News and Resources from the National Institutes of Health

Digestive Diseases
NEWS
National Digestive Diseases Information Clearinghouse
Spring 2012

Vitamin E Helps Diminish a Type of Fatty Liver Disease in Children

Adapted from NIH News

A specific form of vitamin E improved the most severe form of fatty liver disease in some children, according to a study funded by the National Institutes of Health (NIH). Results appeared in the April 27, 2011, issue of the *Journal of the American Medical Association*. A previous study found vitamin E effective in some adults with the disease.

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease among U.S. children. NAFLD ranges in severity from steatosis (fat in the liver without injury) to nonalcoholic steatohepatitis, or NASH (fat, inflammation, and liver damage). Fatty liver increases a child's risk of developing heart disease and liver cirrhosis. The only way to distinguish NASH from other forms of fatty liver disease is with a liver biopsy. Weight loss may reverse the disease in some children, but other than dietary advice, there are no specific treatments. Excess fat in the liver is believed to cause injury by increasing levels of oxidants, compounds that damage cells.

Most children with fatty liver disease are overweight and resistant to insulin, a critical hormone that regulates energy. Boys are more likely affected than girls, as are Hispanic children compared to African-Americans and whites.

Using liver biopsies, researchers found that after 96 weeks of treatment, 58 percent of the children on vitamin E no longer had NASH, compared to 41 percent of the children on metformin (a diabetes drug), and 28 percent on placebo. Vitamin E was better than placebo because it significantly reduced enlargement and death of liver cells.

"These results suggest that vitamin E improves or resolves NASH in at least half of children, which we previously showed to be true in adults,"

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NIDDK
National Institute of Diabetes and Digestive and Kidney Diseases

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said Stephen P. James, M.D., director of the digestive diseases and nutrition division at NIH's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), which funded the study. While the results are encouraging, patients using vitamin E for NASH should be under a doctor's care. "We hope to build on these results by looking for other therapies and reliable, non-invasive ways to monitor the disease and response to therapy."

"These results suggest that vitamin E improves or resolves NASH in at least half of children, which we previously showed to be true in adults."

Stephen P. James, M.D.
Director, Digestive Diseases and Nutrition Division, NIDDK

The Treatment of Nonalcoholic Fatty Liver Disease in Children (TONIC) trial studied whether vitamin E (an antioxidant) or metformin could improve fatty liver disease. The endpoint to measure success was either a sustained reduction in the liver enzyme alanine aminotransferase (ALT) or improvements in the liver as shown by biopsies. A total of 173 children, mostly whites and Hispanics ages 8 to 17, were recruited into three treatment groups. The children received either 500 milligrams of metformin or 400 international units of a natural form of vitamin E or placebo twice a day for 2 years.

Neither vitamin E nor metformin were significantly better than placebo in reducing ALT levels. Twenty-six percent of patients on vitamin E, 16 percent on metformin, and 17 percent of those on placebo had reduced liver enzyme levels. Interestingly, ALT levels improved more rapidly among patients on vitamin E (within 6 months) compared to those on placebo. The ALT levels among the children on placebo improved over the 2 years.

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Would you like to know more about NIDDK-supported research?

The National Institutes of Health (NIH) provides access to a variety of reporting tools, reports, data, and analyses of NIH research activities at the Research Portfolio Online Reporting Tools (RePORT) website, *www.projectreporter.nih.gov/reporter.cfm.* One of the tools available is RePORT Expenditures and Results (RePORTER), which allows users to search a repository of NIH-funded research projects and access and download publications and patents resulting from NIH funding. ■

Digestive Diseases
News

Digestive Diseases News, an email newsletter, is sent to subscribers by the National Digestive Diseases Information Clearinghouse (NDDIC). The newsletter features news about digestive diseases, special events, patient and professional meetings, and new publications available from the NDDIC and other organizations.

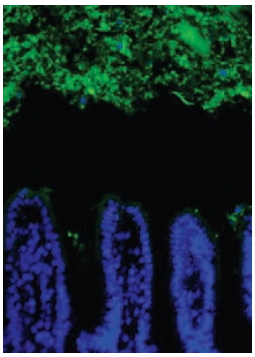
You can read or download a PDF version or subscribe to the newsletter at *www.digestive.niddk.nih.gov/about/newsletter.aspx.*

Executive Editor: Stephen P. James, M.D.

Dr. James is the director of the Division of Digestive Diseases and Nutrition within the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). As director, Dr. James oversees planning, implementation, and evaluation of a national research effort focused on gastrointestinal, pancreatic, hepatobiliary, and nutrition diseases and conditions. Before joining the NIDDK in 2001, Dr. James directed the division of gastroenterology at the University of Maryland's School of Medicine for 10 years.

Protein Creates Partition between Bacteria and the Gut

Originally published in NIH Research Matters
By Vicki Contie



Cells that make up the intestinal wall form fingerlike projections (blue) and release antibacterial proteins that keep bacteria (green) at a distance. *Image courtesy of Shipra Vaishnava and Lora Hooper.*

Scientists have identified a microbe-fighting protein that helps create a buffer zone between the inner walls of the intestines and the bacteria within. The finding may explain how helpful bacteria can survive in the digestive tract without triggering an immune attack.

"Our research shows that RegIIIγ is critical for maintaining what we call the demilitarized zone—the zone of separation between the surface of the intestine and the bulk of bacteria."

