

DIRECTIONS

WINTER 2006

DIRECTIONS
*is the biannual research
publication of the
Diabetes Association
of Greater Cleveland's
Dietrich Diabetes Research
Institute (DDRI)*

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CLEVELAND DIABETES CENTER

Shaping the Future of Medicine

Excitement is building for the projected 2007 groundbreaking of Case's West Quad. The 14-acre former site of Mt. Sinai Hospital in University Circle will be the home of a new medical research campus and the Cleveland Diabetes Center. The West Quad project - one of the largest development projects in the history of Ohio - will create a multidisciplinary environment for collaborative biomedical research with the medical school's university and commercial partners.

Plans call for a 1.5 - 2 million square feet campus with half dedicated to commercial life sciences and half to academic activities related to clinical research. At full build out, the West Quad is expected to create up to 6,000 new jobs at a variety of skill levels. Master planning and construction will begin early this year, with occupation of the first phase in early 2009.

At the 2005 Diabetes Research Retreat, members of the Diabetes Center Steering Committee and Dr. Ralph Horwitz, Dean of the Case School of Medicine, discussed the Cleveland Diabetes Center (CDC) within the development for the West Quad.

The proposed Cleveland Diabetes Center will be composed of the 5 major institutions - Case Western Reserve University, The Cleveland Clinic, MetroHealth Hospital, University Hospitals of Cleveland, and the Department of Veterans Affairs Medical Center and have approximately 40,000 square feet of dedicated space with offices and facilities at the West Quad.



Diabetes Center Steering Committee Members: back (left to right) Sethu Reddy, MD [DDRI Task Force]; Michael Weiss, MD, PhD (co-chair); Patrick Catalano, MD; Henri Brunengraber, MD, PhD; Nathan Berger, MD; Tim Kern, PhD; front: Saul Genuth, MD (co-chair); Harriet Fader, CAE; Byron Hoogwert, MD; Faramarz Ismail-Beigi, MD, PhD; Richard Hanson, PhD. Not pictured: Pamela Davis, MD, PhD.; Joseph Nadeau, PhD; John Sedor, PhD; Roy Silverstein, MD]

Direct clinical care is not planned at the Center at this time; each of the respective institutions would continue their clinical care activities and translational research would be done cooperatively at these institutions. This state-of-the-art research campus intends to be a major force in the improvement of health in our city.

The Center will 1) focus research and education in diabetes; 2) develop mechanisms to encourage translational research; 3) facilitate approval of animal protocols; 4) fund Pilot Grants; 5) work closely with funding agencies like DAGC/DDRI; 6) develop educational programs in diabetes in the School of Medicine and affiliated hospitals; 7) develop a strong interaction with health agencies in Cleveland; and 8) apply for NIH funding and grant support from other agencies. The Center will spin out

Continued on Page 2

companies from its own technology and work to attract Cleveland companies that would like access to the facilities and intellectual capital available.

As stated by Dr. Michael A. Weiss, Chair of Biochemistry Department at Case School of Medicine and DAGC Board member, the overall vision for Cleveland Diabetes Center is to develop a unique approach involving the whole city in an attack on diabetes by bringing together virtually every discipline in the basic and clinical sciences and by harnessing the strengths and insights of different institutions, different departments, and different disciplines to effect a cure and improve the lives of patients with diabetes.

The work at CDC will link biology to clinical research both to identify patients at highest risk for the development of diabetes, obesity and metabolic syndrome and to develop novel ways of treating the disorder. Case School of Medicine is committed to initiate the CDC within the next year; the Diabetes Center will be located on the West Quad when it opens in late 2008/ early 2009. The first phase of the West Quad project would have 500,000 square feet of developed space, with the Diabetes Center as a central element.

Dean Horwitz stated that it is his "intention that the Cleveland biomedical community... will project itself over the next decade into the forefront of a new kind of science that will shape not only the research that goes on in medicine, but the education and practice of medicine. This effort will be one of the critical elements that makes that possible."

STATUS UPDATE:

Since the Retreat, a diabetes center is actively being formed within the walls of Case School of Medicine. Dr. Faramarz Ismail-Beigi, MD, PhD has been named as Director, with Dr. Richard Hanson, PhD as Co-Director. Investigators dedicated to diabetes research are being co-located to serve as the foundation of this concerted effort to establish the Cleveland Diabetes Center.

