



Diabetes

Dateline

National Diabetes Information Clearinghouse

Fall 2007

Researchers Identify New Genetic Risk Factors for Type 2 Diabetes

In the most comprehensive look at genetic risk factors for type 2 diabetes to date, a U.S.-Finnish team, along with two consortia—the Diabetes Genetics Initiative at the Broad Institute and the Wellcome Trust Case Control Consortium/U.K. Type 2 Diabetes Genetics Consortium—has identified at least four new genetic variants associated with increased diabetes risk and confirmed the existence of another six. The groups' findings boost the number of genetic variants linked to increased susceptibility to type 2 diabetes to at least 10.

The U.S.-Finnish team received major support from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Human Genome Research Institute's (NHGRI) Division of Intramural Research, both part of the National Institutes of Health (NIH). The laboratory analysis of genetic variants in the first stage of the study was conducted by the Center for Inherited Disease Research with funding from the NIH and Johns Hopkins University.

“It has been a formidable challenge to identify the complex genetic factors involved in common diseases, such as type 2 diabetes,” said NHGRI Director Francis Collins, M.D., Ph.D. “Now, thanks to the tools and technologies generated by the sequencing of the human genome and subsequent mapping of common human genetic variations, we finally are making significant progress.”

In addition to lifestyle factors like obesity, poor diet, and lack of exercise, doctors have long known that heredity is a significant risk factor for developing type 2 diabetes—people who have a parent or sibling with type 2 diabetes face a



3.5 times greater risk of developing the disease than people with no family history. However, researchers have only just begun to zero in on particular genetic variants that increase or decrease disease susceptibility.

To make their discoveries, researchers used a relatively new, comprehensive strategy known as a genome-wide association study. For this kind of study, researchers use two groups of participants: a large group of people with the disease being studied and a large group of otherwise similar people without the disease. Using DNA purified from blood cells, researchers quickly survey each participant's complete set of DNA, or genome, for strategically selected markers of genetic variation.

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National Institute of
Diabetes and Digestive
and Kidney Diseases





“These genetic findings are exciting news for diabetes research. While more work remains to be done, the newly identified genetic variants may point us in the direction of valuable new drug targets for the prevention or treatment of type 2 diabetes.”

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NIDDK Director

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If certain genetic variations are found more frequently in people with the disease compared with healthy people, the variations are said to be associated with the disease. The associated genetic variations can serve as a strong pointer to the region of the genome where the genetic risk factor resides. However, the first variants detected may not themselves directly influence disease susceptibility, and the actual causative variant may lie nearby. This means researchers often need to take additional steps, such as sequencing every DNA base pair in that particular region of the genome, to identify the exact genetic variant that affects disease risk.

Major Effort

The genomes of more than 32,000 people were tested for the study, making it one of the largest genome-wide association efforts conducted to date.

The newly identified diabetes-associated variations lie in or near

- *IGF2BP2*. This gene codes for a protein called insulin-like growth factor 2 mRNA binding protein 2. Insulin-like growth factor 2 is thought to play a role in regulating insulin action.
- *CDKAL1*. This gene codes for a protein called CDK5 regulatory subunit associated protein1-like1. The protein may affect the activity of the cyclin-dependent kinase 5 (CDK5) protein, which stimulates insulin

production and may influence other processes in the pancreas’ insulin-producing, or beta, cells.

- *CDKN2A* and *CDKN2B*. The proteins produced by these genes inhibit the activity of cyclin-dependent protein kinases, including one that has been shown to influence the growth of beta cells in mice.
- chromosome 11. One association is located in a region of chromosome 11 not known to contain any genes. Researchers speculate that the variant sequences may regulate the activity of genes located elsewhere in the genome, but more work is needed to determine the exact relationships to pathways involved in type 2 diabetes.

Genetic variants associated with diabetes that were confidently confirmed by the new research are *TCF7L2*, *SLC30A8*, *HHEX*, *PPARG*, and *KCNJ11*.

“These genetic findings are exciting news for diabetes research,” said NIDDK Director Griffin P. Rodgers, M.D. “While more work remains to be done, the newly identified genetic variants may point us in the direction of valuable new drug targets for the prevention or treatment of type 2 diabetes.”