Lora Hooper, Ph.D.
Associate Professor, Department of Immunology, University of Texas Southwestern Medical Center

Researchers have long known that about 100 trillion bacteria reside in our intestines. Many of these microbes help us digest food and absorb important nutrients. In the colon, a dense layer of mucus creates a physical barrier between the gut's walls and microbes. The mucus helps to prevent bacterial infection and an immune attack. However, in the small intestine, the mucus layer is thin and permeable to allow absorption of nutrients. Scientists have puzzled over how the mutually beneficial relationship between bacteria and host is maintained.

Dr. Lora Hooper of the University of Texas Southwestern Medical Center and her colleagues suspected that certain immune mechanisms might work in partnership with the mucus layer in the small intestine to keep bacteria at bay. Their investigation, focusing on mice, was funded in part by NIH's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

As reported in the October 14, 2011, issue of *Science,* the researchers first assessed how microbes are naturally positioned relative to the intestinal lining. Using a technique that makes bacteria glow green and intestinal walls blue, the scientists found a 50-micron zone of separation between the bacteria and the lining. Other researchers had previously found that the colon lining in mice also has a 50-micron bacteria-free zone.

The researchers then studied mice lacking the signaling protein MyD88, which activates the innate immune system. This branch of the immune system recognizes certain molecular patterns in disease-causing microbes. With the innate immune system impaired, bacteria invaded the protective zone and came in direct contact with the intestinal lining.

MyD88 controls the production of several antimicrobial proteins in specialized cells in the intestine's lining. Following this clue, the researchers identified a protein called RegIIIγ as responsible for the bacteria-free zone. Mice lacking RegIIIγ lacked the buffer zone between bacteria and the intestinal wall. The intestinal lining had increased numbers of bacteria adhering to it—a feature sometimes seen with digestive disorders such as inflammatory bowel disease.

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"We believe all children in the trial benefited from the frequent diet and exercise advice provided throughout the study," said Joel E. Lavine, M.D., Ph.D., a TONIC principal investigator and professor of pediatrics at Columbia University, New York. "Now we have information on the natural history of a placebo group over time, which will help us design future trials."

Using biopsies in children with liver disease is unique. "TONIC is ground-breaking on two fronts. It is the first study to use liver biopsy to evaluate potential treatments for any liver disease in children," said Patricia Robuck, Ph.D., M.P.H., the project scientist at NIDDK. "It is also the first multi-center, randomized, controlled trial to use a liver biopsy to evaluate a therapy for fatty liver in children, considered the most rigorous design for studies of liver disease."

TONIC was conducted by NASH Clinical Research Network investigators at:

- Case Western Reserve University and the Cleveland Clinic, Cleveland
- Children's National Medical Center, Washington, D.C.
- Indiana University, Indianapolis
- Johns Hopkins University, Baltimore (data coordinating center)
- Saint Louis University and Washington University, St. Louis
- Texas Children's Hospital, Houston
- University of California, San Diego
- University of San Francisco
- Virginia Commonwealth University, Richmond
- Virginia Mason Medical Center, teamed with the University of Washington, Seattle

Additional NIH support for TONIC was provided by the National Cancer Institute, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, and the National Center for Research Resources. Learn more about TONIC at *www.clinicaltrials.gov*—search for NCT00063635—and about the NASH network at *www.jhucct.com/nash/open/centers/centers.htm.*

The National Digestive Diseases Information Clearinghouse, an information service of the NIDDK, has free fact sheets and easy-to-read booklets about digestive diseases. For more information or to learn how to obtain copies, visit *www.digestive.niddk.nih.gov.* ■

Protein Creates Partition,
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"Maintaining a protective zone between you and your bacteria seems to be important for maintaining intestinal health," says Hooper. "Our research shows that RegIIIγ is critical for maintaining what we call the demilitarized zone—the zone of separation between the surface of the intestine and the bulk of bacteria." RegIIIγ and related proteins might represent a potential new target for treating or preventing certain digestive disorders.

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Long-Term Diet Linked to Microbe Type in the Gut

Adapted from University of Pennsylvania news release

"You are what you eat" is familiar enough, but how deep do the implications go? An interdisciplinary group of investigators from the Perelman School of Medicine at the University of Pennsylvania have found an association between long-term dietary patterns and the bacteria of the human gut.

"We found that diet is linked to the types of microbes in the gut, which provides a potential mechanism connecting diet with health."

Frederic D. Bushman, Ph.D.
Professor of Microbiology, Perelman School of Medicine, University of Pennsylvania

In a study of 98 healthy volunteers, the gut bacteria separated into two distinct groups, called enterotypes, that were associated with long-term consumption of either a typical Western diet rich in meat and fat versus a more agrarian diet rich in plant material. A subsequent controlled-feeding study of 10 subjects showed that gut microbiome composition changed detectably within 24 hours of initiating a high fat/low fiber or low fat/high fiber diet, but that the enterotype identity of the microbe group remained stable during the 10-day study, emphasizing the short-term stability of the enterotypes. The findings, [published first online in *Science Express* and in the October 7, 2011, issue of *Science,*] may have implications for exploring the relationship between diet and therapies for gastrointestinal disorders.