Watch the West Quad progress at <http://westquad.case.edu>. ■

2005 DIABETES RESEARCH RETREAT

DDRI Continues to Foster Collaboration in Diabetes Research

Northeast Ohio diabetes investigators gathered in November for the second annual Diabetes Research Retreat. Presentations by internationally renowned experts filled the morning, while the afternoon focused on the plans for the Cleveland Diabetes Center. (see front page)

The 2005 Retreat boasted 189 participants and 61 posters representing 40 different disciplines/departments and 28 different institutions/organizations.

DDRI continues to promote these dynamic interactions as a springboard to better diabetes treatment and, ultimately, a cure. ■



2005 Diabetes Research Retreat



March is Save Your Vision Month.

This awareness campaign is a reminder for at-risk groups like those with diabetes that regular, comprehensive vision exams are critical in detecting problems affecting eye health such as cataracts, age-related macular degeneration (ARMD), glaucoma, and diabetic retinopathy.

For the many people who have diabetes but don't know it, a comprehensive eye exam may be the first indication that they have the disease.

After dilating the pupil, an optometrist can see inside your eye using an ophthalmoscope that lights and magnifies the blood vessels. Changes to these blood vessels may indicate various stages of diabetic retinopathy. Left untreated, retinopathy can cause blindness.

Other eye diseases, like glaucoma, may cause vision damage and eventual blindness without the patient ever experiencing any symptoms. During a comprehensive eye exam, an optometrist measures the pressure within the eye and examines the optic nerve to determine the existence of glaucoma.

When was the last time you had a comprehensive eye exam? Maybe it's time to make an appointment. ■

Find out more about:

Prevent Blindness Ohio at www.preventblindness.org. Prevent Blindness America is the nation's leading volunteer eye health and safety organization dedicated to fighting blindness and saving sight.

Diabetic Retinopathy at the Website of the National Eye Institute <http://www.nei.nih.gov/health/diabetic/retinopathy.asp>

Save Your Vision month at <http://www.aoa.org/x1688.xml>

Oxygen Therapy for Macular Edema

Fluid buildup in the part of the eye responsible for central vision, the macula, causes poor vision in many people with diabetes. In a pilot study at Johns Hopkins, scientists used oxygen therapy to treat macular edema in 9 affected eyes of five patients who had diabetes for an average of 9 years. Patients were instructed to use the oxygen continuously for 3 months. Macular thickness was reduced an average of 43% in all cases. ■

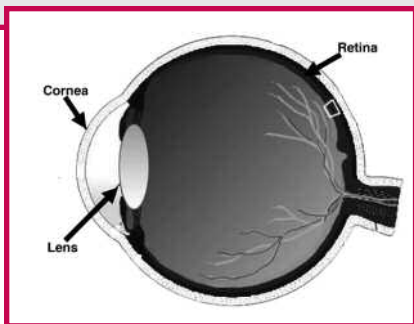
ASK THE EXPERT

One of the most frightening complications of diabetes is vision loss. Using animal models, **Tim Kern, PhD** investigates the causes of diabetic retinopathy and looks for ways to prevent it. Dr. Kern is the Director of Diabetes Research in the Division of Endocrinology of the Department of Medicine at Case, served as Co-Chair of the first of its kind Vision Loss Prevention Research Symposium last year in Columbus, and is a member of the DAGC Board of Directors. He is

internationally recognized as an expert in experimental studies of diabetic retinopathy, and his expertise frequently is called on by the National Institutes of Health (National Eye Institute as well as the National Institute of Diabetes & Digestive & Kidney Diseases). You may also recognize his name from the research section of the DAGC Website – Dr. Kern received the Kristin C. Dietrich Diabetes Research Award in 1998 for his work on advanced diabetic complications. ■



Photo: Tim Kern, PhD, second from right, back row, conducted a seminar for the 2005 DAGC Summer Interns at Camp Ho Mita Koda.