Visit www.diabetes.niddk.nih.gov/dm/pubs/overview for more information about diabetes and www.genome.gov/20019523 for more information about genome-wide association studies. ■

Diabetes Dateline



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, send an email to niddk@info.niddk.nih.gov. 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.



Rodgers Renews Commitment to Diabetes Research

Griffin P. Rodgers, M.D., director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH), shares his vision and the Institute's goals for diabetes research.



"At all levels of the NIDDK, we will continue to pursue the most compelling research to combat type 1 diabetes and type 2 diabetes and obesity, its most important risk factor."

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NIDDK Director

The rapidly growing problem of diabetes in this country poses a major public health challenge that shows no signs of abating. With each passing year, the human and economic costs of diabetes continue to mount, while the burden of managing the disease overwhelms many people with diabetes and their families.

As the recently appointed director of the NIDDK, I am committed to a vigorous, multipronged research program in diabetes and its many debilitating complications. Diabetes affects almost 21 million Americans and costs an estimated \$132 billion annually in medical expenses and indirect costs. Eye, kidney, nerve, heart, and other complications of diabetes reduce the lifespan and quality of life for people with this disease.

At all levels of the NIDDK, we will continue to pursue the most compelling research to combat type 1 diabetes and type 2 diabetes and obesity, its most important risk factor. Moreover, we will remain firmly committed to basic, translational, and clinical research; research training and career development; and the dissemination of health information to improve the lives of people with diabetes, their families, and those at risk for the disease.

In particular, the NIDDK will work to

- strengthen a vigorous investigator-initiated research portfolio. The capability of individual investigators is crucial for research progress. Therefore, the NIDDK will continue to fund investigator-initiated grants
- support pivotal clinical studies and trials. The NIDDK will continue to seek out and support critical studies. The NIDDK's ongoing support of the Epidemiology of Diabetes Interventions and Complications study and the Diabetes Prevention Program Outcomes study are just two examples of important large-scale studies under way—studies that can help change the way diabetes is treated.
- preserve a stable pool of talented new investigators. The ideas and fresh perspectives of new investigators invigorate the diabetes research community. We will take steps to encourage today's generation of young scientists to dedicate their careers to diabetes research and will work to foster exceptional research training and mentoring opportunities. These programs help to ensure a cadre of well-trained Ph.D. scientists and physician scientists specializing in endocrinology and diabetes research.
- ensure knowledge dissemination through outreach and communications. We are continuing efforts to impart science-based

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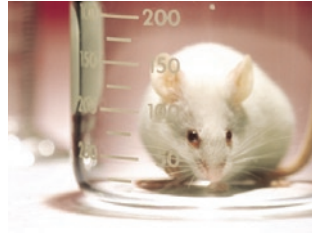
NIH Funds Knockout Mouse Repository

The National Institutes of Health (NIH) is creating a repository for its Knockout Mouse Project, a trans-NIH initiative to increase the availability of genetically altered mice and related materials. The repository will archive, maintain, and distribute up to 8,500 strains of embryonic stem cell clones, live mouse lines, frozen embryos and sperm, and vectors.

“This initiative will ensure knockout mouse strains are made available to the research community in an economical and timely manner.”

Barbara Alving, M.D.
Director, NIH National Center for Research Resources

Knockout mice are lines of mice in which specific genes have been completely disrupted, or knocked out. Researchers can use knockout mice to develop better models of many inherited human diseases.



“Knockout mice are useful tools that allow researchers to study human conditions such as cancer, diabetes, and Alzheimer’s disease and then translate discoveries into cures and treatments that will improve public health,” said Barbara Alving, M.D., director of the NIH National Center for Research Resources. “This initiative will ensure knockout mouse strains are made available to the research community in an economical and timely manner.”

The National Institute of Diabetes and Digestive and Kidney Diseases is one of several NIH institutes supporting the \$50 million Knockout Mouse Project. Nearly \$5 million of that amount supports the creation and maintenance of the repository, which is overseen by

the University of California, Davis, and the Children’s Hospital Oakland Research Institute in Oakland, CA.