"It's well known that diet strongly affects human health, but how diet influences health is not fully understood," says Frederic D. Bushman, Ph.D., professor of Microbiology, who led the study together with co-principal investigators James Lewis, M.D., MSCE, professor of Medicine in the Division of Gastroenterology and professor of Epidemiology, and Gary Wu, M.D., professor of Medicine in the Division of Gastroenterology. "We found that diet is linked to the types of microbes in the gut, which provides a potential mechanism connecting diet with health."

Wu noted, "Although the mechanisms by which diet influences gut microbes remain to be fully characterized, our findings also provide insights into the differences in the types of gut bacteria observed in various societies across the globe."

The team used diet inventories—surveys that catalog what people have eaten in the last 24 hours and also what they usually eat long-term—and compared that to sequenced DNA from stool samples from 98 healthy individuals. The sequencing allowed the researchers to count and identify gut bacteria. Fecal bacterial communities clustered into two broad groups, or enterotypes, distinguished primarily by levels of *Bacteroides* and *Prevotella.*

The enterotypes were strongly associated with diet, particularly protein and animal fat (*Bacteroides* genus) versus carbohydrates (*Prevotella* genus). Both *Bacteroides* and *Prevotella* are broad genera of bacteria species that typically live in the human gut. Humans tend to have mostly a species from one bacterial group but not both. Vegetarians were more likely to be in the *Prevotella* group, the enterotype associated with diets enriched in carbohydrates and lacking meat, and the one vegan was also in the *Prevotella* group.

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NIDDK Workshop on Acute Diarrheal Diseases Focuses on Translational Approaches for New Drug Development

The National Institute of Diabetes and Digestive and Kidney Diseases hosted a workshop in September 2011 on Translational Approaches for Pharmacotherapy Development for Acute Diarrhea. The workshop brought together investigators to examine the current understanding and challenges of acute diarrhea treatment, the pathogenesis of acute diarrhea, the pathophysiologic mechanisms involved, and the advances needed to develop new drug therapies for treating diarrheal diseases.

Workshop attendees summarized the present-day challenges of treating diarrheal diseases:

- New epidemics of infectious diarrhea—such as the 2011 European Shiga-toxin-producing *Escherichia coli* and ongoing Haitian cholera outbreaks—have added to the burden of worldwide diarrheal disease.
- Despite improvements in oral rehydration solution (ORS) therapy, its use has dropped since the 1990s, which may be due to several factors including failure to significantly reduce the duration or volume of diarrhea.
- Repeated diarrheal episodes in children have been linked to malnutrition, stunting, and impaired physical and mental development. Further research must determine how to address not only mortality from diarrheal disease, but these long-term effects as well.
- Other than ORS, few safe and effective drugs are available for treating acute diarrhea. New types of drugs may be needed to prevent complications like those described above.

Workshop participants also discussed how the host-microbe interactions that facilitate infection can vary from one case to another. For this reason, targeting a common mechanism involved in how a bacterium, virus, or parasite initially infects a host may not be possible. However, the host response to infection, no matter the cause, may include some common features, such as altered electrolyte and water transport, alterations in tight junction function and regulation, and interactions with certain cellular signaling pathways.

Recent advances have identified genetic variations that are associated with increased susceptibility to acute diarrheal diseases. These discoveries present a need for new screening approaches to learn about new genetic factors as well as susceptibility and response to treatment. The intestinal microbiome should also be examined for its role in affecting susceptibility to infection.

Referencing these elements of diarrhea infection, workshop participants highlighted the possibility for potential drug development based on:

- stimulating sodium absorption
- inhibiting anion secretion
- correcting defects in specific transport proteins or in pathways that regulate transporter function
- targeting factors linked to electrolyte transport, including epithelial tight junctions, signaling by intestinal hormones and neurotransmitters, and the enteric nervous system
- increasing epithelial proliferation and restoration in cases where mucosal destruction also occurs

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Attendees recommended additional research into existing candidates for drug development, including zinc, clotrimazole, probiotics, ORS, and antimotility agents. The workshop examined not only the ways that these compounds and mechanisms might yield new treatment options, but also the methods and models for translational research that will produce the most useful results.

In conclusion, the meeting participants created a summary of recommendations for translational research to advance the development of diarrheal disease pharmacotherapy. The recommendations in part addressed research methods, by encouraging more in vivo research in animal models, and more in vitro human models for testing drugs. The summary concluded that a modified ORS should be developed. Finally, the report advised of areas in need of further research inquiry, including in genetic risk factors for diarrheal diseases, the mechanisms involved in pathogenesis, and the impact of early development and aging.

A report of this meeting was published online January 24, 2012, in the journal *Gastroenterology*, available online at *www.gastrojournal.org*.

For more information about upcoming meetings and workshops, visit *www2.niddk.nih.gov/News/Calendar*.

The National Digestive Diseases Information Clearinghouse, an information service of the National Institute of Diabetes and Digestive and Kidney Diseases, has free fact sheets and easy-to-read booklets about diarrhea. For more information or to obtain copies, visit *www.digestive.niddk.nih.gov*. ■

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Subsequently, 10 healthy volunteers were enrolled in a controlled feeding experiment in which their diets were fixed for a 10-day period. All 10 subjects in the controlled-feeding experiment were in the *Bacteroides* group at the start, during, and at the end of the experiment. Their gut microbiomes changed within one day but stayed within the same broad *Bacteroides* group, even if they ate a diet high in carbohydrates over the 10-day period, emphasizing the short-term stability of the enterotypes.