Diabetes can affect many organs throughout the body, but impairment of vision is one of the most significant. Two of the most important problems in the eye caused by diabetes affect the lens (cataract) and retina (diabetic retinopathy). The retina is in the back of the eye, and converts light energy into a signal that the brain can recognize and interpret, thus allowing us to see. In the early stages of diabetic retinopathy, the tiny blood vessels that nourish the retina can leak (causing retinal or macular edema) or get plugged up, and retinal nerves begin to die. In the later stages of diabetic retinopathy, these abnormalities of the blood vessels cause the retina to become starved of oxygen and nutrients, and so new “replacement” blood vessels grow. Unfortunately, these new blood vessels are leaky and grow wildly, ultimately leading to vision loss by preventing light from reaching the retina in some areas. Only a fraction of all diabetics progress to the sight-threatening (or neovascular) stages of diabetic retinopathy, but presently it is impossible to predict which patients will show the progression until the damage has already started.

Convincing data exists showing that keeping blood sugar as normal as

DIABETIC RETINOPATHY RESEARCH

By Timothy S. Kern, PhD

possible can slow or prevent the development of diabetic retinopathy and other complications of diabetes, but such metabolic control is difficult to achieve and maintain in many patients. As a result, researchers are trying to identify additional therapies by which the retinopathy and other complications can be reliably prevented or arrested.

Our laboratory has been studying how diabetic retinopathy develops, and using that information to develop new therapies to inhibit the development of the retinopathy. Over the past several years, we have developed novel information that suggests that diabetic retinopathy is actually caused by inflammation. This is not the typical inflammation that can happen when you get a cut or an infection, but a disease that is unique to the retina as a result of prolonged exposure to concentrations of sugar in the blood. Along with collaborators in Cleveland (Drs. Mohr, Zheng, and Zhang) and in other parts of the country, we have demonstrated that a number of experimental treatments that block biochemical abnormalities of inflammation in the retina can slow or prevent the degeneration of retinal blood vessels in diabetic animals. This is important because the degeneration of retinal blood vessels seems to be a critical abnormality which initiates the steps leading to vision loss in diabetes. Some of the therapies identified so far are very specific (such as inhibitors of the inducible isoform of

nitric oxide synthase or of poly(ADP-ribose) transferase), whereas others act more generally and are readily available (aspirin at higher than normal doses, or vitamin E). Efforts are being initiated now to test these findings in diabetic patients, and ultimately translate these findings into clinical care. Even if some of these therapies are judged to be less suitable for use in patients, they can help us understand the sequence of abnormalities that cause diabetic retinopathy, and thereby help in our search for better and safer ways to stop vision loss in diabetes. ■

DID YOU KNOW...

You can order diabetes self-management audio recordings for the visually impaired from DAGC

on our Website at
<http://www.dagc.org/visimpaired.asp>.

One click will place your order for *Diabetes: the Basics* or *Living With Diabetes and Visual Impairment*. Both recordings are available on cd or tape.

FAQ ~ FREQUENTLY ASKED QUESTIONS



Given all the advances in diabetes research in the last few years, people often ask why someone doesn't come up with an easier way to test for glucose levels – something painless and simpler than the fingerstick method. We turned to Dr. Rafat Ansari from NASA to tell us about his research on glucose level sensing for astronauts.

Rafat R. Ansari, PhD is a Biofluid Sensor Systems Scientist in the Microgravity Science Division at NASA's Glenn Research Center and leads the Vision Research Laboratory. He has promoted light scattering technology both for space experiments aboard the space shuttle orbiter and for Earth-based clinical, biomedical, and industrial applications. NASA supports Dr. Ansari's developments because the effects of aging, like cataracts, have implications for what happens to the body during space travel and new instruments are always being sought to diagnose and improve astronaut health. He is currently researching and developing the "Built-for-Space" fiber-optic probe for the early detection of cataracts, glaucoma, retinopathy, macular degeneration, and systemic diseases such as diabetes before clinical symptoms appear. ■