For more information about the Knockout Mouse Project, visit www.komp.org. To request information or products, researchers can call 1-888-KOMP-MICE (566-7642) or send an email to service@komp.org. ■

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knowledge gained from research funded by the NIH and other agencies, such as the Centers for Disease Control and Prevention, to health care professionals and the public for the direct benefit of people with diabetes and their families.

The NIDDK is also committed to the National Diabetes Education Program (NDEP). As we enter a new era of translating the most rigorous findings in diabetes research to improve diabetes prevention and treatment, the NDEP is urgently committed to slowing the diabetes epidemic and improving diabetes care. I look forward to working with the leadership and volunteers of the NDEP to make a difference in the lives of people affected by diabetes. ■



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- support pivotal clinical studies and trials
- preserve a stable pool of talented new investigators
- ensure knowledge dissemination through outreach and communications

NIDDK Unveils Website Makeover

Dynamic graphics and an enhanced layout define the redesigned website launched by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

The NIDDK's website reformat is aimed at best directing the site's users—scientists, health care professionals, and the general public—to the topics and sections they seek.

While the fundamental architecture of information remained stable in the redesign process, the committee advancing the design sought to update the website's look and feel and improve the immediate success of information seekers.

“Our new design should save researchers, health professionals, and the public valuable time finding important scientific and consumer health information,” said NIDDK Director Griffin P. Rodgers, M.D. “We are continually striving to make our resources more readily available to a wider audience and in the latest formats. The website plays a key role in helping to disseminate this information.”

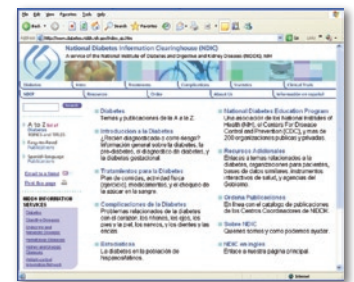
NIDDK Website Features Health Information in Spanish

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) has launched a new portal to feature Spanish-language diabetes materials and resources on its website.

People looking for information about diabetes in Spanish can now go directly to the Spanish-language portal page, where they will find an A to Z list of topics and titles. The online system for ordering NIDDK materials now includes descriptions in Spanish of available publications to help visitors choose the resources they want. The National Diabetes Information Clearinghouse has 35 publications about diabetes in Spanish and will be adding more in the future, including one-page fact sheets that are part of the NIDDK's Awareness and Prevention Series.

The NIDDK website, which receives nearly 2 million visits per month, scored an 83 out of 100 possible points on the American Customer Satisfaction Index (ACSI) for March to June 2007, making it a top-performing site. The ACSI measures the performance of about 200 private-sector companies and many government agencies. Visitors rate government websites on various components of overall satisfaction, such as ease of search and navigation, look and feel, functionality, and content. Ratings are converted to a score on a 100-point scale using ACSI methodology.

The website features a reference collection, an interactive health tools portal, an image library, and portals containing health information in Spanish. ■



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To visit the site, go to www.niddk.nih.gov.

The new Spanish-language portal is available at www.diabetes-espanol.niddk.nih.gov.

The NIDDK website also links to the Spanish-language portal for MedlinePlus and the NIDDK Reference Collection, a free, online database that includes 78 resources in Spanish.

To help people order materials in Spanish, two full-time bilingual information specialists respond to requests for health information. In the past 12 months, more than 17,500 Spanish-language publications were ordered through the three NIDDK Clearinghouses. The NIDDK responded to more than 700 information requests in Spanish during that time. ■

NIDDK-funded Video Game Touting Healthy Lifestyle Wins Award

A kids' video game promoting healthy eating and physical activity, funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), won a 2007 Horizon Interactive Gold Award, its fourth international honor.

"Escape from Diab," a science fiction adventure video game, is one of two video game-based behavioral interventions supported by a \$9 million NIDDK grant. Archimage, Inc., an architectural design firm that develops video games, created "Escape from Diab" and its sister title, "Nanoswarm: Invasion from Inner Space," in collaboration with experts at the Children's Nutritional Research Center of Houston's Baylor College of Medicine. Both games run on Windows personal computers and have dedicated websites that feature elements of the games.