There are several potential applications of this research. The Penn investigators are currently exploring the relationship between dietary therapies for Crohn's and the composition of the gut microbiome.

"Crohn's disease is caused in part by the way our body responds to the microbes in our intestines," explains Lewis. "Dietary therapies are different from most other Crohn's disease therapies because the dietary therapies don't suppress the immune system. One hypothesis is that these dietary therapies work by changing what organisms live in the intestines."

Roughly 1.5 million people in the United States suffer from ulcerative colitis or Crohn's disease, whose symptoms include abdominal pain, bleeding, nausea, and diarrhea.

The next line of study will be to identify changes in microbial composition associated with successful dietary intervention for these diseases, then optimize ways of creating these changes for improved therapy.

This work was funded as a Human Microbiome Project by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the NIH Common Fund, and the Joint Penn-CHOP Center for Digestive, Liver, and Pancreatic Medicine.

The National Digestive Diseases Information Clearinghouse, an information service of the NIDDK, has free fact sheets and easy-to-read booklets about digestive diseases, including Crohn's disease and ulcerative colitis. For more information or to obtain copies, visit *www.digestive.niddk.nih.gov*. ■

NIH Research Model Predicts Weight with Varying Diet, Exercise Changes

Findings Challenge One-Size-Fits-All Weight Assumptions

Adapted from NIH News

Researchers at the National Institutes of Health (NIH) have created a mathematical model—and an accompanying online weight simulation tool—of what happens when people of varying weights, diets, and exercise habits try to change their weight. The findings challenge the commonly held belief that eating 3,500 fewer calories—or burning them off exercising—will always result in a pound of weight loss.

"This research helps us understand why one person may lose weight faster or slower than another, even when they eat the same diet and do the same exercise."

Kevin Hall, Ph.D.
NIDDK

Instead, the researchers' computer simulations indicate that this assumption overestimates weight loss because it fails to account for how metabolism changes. The computer simulations show how these metabolic changes can significantly differ among people. Findings were published Aug. 26, 2011, in a *Lancet* issue devoted to obesity.

However, the computer simulation of metabolism is meant as a research tool and not as a weight-loss guide for the public. The computer program can run simulations for changes in calories or exercise that would never be recommended for healthy weight loss. The researchers hope to use the knowledge gained from developing the model and from clinical trials in people to refine the tool for everyone.

"This research helps us understand why one person may lose weight faster or slower than another, even when they eat the same diet and do the same exercise," said Kevin Hall, Ph.D., an obesity researcher and physicist at the NIH's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the paper's first author. "Our computer simulations can then be used to help design personalized weight management programs to address individual needs and goals."

The online simulation tool based on the model enables researchers to accurately predict how body weight will change and how long it will likely take to reach weight goals based on a starting weight and estimated physical activity. The tool, at *http://bwsimulator.niddk.nih.gov,* simulates how factors such as diet and exercise can alter metabolism over time and thereby lead to changes of weight and body fat.

To test the model, the researchers compared predicted weight changes to actual changes in people. "Mathematical modeling lets us make and test predictions about changes in weight and metabolism over time," Hall said. "We're developing research tools to accurately simulate physiological differences between people based on gender, age, height, and weight, as well as body fat and resting metabolic rate."

For example, the team found that people's bodies adapt slowly to changes in dietary intake. They also found heavier people can expect greater weight change with the same change in diet, though reaching a stable body weight will take them longer than people with less fat.

The model also points to a potential simplified method to approximate weight loss in an average overweight person. An adult who has a body mass index (a measure of a person's weight

Model Predicts Weight,
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New NIH Center Will Translate Research Discoveries into New Drugs, Devices

From NIH News

In a move to re-engineer the process of translating scientific discoveries into new drugs, diagnostics, and devices, the National Institutes of Health has established the National Center for Advancing Translational Sciences (NCATS). The action was made possible by Congress' approval of a fiscal year 2012 spending bill and the president's signing of the bill, which includes the establishment of NCATS with a budget of $575 million.

NCATS will serve as the nation's hub for catalyzing innovations in translational science. Working closely with partners in the regulatory, academic, nonprofit, and private sectors, NCATS will strive to identify and overcome hurdles that slow the development of effective treatments and cures.

"Congressional support for the National Center for Advancing Translational Sciences marks a major milestone in mobilizing the community effort required to revolutionize the science of translation," said NIH Director Francis S. Collins, M.D., Ph.D. "Patients suffering from debilitating and life threatening diseases do not have the luxury to wait the 13 years it currently takes to translate new scientific discoveries into treatments that could save or improve the quality of their lives. The entire community must work together to forge a new paradigm, and NCATS aims to catalyze this effort."

A prime example of the type of innovative projects that will be led by NCATS is the new initiative between NIH, the Defense Advanced Research Projects Agency, and the U.S. Food and Drug Administration to develop cutting-edge chip technology. This new technology will allow researchers to screen for safe and effective drugs far more swiftly and efficiently than current methods. A great deal of time and money can be saved testing drug safety and effectiveness much earlier in the process.

To meet the goals of NCATS, NIH is reorganizing a wide range of preclinical and clinical translational science capabilities within NIH into an integrated scientific enterprise with new leadership and a bold new agenda. While the effort to recruit an NCATS director continues, organizational changes and realignment of resources will move forward under the leadership of Acting Director Thomas R. Insel, M.D., and Acting Deputy Director Kathy Hudson, Ph.D. Dr. Insel is the director of the National Institutes of Mental Health and Dr. Hudson is the deputy director for science, outreach, and policy at the National Institutes of Health.