NON-INVASIVE GLUCOSE MONITORING THROUGH THE EYE

By Rafat R. Ansari, PhD

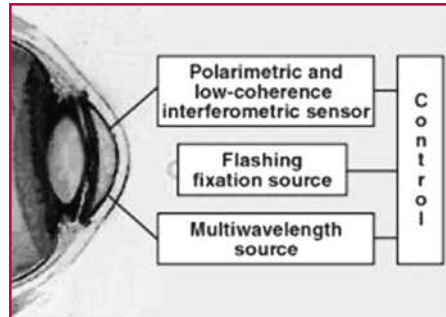
Astronauts are very active and healthy people and generally are free of diabetes. So far the space travel to low earth orbit (about 300 Km above the earth's surface) in space shuttle or six months to a year stay on space stations have not shown diabetes to be a risk factor for astronauts. However, it is important to monitor health of astronauts during long-duration travel e.g., to Mars. A round trip to Mars is expected to take about three years. The conditions for human survival on Mars can be very harsh and travel in confined spaces, effects of radiation, and zero gravity may alter immune system and other important organ functions. The effects of space travel are very similar to those of aging e.g., muscle and bone loss can lead to osteoporosis.

A user friendly goggles-like head-mounted device equipped with a suite of instruments for several non-invasive and quantitative medical evaluation of the eye, skin, and brain is being built at NASA's Glenn Research Center in Cleveland. This device will monitor



Glucose Sensing Prototype Laboratory Setup

astronaut health during long-duration space travel by detecting aberrations from pre-established "norms", enabling prompt diagnosis and possibly the initiation of early preventative/curative therapy. The non-invasive nature of the device technologies permits frequent repetition of tests, enabling real-time complete crew health monitoring. This device may ultimately be useful in telemedicine to bring modern healthcare to under-served areas on Earth as well as in so-called "advanced" care settings (e.g. diabetes in the USA).

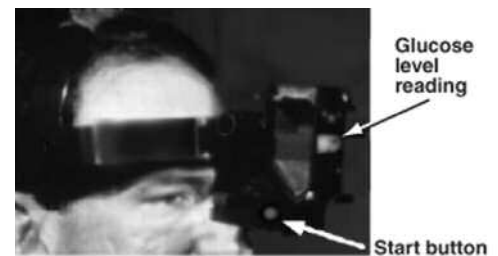


One of the sensors under development in this device is a non-invasive glucose sensor to monitor glucose levels through the eye. The concept is very simple. Certain objects possess chiral properties. For example, left and right hands are non superimposable mirror images and thus are chiral objects. Glucose molecules being chiral are optically active which means they rotate the plane of polarized light to right (clockwise). The rate of rotation is directly proportional to the amount of glucose present in a solution. The aqueous humor of the eye exhibits low scattering properties and its glucose concentration closely matches blood glucose levels in the serum. Thus the polarimetric optical approach is attrac-

tive since the visible spectrum and significant path lengths in the anterior chamber of the eye can be used. The patented device¹ (US Patent) was calibrated against known concentration of glucose solutions in an eye model. It showed good correlation in hypo- and hyper-glycemic concentrations². Presently the device is being tested in humans (figure 1). In future the device will be miniaturized as shown in figure 2.

The goal of Glenn's Vision Research and Human Health Diagnostics Laboratory is to provide non-invasive monitoring of ocular health and systemic diseases before the appearance of clinical symptoms in a telemetry setting.

For further information, contact Dr. Rafat Ansari at 216-433-5008 or e-mail rafat.r.ansari@nasa.gov or visit the website: <http://exploration.grc.nasa.gov/grc bio/VisionResearch/> ■



REFERENCES:

- Rafat R. Ansari and Luigi Rovati, *Method and Apparatus for the Non-Invasive Measurements of Blood-Glucose Levels in Humans*, US Patent 6,704,588, March 9, 2004.
- Ansari, R.R., Bockle, S., Rovati, L. "New Optical Scheme for A Polarimetric-Based Glucose Sensor" J. Biomed. Optics, 9(1) 103-115, 2004.

SUMMER INTERNSHIPS IN DIABETES RESEARCH CELEBRATES 20TH ANNIVERSARY

Individual Support Makes Local Projects Happen

This year marks the 20th anniversary of DAGC's Summer Internship in Diabetes Research program. The unique program began with individual contributions totaling \$1,106 to DAGC in honor of Andrea Vigliotti. Contributions that followed made it possible to award the \$1,200 Andrea Vigliotti Summer Research Internship to five outstanding students in 1986.