The Horizon Interactive Awards is a leading international, interactive media awards competition. The video game also was nominated for 2007 Best Youth Website in the 11th Annual Webby Awards, the top international award honoring excellence on the Internet, including websites, interactive advertising, online film and video, and mobile websites. ■



"Escape from Diab" is a serious video-game adventure in healthy eating and exercise. It puts players inside a sci-fi action and adventure where healthy lifestyle choices are the keys to winning. To access the game, go to www.escapefromdiab.com.

News Brief

UN Celebrates World Diabetes Day

World Diabetes Day, recognized on November 14, will also be celebrated as a United Nations (UN) Day for the first time this year, thanks to a resolution passed late last year by the UN General Assembly.

The landmark resolution acknowledged the global threat of the diabetes epidemic and stipulated that World Diabetes Day be celebrated as a United Nations Day beginning in 2007. The resolution calls on all nations to work toward the prevention, treatment, and care of diabetes.

World Diabetes Day was established by the World Health Organization (WHO) and the International Diabetes Federation in 1991 to coordinate diabetes advocacy worldwide. The WHO estimates that more than 180 million people worldwide have diabetes, and the number is likely to more than double by 2030. For more information about World Diabetes Day, visit www.worlddiabetesday.org. ■



NDEP Announces National Campaign to Promote Free Diabetes Resources

The National Diabetes Education Program (NDEP) announced a new national campaign to coincide with its 10th anniversary this year.

The *One Call. One Click.* initiative, designed to promote the NDEP as the public's number one source for free diabetes information, includes distributing media kits that contain new print, online, and radio public service announcements in English and Spanish to the program's 200 partners and the public media. The NDEP announced the campaign at its June 7 steering committee meeting in Bethesda, MD.

As part of the campaign, the NDEP established a new toll-free phone number, 1-888-693-NDEP (6337), and has established a new website address to make it easier for people to remember: www.YourDiabetesInfo.org. This new phone number and website address are simply "aliases," which will connect to the traditional NDEP phone number and website still in effect, NDEP Director Joanne Gallivan told steering committee meeting attendees.

Gauging Public Awareness

In addition to the campaign, Gallivan said the NDEP commissioned a survey of the public's knowledge, attitudes, and practices related to diabetes. The survey, which had a target sample size of 1,600 people aged 45 and older, found that

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89 percent of respondents considered diabetes to be a serious condition. Other results culled from the survey include

- 46 percent of the surveyed population is at high risk for diabetes as defined by risk factors, but only a quarter of them reported feeling at risk for diabetes
- being overweight, heredity, and lack of exercise are well-known risk factors for diabetes, but belonging to a particular race or ethnic group is not a recognized risk factor
- 57 percent of people with diabetes have heard the term "A1C," and 30 percent of people with diabetes can report their last A1C level
- 39 percent of the public and half the people with diabetes are aware of the link between diabetes and heart disease and identify heart disease as a serious health problem caused by diabetes
- the public—especially people with diabetes—have heard of the NDEP's campaigns

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



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Featured in the NIDDK Reference Collection

Diabetes Self-management



Go to www.aadenet.org/products/desk_reference.shtml for more information about this desk reference.

The American Association of Diabetes Educators has published a comprehensive desk reference entitled *The Art and Science of Diabetes Self-Management Education* for health care professionals, community professionals, and others who provide education to people with diabetes. The textbook is divided into three sections: “Understanding the Individual’s Health Behaviors and Choices,” which provides background and theoretical foundations necessary for effective self-management education; “Translating Science to Art: Understanding the Disease and Its Treatment,” which provides technical information about the different aspects of diabetes, its therapies, and chronic complications; and “Facilitating Successful Self-Management,” which lays out the new “core” of knowledge for well-designed diabetes education. Each chapter ends with teaching strategies, resources, and patient education tips. The textbook is available from the American Association of Diabetes Educators, 100 West Monroe, Suite 400, Chicago, IL 60603, 1-800-338-3633. The cost to members is \$199; the nonmember price is \$249.

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

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

- Fathers Take Care of Yourselves When Dealing with CVD and Diabetes
- National Diabetes Education Program Promotes Diabetes Prevention
- Cardiovascular Disease Linked to Diabetes
- Eye Diseases in Women

Videos

- Demystifying Medicine—Diabetes: New Clinical and Basic Dimensions

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. ■