The following programs will comprise NCATS:

- Bridging Interventional Development Gaps, which makes available critical resources needed for the development of new therapeutic agents
- Clinical and Translational Science Awards, which fund a national consortium of medical research institutions working together to improve the way clinical and translational research is conducted nationwide
- Cures Acceleration Network, which enables NCATS to fund research in new and innovative ways
- FDA-NIH Regulatory Science, which is an interagency partnership that aims to accelerate the development and use of better tools, standards and approaches for developing and evaluating diagnostic and therapeutic products

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in relation to his or her height) between 25 and 29.9 is considered overweight. One example: For every pound you want to lose, permanently cut 10 calories from your current intake per day. At that rate, it will take about 1 year to achieve half of the total weight loss, and almost all of the weight loss will have occurred by 3 years. This calculation shows how long it takes to achieve a weight-loss goal for a single permanent change of diet or exercise. Researchers can use the Web simulation tool to plan for a phase of more-rapid weight loss followed by a weight maintenance phase. People should consult with their physician prior to embarking on a diet plan.

"By using our model to track progress, clinicians can help people re-evaluate their goals and ability to achieve them at the pace they want," Hall said. "It's a good reality check for how long weight loss takes, and what changes in eating and exercise are required to achieve and maintain goal weight." Hall and collaborators also published findings, first published online May 11, 2011, in the *American Journal of Clinical Nutrition,* illustrating a method for precisely measuring how much a person's eating changed when he or she went on a diet.

"This research illustrates how the interdisciplinary skills of NIH scientists, like a physicist doing obesity research, can help lead to innovative ways to test, understand and treat a major public health epidemic," said NIDDK Director Griffin P. Rodgers, M.D., M.A.C.P. "Advancing research from the laboratory to the bedside enables us to make the discoveries that can better people's lives."

The National Digestive Diseases Information Clearinghouse, an information service of the NIDDK, has free fact sheets and easy-to-read booklets about digestive diseases. For more information or to obtain copies, visit *www.digestive.niddk.nih.gov.* ■

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- Office of Rare Diseases Research, which coordinates and supports rare diseases research
- Components of the Molecular Libraries, which is an initiative that provides researchers with access to the large-scale screening capacity necessary to identify compounds that can be used as chemical probes to validate new therapeutic targets
- Therapeutics for Rare and Neglected Diseases, which is a program to encourage and speed the development of new drugs for rare and neglected diseases

The budget for NCATS is primarily a reallocation of funds from programs previously located in the NIH Office of the Director, National Human Genome Research Institute, and National Center for Research Resources. NIH is committed to both basic and applied research and has maintained a relatively stable ratio of funding across these two areas of focus. The funding ratio will not be disturbed by the establishment of this new center.

The formation of NCATS has been a methodical process highlighted by the recommendation of the NIH Scientific Management Review Board in December 2010 to create a new center dedicated to advancing translational science. This recommendation was followed by a year of intensive feedback and expert insight from all sectors of translational science through advisory meetings and extensive public consultation.

"I am deeply grateful for the expertise and insight provided by the many researchers, industry executives, patients, voluntary organizations, and NIH staff that helped NIH evaluate NCATS' purpose and crystallize its vision," said Dr. Collins.

To learn more about the impetus and development of NCATS, go to:

- NCATS web page: *www.ncats.nih.gov*
- NCATS on the Feedback NIH website: *http://feedback.nih.gov/index.php/category/ncats* ■

Brown Medicine Magazine Profiles NIDDK Director Griffin P. Rodgers

Excerpted from Brown Medicine
By Sarah Baldwin-Beneich and David Peterson

"I saw that diabetes, obesity, and kidney disease hit African Americans harder than others. This was my first exposure to the effects and interaction of genetics and the environment."

Griffin P. Rodgers, M.D., M.A.C.P.
NIDDK Director

Brown Medicine magazine featured Griffin P. Rodgers, M.D., M.A.C.P., director of the National Institute of Diabetes and Digestive and Kidney Diseases, on the cover of its Fall 2011 issue. Read an excerpt from the story, "The Ambassador," below:

"A hematologist by training, Rodgers first became interested in medicine growing up in the '60s and '70s in New Orleans. He excelled in math and science early on. His father taught physical education and science. But it was his mother, a public health nurse, who first exposed him to the practice and potential of medicine.

"Many of my mother's patients weren't able to get to the clinic during the workweek. She'd take it upon herself to visit them at their homes during the weekend. We went to some rough neighborhoods," Rodgers recalls, laughing softly, "and she took me along as protection." He watched as she applied her nursing training and practical approaches to solve medical problems.

"I learned quite a bit this way. Her knowledge, compassion, and ability to get along with people went a long way in getting them to follow instructions, do follow-up."

Making the rounds with his mother was formative in another sense, as well: "I saw that diabetes, obesity, and kidney disease hit African Americans harder than others. This was my first exposure to the effects and interaction of genetics and the environment."