Since the program's inception, the Diabetes Association of Greater Cleveland has awarded \$168,000 to 88 exceptional students who spend their summer working with local diabetes researchers. Six more internships will be awarded this year to undergraduate, graduate, and medical students who will add to the body of knowledge about diabetes. On behalf of the people we serve, we again offer our sincere thanks for the

contributions of all these students and particularly to the 53 Summer Intern Sponsors who dedicated their time to nurture these young researchers through this program.

We also would like to thank those special individuals whose vision started this program. As a local and independent diabetes organization, DAGC depends on a variety of funding sources to make our programs possible. Research activities throughout DAGC's 51 years have depended solely on contributions from individual donors.

We are proud to be able to offer research awards to students who may one day – because of your help – find that one piece to complete the puzzle and make diabetes a disease of the past. ■

DIABETES RESEARCH MAKES A DIFFERENCE – AND SO CAN YOU!

Research awards to local diabetes investigators are one of the ways that DAGC contributes to the fight against this life altering and life threatening disease.

DAGC/DDRI research programs depend entirely on support from individual donors like you! Your donations to diabetes research help us continue the fight right here at home. Without your support, programs like the Summer Internship in Diabetes Research would not be possible.

According to newly released statistics from the Center for Disease Control, 21 million Americans have diabetes – 1 million of them are in Ohio! **And 1 in 14 of every northeast Ohioan has diabetes.**

Every day in the US 4,100 new cases are diagnosed, 810 people die from diabetes, 230 have a diabetes-related amputation, 120 new cases require dialysis or kidney transplant, and 55 people go blind.

You make a difference when you use the enclosed envelope or donate online at www.dagc.org. Remember – every dollar donated stays right here in northeast Ohio. ■

GENERAL RESEARCH UPDATES . . .

More on Diabetic Retinopathy

For the first time, extensive human data has shown that erythropoietin, a protein that stimulates red blood cell formation, is involved in the development of diabetic retinopathy. Japanese researchers found erythropoietin levels that were 12 times higher in patients in the last stages of retinopathy vs. those in people without diabetes. Earlier studies also suggested that erythropoietin acts to protect the retina from damage during stress, so simply blocking it in people with diabetes might not be safe. In addition, these researchers found excessively elevated levels of vascular endothelial growth factor (VEGF) in the diabetes patients – another molecule that has previously been indicated as a contributor to retinopathy. Drugs designed to block the action of VEGF are being tested, but as shown in this work, another molecule is independently involved.

Using rodent models of diabetes, a Pennsylvania research team found that the antibiotic minocycline limits the retinal damage caused by microglia by around 50%. Microglia release toxins to destroy damaged cells and then engulf them, serving as

the “cleanup” cells for the central nervous system. If they are activated and release their toxins in the retina, healthy neurons critical to normal vision are also destroyed. In diabetes, there is an increase in the production of cytokines - proteins that cause neuronal inflammation by activating the microglia. This study showed increased cytokine production in rat retinas in the early stages of diabetes that correlated with increased microglia activation. When treated with minocycline, inflammation in the retina caused by cytokines was reduced. This meant reduced microglia activation, fewer neurotoxins released, and less cell death. ■

Low-Fat Dairy For Men

Including more dairy products in the diet - especially those low in fat – appears to reduce the risk of type 2 diabetes in men. Analyzing data from over 41,000 male participants in the Health Professionals Follow-up Study, Boston researchers documented 1,243 new type 2 cases. They found a significant relationship between total dairy intake and the development of diabetes. Each serving-per-day increase in dairy was associated with a 9% lower risk for type 2. Further

analysis showed that the relationship was primarily a result of low-fat dairy intake. Next time you are thirsty, reach for the skim milk! ■

Is Alzheimer's a New Diabetes?

Following the recent discovery that the brain produces insulin, scientists found significant drops in insulin levels and insulin receptors in the brains of patients with early stage Alzheimer's disease. The postmortem studies suggest a link between abnormalities in insulin signaling and unexplained features of Alzheimer's like cell death and “tangles in the brain”. These Rhode Island researchers think that this may indicate that Alzheimer's is a new type of diabetes specific to the brain. There is no evidence that people with diabetes are at higher risk for Alzheimer's and most of those with Alzheimer's disease do not have diabetes.

