETES EDUCATION PROGRAM

For more information about the NDEP, visit *www.ndep.nih.gov.*

Toolkit Helps Employers Tackle Diabetes in the Workplace



A new NDEP toolkit gives employers the tools they need to conduct a diabetes workshop in the workplace. The "Diabetes At Work Workshop Toolkit" is the product of nationwide workshops about the key role employers could play in diabetes prevention and control through workplace interventions. The free toolkit includes all the resources needed to get started, including a step-by-step plan for coordinating and executing a Diabetes At Work workshop and articles about the benefits of diabetes workplace programs. The toolkit is available on CD–ROM at *www.ndep.nih.gov/diabetes/pubs/catalog.htm#PubsHCPrev.* ■

Upcoming Meetings, Workshops, and Conferences

The following meetings will be held at the National Institutes of Health (NIH) in Bethesda, MD:

Genes, Environment, and Health Initiative: Translating Whole Genome Association Data into Clinical Practice

This meeting will explore the challenges in using basic findings from the Genes, Environment, and Health Initiative to positively affect health. The NIH Genes, Environment, and Health Initiative was launched in 2006 to help identify major genetic susceptibility factors for diseases with substantial public health impact and to develop technologies for measuring potentially causative environmental exposures. The meeting, scheduled for March 10 to 11, 2008, will feature presentations about important new genetic findings for diabetes and other diseases, approaches to using those findings for therapeutic or diagnostic purposes, and ethical and social issues inherent in such research. For more information and to register, visit *www3.niddk.nih.gov/fund/other/GeiTranslation*.

Workshop on the Establishment, Maintenance, and Turnover of Fat Depots

This workshop, to be held May 21 to 22, 2008, will focus on the molecular players involved in the establishment, maintenance, and turnover of different fat depots. Speakers will present what is known about the molecular determinants of depot size and deposition sites, cellular makeup, and factors that control remodeling and turnover of different fat depots. Plenary talks, selected "hot topic" presentations, and a poster session will provide a forum for basic scientists and clinical researchers working across these areas to share information. For more information, go to *www3.niddk.nih.gov/fund/other/FatDepots2008*.

National Conferences

The National Institute of Diabetes and Digestive and Kidney Diseases Information Clearinghouses will be exhibiting at the following upcoming conferences:

- **American College of Physicians Internal Medicine 2008**
  May 15 to 17 in Washington, DC.

  For more information, go to *www.acponline.org/cme/as/im08.htm?hp*.

- **American Academy of Physician Assistants Annual Conference**
  May 24 to 29 in San Antonio.

  For more information, go to *www.aapa.org/annual-conf*. ■

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