For more information or to read the full article, visit the *Brown Medicine* magazine website at *www.brownmedicinemagazine.org/index.php.* ■

NIDDK Advisory Council Member Receives 2011 Physician Clinician in Diabetes Award

Adapted from the University of Washington Office of News and Information

Dr. Jerry P. Palmer, professor of medicine, has received the American Diabetes Association's prestigious 2011 Outstanding Physician Clinician in Diabetes Award. The award was presented at the Association's 71st Scientific Sessions in San Diego, Calif.

Dr. Jerry Palmer

The Outstanding Physician Clinician in Diabetes Award is given to an individual who has made major contributions to diabetes care as a widely respected clinician and educator.

Palmer is a member of the Advisory Council of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and is the director of the UW Diabetes Endocrinology Research Center and chief of the Division of Endocrinology, Metabolism, and Nutrition, Puget Sound Veterans Affairs Health Care System. Palmer has a distinguished career as clinician, educator, mentor, and scientist.

Known internationally for his discovery of insulin autoantibodies, Palmer also is highly regarded locally as a clinician, in part because he implements research findings to help patients.

Palmer was a principal investigator of the Seattle Diabetes Control and Complications Trial (DCCT) site. Realizing the importance of the multidisciplinary approach, he created the UW Diabetes Care Center. This clinic has an international reputation as a premier academic diabetes center. Palmer is also a clinician and teacher in the Puget Sound Veterans Affairs Health Care System's Endocrine Clinic, a popular training site for UW students, residents and fellows.

Palmer is a past recipient of the Robert H. Williams Rachmiel Levine Award and has been repeatedly named among the Best Doctors in America. He is a past president of the Immunology of Diabetes Society.

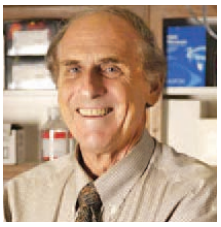
He has served on the board of the American Diabetes Association's Washington affiliate (1975-1983), and on its national board (1994-1997). He was on the National Institutes of Health steering committee for the Diabetes Prevention Trial–Type 1 (DPT-1) and now for Type 1 Diabetes TrialNet, and is on the international executive committee for TRIGR (Trial to Reduce Insulin Dependent Diabetes in the Genetically at Risk). ■

NIH Grantees Win 2011 Nobel Prize in Physiology or Medicine

From NIH News

Bruce A. Beutler, M.D.

Jules A. Hoffmann, Ph.D.



Ralph M. Steinman, M.D.

The 2011 Nobel Prize in Physiology or Medicine has been awarded to National Institutes of Health grantees Bruce A. Beutler, M.D., of The Scripps Research Institute, La Jolla, Calif., and Jules A. Hoffmann, Ph.D., for their discoveries concerning the activation of innate immunity; and the late Ralph M. Steinman, M.D., of Rockefeller University, New York City, for his discovery of the dendritic cell and its role in adaptive immunity.

"Their discoveries have opened up the possibility of harnessing the body's own cells and immune processes to prevent infectious diseases, autoimmune disorders, allergic diseases, cancer, and rejection of organ transplants."

Anthony S. Fauci, M.D.,
NIAID Director

"The work of these three NIH-supported scientists has provided fundamental understanding of the body's immune system, and has been pivotal to the development of new vaccines against infectious diseases and treatments for cancer," said NIH director Francis S. Collins, M.D., Ph.D.

The NIH began supporting the work of Dr. Beutler in 1984 and has provided almost $58 million in support. Dr. Beutler's work has been supported by the National Institute of Allergy and Infectious Diseases (NIAID), the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of General Medical Sciences, and the National Cancer Institute. Dr. Hoffmann has received almost $7 million in support from NIAID since 1998. NIAID began supporting the work of Dr. Steinman in 1976 and provided more than $49 million in support.

"NIAID has had the honor of supporting all three awardees," says NIAID Director Anthony S. Fauci, M.D. "Their elegant work has been — and will continue to be — extraordinary in its impact. It is rare that an investigator makes a discovery so important that it influences virtually every aspect of a scientific discipline. Their discoveries have opened up the possibility of harnessing the body's own cells and immune processes to prevent infectious diseases, autoimmune disorders, allergic diseases, cancer, and rejection of organ transplants."

The Office of the Director, the central office at NIH, is responsible for setting policy for NIH, which includes 27 Institutes and Centers. This involves planning, managing, and coordinating the programs and activities of all NIH components. The Office of the Director also includes program offices which are responsible for stimulating specific areas of research throughout NIH.

Additional information is available at *www.nih.gov/icd/od.* ■

NIH Clinical Center Receives 2011 Lasker~Bloomberg Public Service Award

Adapted from NIH News

John I. Gallin, M.D., director of the NIH Clinical Center (second from left), accepts the 2011 Lasker~Bloomberg award on behalf of the Clinical Center and the NIH.

The NIH Clinical Center, the clinical research hospital at the National Institutes of Health in Bethesda, Md., is the 2011 recipient of the Lasker~Bloomberg Public Service Award. The award was presented by the Albert and Mary Lasker Foundation, which has recognized outstanding advances in medical research each year since 1945. The award honors the Clinical Center for serving as a model institution that has transformed scientific advances into innovative therapies and provided high-quality care to patients.

"The NIH Clinical Center has been pivotal in advancing clinical studies that are at the forefront of solving the nation's most pressing public health issues."