Other studies in Philadelphia have shown that blood levels of a protein, amyloid-beta 42, increase as body fat increases. This amyloid peptide is believed to be responsible for the buildup of amyloid plaques in the brain associated with Alzheimer's disease. According to this team, these data suggest that the amyloid-beta is stored in the fat instead of being metabolized. ■

Fracture Risk in Women

Compared to women without diabetes, women with type 1 diabetes have 3-8% lower bone mineral density and are significantly more likely to experience a bone fracture after the age of 20. More research is needed to understand the connection, but these findings highlight the importance of screening for osteoporosis and fracture prevention as these women near menopause. ■

Pump Therapy for Children

Use of an insulin pump rather than multiple daily injections improves glycemic control in children under 12. Comparing A1c levels at the beginning of the study and after 6 and 12 months of treatment, the twelve year olds showed significantly lower readings at each measurement. For children over 12, small improvements in A1c levels were noted after 6 months of continuous infusion therapy, but these improvements were not sustained. These adolescents did show less weight gain when using the pump than those receiving insulin injections. Although uncommon according to the researchers, the risk of diabetic ketoacidosis was 2-1/2 times greater in the children on the pump. Continuing to educate patients should decrease this risk. ■

Hypoglycemia Affects Children's Brain Development

Cognitive function in children 6 to 18 years old was reduced on long-term spatial memory performance in those who had experienced 3 episodes of severe hypoglycemia, particularly if those episodes began before age five. Investigators think this might indicate a vulnerability to these severe low glucose levels in the developing brain of the very young. The risk and benefits of tight control at early ages needs to be assessed fully. ■

Stress Effects

Psychological stress may be a trigger for diabetes-related autoimmunity in children. A study of 6,000 children and their families indicates that 2-1/2 year old children were 3 times as likely to develop type 1 diabetes if the mother experienced a stressor like divorce or violence. The stress-

autoimmune connection was not explained by other known risk factors of type 1 such as familial history of diabetes, increased parental age, childhood infections, child's body weight, delivery by Cesarean section, or neonatal intensive care for the baby. The mother's stress levels may influence stress in the children and raise levels of the stress hormone, cortisol. The cortisol may then lead to insulin resistance that stresses the beta cells and triggers an autoimmune response for those genetically predisposed to developing type 1 diabetes. Investigators suggested that attending to stress levels and coping skills in children, as well as the whole family, should be a priority among clinicians.

Other research on the effects of psychological stress in type 1 diabetes patients shows that stress slows glucose metabolism following a meal, but has no effect on glucose levels during fasting. Exposure to stress delayed the expected lowering of glucose concentrations following the post-meal spike by 45 minutes. This effect was noticed a half an hour after the stressor and lasted about 2 hours. ■

Cholesterol and Vision

Harvard scientists analyzed data from over 1,400 patients with type 1 diabetes who were in the famous Diabetes Complications and Control Trial (DCCT). Those with the highest levels of low-density lipoprotein (LDL or "bad" cholesterol) were at twice the risk of developing macular edema than those with the lowest levels. People with the largest ratio of total cholesterol to high-density lipoprotein (HDL or "good" cholesterol) had 4 times the risk of developing the disorder. Interestingly, no relationship was evident between cholesterol levels and diabetic retinopathy. ■

Predicting Type 1

Researchers at Children's Hospital of Pittsburgh tracking about 1,500 close relatives of people with type 1 diabetes since 1979 used a combination of three tests to predict who would develop the disease – and did so with 80% accuracy. Each individual test alone was relatively inaccurate. The islet cell antibody screen, an expen-

sive and cumbersome test, only predicts the risk correctly half the time. Two newer tests that check for biomarkers GAD65 and IA-2 are also inaccurate, although they are easier and cheaper. Using all 3 tests together will help researchers design clinical trials to delay the onset and prevent the disease.