Griffin P. Rodgers, M.D., M.A.C.P.
NIDDK Director

The award recognizes the Clinical Center's rich history of medical discovery through clinical research since it opened in 1953. Over the decades, nearly half a million volunteers have participated in clinical research at the Clinical Center. Its mission has remained providing exceptional clinical care for research volunteers, an environment for innovative bench-to-bedside clinical research, and training for clinical researchers.

"The Clinical Center, the world's largest clinical research hospital, exists to help scientists who are clinicians rapidly translate promising discoveries in the laboratory into new and better ways to treat and prevent disease," said NIH Director Francis S. Collins, M.D., Ph.D. "The Clinical Center's 58-year research portfolio has resulted in remarkable medical advances."

Those medical milestones include development of chemotherapy for cancer; the first use of an immunotoxin to treat a malignancy (hairy cell leukemia); identification of the genes that cause kidney cancer, leading to the development of six new, targeted treatments for advanced kidney cancer; the demonstration that lithium helps depression; the first gene therapy; the first treatment of AIDS (with AZT); and the development of tests to detect AIDS/HIV and hepatitis viruses in blood, which led to a safer blood supply.

"By enabling some of the world's top medical researchers to collaborate in innovative, interdisciplinary ways, the NIH Clinical Center has been pivotal in advancing clinical studies that are at the forefront of solving the nation's most pressing public health issues," said Griffin P. Rodgers, M.D., M.A.C.P., director of the National Institute of Diabetes and Digestive and Kidney Diseases.

"The Clinical Center's work has always depended on patients and healthy individuals from around the world who volunteer for clinical research here," said John I. Gallin, M.D., director of the NIH Clinical Center. "Our patients

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Former NIH Director Healy Dies at 67

From NIH Record

Bernadine P. Healy, M.D.

Dr. Bernadine Healy, who became the 13th NIH director in April 1991 and was the first woman to head the agency, died Aug. 6 of a brain tumor at age 67. She had battled brain cancer for 13 years.

"How wonderful to be in a career that in almost any dimension of it—whether you're the doctor at the bedside, or the scientist in the laboratory … that you are doing something that is pure in its fundamental purpose, which is helping another human being."

Bernadine P. Healy, M.D.
Former NIH Director

Healy served as NIH director for 2 years, during which she launched the $625 million Women's Health Initiative and established the Shannon Awards, which fostered innovative approaches in research. She also established a policy that all NIH-funded clinical trials on conditions that affect both genders must include both men and women.

"I am deeply saddened by the death of former NIH Director Bernadine P. Healy, and will greatly miss her courageous leadership on behalf of biomedical research," said NIH director Dr. Francis Collins. "Dr. Healy will be long remembered for her visionary efforts that transformed the landscape of women's health research."

Healy came to NIH from the Cleveland Clinic Foundation, where she had been a research director and cardiologist for 6 years. She had also been deputy director of the Office of Science and Technology Policy at the White House and a professor of medicine at Johns Hopkins University.

Healy was president of the American Heart Association in 1988-1989 and was a member of the Institute of Medicine. A native of Queens, N.Y., she had earned her medical degree at Harvard Medical School.

After leaving NIH, she was dean of Ohio State University Medical School (1995-1999) and president and chief executive officer of the American Red Cross (1999-2001). She was also a columnist for *U.S. News & World Report*. In 1994, she ran unsuccessfully for the U.S. Senate from Ohio.

Collins, whom Healy recruited from the University of Michigan to head the nascent Human Genome Project at NIH, said, "I will be forever grateful to Dr. Healy for her vigorous support of the public effort to sequence the human genome and her keen insights into the potential of genomic research for revolutionizing medicine."

In remarks she made for an NIH exhibit on pioneering women doctors, Healy said, "All of us, I believe, in our hearts are humanitarian. And how wonderful to be in a career that in almost any dimension of it—whether you're the doctor at the bedside, or the scientist in the laboratory, or the public health doc tracking down the latest epidemic—that you are doing something that is pure in its fundamental purpose, which is helping another human being."

Healy is survived by her husband, Dr. Floyd D. Loop, and two daughters. ■

Rotavirus Vaccination Leads to Large Decreases in Health Care Costs and Doctor Visits

Adapted from CDC news release

Vaccinating infants against rotavirus has resulted in dramatic decreases in health care use and treatment costs for diarrhea-related illness in U.S. infants and young children, according to a new study by the Centers for Disease Control and Prevention. The study was published in the *New England Journal of Medicine.*

"This study provides more evidence that vaccinating against rotavirus substantially reduces suffering and health care costs for this common childhood illness."

Mark Pallansch, Ph.D.
Director, Division of Viral Diseases, Centers for Disease Control and Prevention

"This is good news for parents and our health system overall," said Dr. Umesh Parashar, medical epidemiologist and team leader for the Viral Gastroenteritis Team in CDC's Division of Viral Diseases. "Rotavirus vaccine is one of the most effective ways to prevent severe diarrhea-related illness in young children and keep them healthy."

Rotavirus is a major cause of severe diarrhea in infants and young children in the United States. Before vaccines were introduced in 2006, rotavirus was responsible for about 400,000 visits to doctor's offices, 200,000 emergency room visits, 55,000 to 70,000 hospitalizations, and 20 to 60 deaths each year in children under 5 years old.

RotaTeq and Rotarix, the two U.S. licensed rotavirus vaccines, were 85 to 98 percent effective at preventing severe rotavirus disease in clinical trials in middle- and high-income countries, including the United States.

This new study used data from a large U.S. insurance database for 2001 to 2009 to assess rotavirus vaccine coverage and its impact on health care use and treatment costs for diarrhea-related illness in children under 5 years old. The study examined direct benefits to vaccinated children and indirect protective benefits to unvaccinated children. National declines in health care use and treatment costs were estimated by applying the declines seen in this study to children under 5 years old in the U.S population.

By the end of 2008, 73 percent of children younger than 1 year of age, 64 percent of 1-year-olds, and 8 percent of 2-to-4-year-olds had received at least one dose of rotavirus vaccine. Rotavirus-related hospitalizations decreased substantially compared with pre-vaccine levels in children under 5 years old—a 75 percent decline for 2007–2008 and 60 percent decline for 2008–2009.

Vaccinated children had 44 to 58 percent fewer diarrhea-related hospitalizations and 37 to 48 percent fewer emergency room visits for diarrhea than unvaccinated children during the 2008 and 2009 rotavirus seasons (January to June). Even in unvaccinated children, there were substantial declines in health care use during the 2008 rotavirus season compared with pre-vaccine levels—showing indirect protective benefits.

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Rotavirus Vaccination, continued from page 16

The study estimated that about 65,000 hospitalizations of children under 5 years old from 2007 to 2009 were averted nationally with a health care cost savings of about $278 million.

"This study provides more evidence that vaccinating against rotavirus substantially reduces suffering and health care costs for this common childhood illness," said Dr. Mark Pallansch, director of CDC's Division of Viral Diseases. "As more children get vaccinated against rotavirus, we expect to see even greater reductions in disease among all age groups."

An electronic copy of the article is available upon request from CDC by emailing *jstpierre@cdc.gov.* For more information about rotavirus, visit *www.cdc.gov.*

The National Digestive Diseases Information Clearinghouse, an information service of the National Institute of Diabetes and Digestive and Kidney Diseases, has free fact sheets and easy-to-read booklets about digestive diseases, including viral gastroenteritis and diarrhea. For more information or to obtain copies, visit *www.digestive.niddk.nih.gov.* ■

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include those with rare diseases, common disorders, and undiagnosed conditions. There are about 1,500 clinical research studies under way today and the patients and healthy volunteers who participate in them are true partners in research."

Advancements through clinical research also depend on having a cadre of investigators trained to do it, Gallin added. "Students in the health sciences and clinicians come here to learn how to conduct clinical research by working closely with NIH investigators. Since 1995, more than 22,000 students around the world have participated in the Clinical Center's clinical research training curriculum offered through distance-learning programs."

The original hospital, the Warren Grant Magnuson Clinical Center, opened in 1953. A new research hospital, the 240-bed Mark O. Hatfield Clinical Research Center, opened in 2004. Most of NIH's 27 institutes and centers conduct clinical research at the Clinical Center through their programs on the NIH campus in Bethesda, Md. NIH plans to open the facility for use by external researchers, based on the 2010 recommendations from the Scientific Management Review Board, established under the NIH Reform Act of 2006, which will allow the Clinical Center to facilitate clinical research on a broader scale.

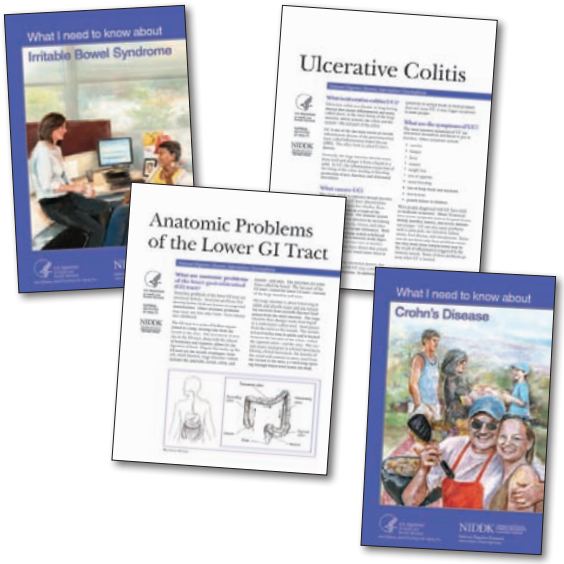
For more information, visit the NIH Clinical Center at *http://clinicalcenter.nih.gov.* ■

Updated Publications

The National Digestive Diseases Information Clearinghouse has updated the following publications:

- *Anatomic Problems of the Lower GI Tract*
- *Crohn's Disease*
- *ERCP (Endoscopic Retrograde Cholangiopancreatography)*
- *Proctitis*
- *Ulcerative Colitis*
- *What I need to know about Crohn's Disease*
- *What I need to know about Gas*
- *What I need to know about Irritable Bowel Syndrome*

These publications are available at *www.digestive.niddk.nih.gov.*



Upcoming Meetings, Workshops, and Conferences

The National Institute of Diabetes and Digestive and Kidney Diseases Information Clearinghouse will exhibit at the following upcoming events:

Society of Gastroenterology Nurses and Associates 39th Annual Course

May 18–23 in Phoenix.
For more information, visit *www.sgna.org/Events/2012AnnualCourse.aspx.*

Digestive Disease Week 2012

May 19–22 in San Diego.
For more information, visit *www.ddw.org.*

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