Meanwhile, Joslin researchers are using MRI (magnetic resonance imaging) to detect the early destruction of the insulin-producing islet cells in the pancreas. Type 1 diabetes is usually diagnosed because of the clinical symptoms that appear later after significant destruction by lymphocytes has occurred. Mice were given IV injections of magnetic nanoparticles (tiny, tiny iron oxide particles). These particles travel through the blood stream. If there is inflammation (an undetectable, early part of the disease process) in the pancreatic blood vessels due to the increase in T lymphocytes (white blood cells), the vessels swell and leak. Magnetic particles escape and are "eaten" by macrophages (scavenger cells). Collections of these magnetic particles can be seen with the MRI and indicate sites of inflammation. Researchers used the information to predict which mice would go on to develop type 1 and to test the effectiveness of immune therapies to reverse it. The investigators have since begun a clinical trial to test the effectiveness one of the drugs to treat pancreatic inflammation in humans. ■

3 Transplant Advances

A promising new technique for islet cell transplantation was developed at the Diabetes Research and Wellness Foundation in Britain and improved upon by a research team in Edmonton, Canada. Clusters of islet cells are removed from a donated pancreas in highly sterile conditions before being injected directly into the recipient's liver. The unique procedure requires staff to pass through progressively cleaner rooms to ensure sterile conditions. Doctors report the injection of cells into the liver as a fairly simple procedure and have hopes of revolutionizing treatment of type 1 diabetes within the

next decade. Immunosuppressant (anti-rejection) drugs are still required.

Even with immunosuppression, prior transplants of islet cells into the pancreas still result in destruction of half of the transplanted cells by the body's own T cells. Japanese scientists used a mouse model to show that specific kinds of T cell, natural killer cells (NKT), instigate the rapid destruction of the transplanted cells. In response to the stress of the transplant, NKT cells are activated and produce interferon (IFN)-gamma (an inflammatory molecule) that then activates the T cells to attack the islet cells. Researchers found that transplanted islet cells survive in mice without NKT cells and in those unable to produce IFN-gamma. The team also showed that multiple doses of a drug alpha-galactosylceramide caused the NKT cells to decrease IFN-gamma production and increase survival in the transplanted cells. Clinical trials are being conducted in Japan.

In a European study of newly diagnosed adults with type 1 diabetes, a six-day course of treatment with a monoclonal antibody resulted in higher residual beta cell function vs. those given a placebo. Type 1 does not destroy all the beta cells at once. Overt diabetes is generally seen when beta cell reserves fall 80%; it is preceded by an incubation period that can be months or years. CD3 is a molecule on the surface of the T cells. The monoclonal antibody, anti-CD-3, targets this molecule and “resets” the T cells to inhibit beta cell destruction. The injections of anti-CD3 lowered insulin dependence in the treatment group by 12% and extended insulin-making capabilities for at least 18 months. Patients with beta cell function over 50% when treatment began responded best. The placebo group required more insulin injections and lost a third of its ability to make insulin. Flu-like symptoms with fever and swollen glands were a temporary side effect of treatment and highlight the need for more testing, particularly long-term. ■

Stem Cell Breakthrough for Type 2

In a novel approach, researchers have implanted autologous bone marrow stem cells directly into the pancreas in 16 type 2 diabetes patients. Autologous means derived from the same individual receiving the transplant; such a transplant doesn't require immunosuppressant drugs to inhibit rejection. The “Argentinean Protocol” has so far resulted in an increase in the body's production of insulin and decreased blood glucose and A1c levels faster than other treatments for those recipients. The team suggests the improvement is due to regeneration of the previously damaged beta cells, but may result from the new beta cells themselves. No complications have been reported. For 13 of the sixteen, the treatment also meant that they no longer needed insulin or their medication to stimulate insulin production. ■

Genetic Breakthroughs

Using DNA technology, investigators at Joslin Diabetes Center identified the first abnormal gene in human pancreatic islet cells linked to the most common form of type 2 diabetes. The team then created a defect in the gene, ARNT, in mice. When given a glucose challenge, mice showed a decrease in insulin secretion similar to that seen in people with type 2. This exciting discovery moves research closer to finding the other genes involved. Once identified, manipulation of these genes could be the key to a cure.

An Icelandic team studying Iceland's comprehensive genetic records found a gene linked to development of type 2 diabetes that may account for 20% of cases in the general population. This gene is a transcription factor – a gene that controls another gene. A person with one copy of the variant, as in 38% of people, has a 40% increased risk of developing diabetes. Seven percent of those studied had 2 copies of the variant; their risk increased 140%. The variant, called TCF7L2, is found on chromosome 10q and is associated with a younger age of onset and patients who are thinner than the “average” type 2 patients. Such findings may lead to diagnostic tests that could forecast risk years ahead of time. ■

Pancreatic Cancer Link

Pancreatic cancer has been difficult to detect until advanced stages. Researchers at the Mayo Clinic analyzed data from 2,122 patients who were 50+ year-old residents of Rochester, Minnesota between 1950 and 1995. Those individuals who were newly diagnosed with type 2 diabetes were 8 times more likely to develop pancreatic cancer within 3 years when compared to same-age individuals. This suggests that onset of diabetes after age 50 could be a signal of underlying pancreatic cancer.

In an unrelated analysis of data from the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study, researchers found that higher glucose levels, insulin, and insulin resistance correlated with increased pancreatic cancer risk. Those subjects with diabetes and highest insulin levels had twice the risk of developing the cancer. Given the length and design of the study, the results suggest that increased insulin levels and insulin resistance were the result of pancreatic cancer. ■

Lose Weight While You Sleep

Not exactly... but researchers have linked a “clock” gene to obesity, metabolic syndrome, and diabetes. Compared to people who slept only 5 hours or less, those who slept at least 7 hours had less risk of developing diabetes or glucose intolerance. It was also true when that group was compared to people sleeping more than 9 hours! In mouse studies, mutation of the clock gene led to overeating, weight gain, metabolic syndrome, and elevated blood glucose levels. ■

Breastfeeding Lowers Mother's Risk

Research suggests that, in addition to the other known benefits to mother and baby, breastfeeding may protect mothers from type 2 diabetes. Analysis of 150,000 mothers from the Harvard Nurses Health Study which tracked nurses over 29 years, showed that the risk for developing diabetes dropped 15% for every year a woman breastfed and the benefit lasted at least 15 years. (One year of breastfeeding can be one child for one year or 2 children for 6 months.) The results were controlled for weight and exercise habits. ■

SERVING THE PROFESSIONAL RESEARCH COMMUNITY

DDRI as a Contact Point and Disseminator of Information

Diabetes is a complex disease that affects the whole body. The Diabetes Association of Greater Cleveland's research component, the Dietrich Diabetes Research Institute (DDRI) brings together northeast Ohio's diabetes research professionals to solve its many puzzles.

DDRI Quarterly Meetings

The March 2006 Quarterly Meeting linked senior scientists with those junior faculty working to establish themselves in the diabetes field. "Fostering Research Among Young Professionals" provided the forum for collegial discussion and networking – another way to stimulate synergy and bring us closer to our goal of unlocking the mysteries of diabetes.

2006 Diabetes Summit on Beta Cell Function

In association with the Diabetes Association of Greater Cleveland's Dietrich Diabetes Research Institute, the Cleveland Clinic will present "The Beta Cell: Function, Protection & Replacement" on May 17 & 18, 2006 at HealthSpace Cleveland.

This exciting conference will welcome local and national experts to focus on new developments in the field.

CLINICAL TRIALS

Interested in finding clinical trials?

Visit the DAGC Website at www.dagc.org for more information on local clinical trials, including those studies on eye disease.

2006 DAGC Advertising Opportunities Available

Looking for a great place to promote your product, web site, or storefront? Whether you are a large national corporation or a small local company, DAGC can provide you with visibility online or in print at a very cost-effective price! We will customize a package to suit your advertising needs!

**For more information, call
216-591-0800 x18**

Monday, June 12, 2006

15th Annual Golf Tournament

Presented by *The Shamrock Companies, Inc.*

at **Canterbury Golf Club**

Visit www.dagc.org or call (216) 591-0800

for more information and to register.

Saturday, November 4, 2006

21st Annual Gala

"P R O M E N A D E "

presented by **Realty One Real Living**

at **Lakeside Courthouse, Cleveland**

Questions? Comments? Feedback?

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