

**OUR VISION IS TO CREATE A WORLD WITHOUT TYPE 1 DIABETES.**

JDRF research and advocacy drives transformational T1D therapies that hold significant promise in turning Type One into Type None.

JDRF's strategic research plan encompasses multiple therapeutic areas designed to deliver a sustained stream of new, life-changing therapies.

JDRF is impacting every stage of the discovery and development pipeline to expedite meaningful scientific progress and speed delivery of advanced therapies to people with T1D.

The path from Type One to Type None is a stream of therapies that steadily remove the daily burden and complications of T1D on the way to a cure and universal prevention.

RESEARCH UPDATES



**ARTIFICIAL PANCREAS**

**Sleeping Without Fear**

**Study: Artificial pancreas systems with predictive low-glucose-suspend help reduce overnight hypoglycemia in individuals with type 1 diabetes**

**KEY MESSAGES**

- Overnight hypoglycemia—or low blood sugar—is a life-threatening complication of T1D, and studies report that 55 percent of severe hypoglycemia episodes occur during sleep<sup>1</sup> and that patients do not respond to 70 percent of their warning alarms<sup>2</sup>.
  - A JDRF-supported home-based clinical trial found that hypoglycemic episodes were significantly reduced when individuals with T1D used predictive low-glucose-suspend technology to monitor and reduce their insulin delivery during sleep.
  - Predictive low-glucose-suspend technology is algorithm-based software that connects to a continuous glucose monitor and an insulin pump to form the basis for forthcoming artificial pancreas systems. The first of its type is expected to be available in Europe later this year.
- [Link to full story >](#)



**RESTORATION**

**A Picture's Worth a Thousand Words**

**JDRF-funded study shows new imaging technique can track beta cell status**

**KEY MESSAGES**

- The number or amount of functioning beta cells a person has is difficult to measure, making the progress of T1D hard to detect and slowing clinical studies of novel beta cell survival or regeneration therapies.
  - Better markers of the T1D disease process and beta cell imaging techniques will speed clinical studies of beta cell survival and regeneration therapies accelerating progress toward a cure for T1D.
  - This JDRF-funded PET imaging technique to measure the amount of beta cells is very promising based on clinical studies including people with T1D.
- [Link to full story >](#)



**RESTORATION**

**Specific Protein May Help Beta Cells Survive in Type 1 Diabetes**

**JDRF-funded researchers find therapeutic potential of MANF protein to reduce beta cell stress in type 1 diabetes**

**KEY MESSAGES**

- JDRF-funded researchers from the University of Helsinki in Finland showed that a protein called MANF (mesencephalic astrocyte-derived neurotrophic factor) may help protect beta cells from excessive or pathologic stress.
  - In the study, mice deficient in the protein MANF developed severe diabetes due to a decrease in beta cell mass after birth, while beta cells proliferated in mice with overexpression of MANF protein. Furthermore, an overexpression of MANF in diabetic mice increased beta cell regeneration.
  - These findings could help lead to potential beta cell restoration therapies for people with T1D.
- [Link to full story >](#)



**RESEARCH PORTFOLIO**

**JDRF Ranked as Top Non-Governmental Diabetes Research Funder**

**Independent analysis of key scientific literature found JDRF among the top organizations funding diabetes research globally**

**KEY MESSAGES**

- JDRF is the leading global organization funding T1D research.
  - An analysis of scientific diabetes publications over the past five years confirmed JDRF's leading role as a supporter of important diabetes research.
  - JDRF was ranked globally as the top non-governmental diabetes research funder.
- [Link to full story >](#)

## Artificial Pancreas

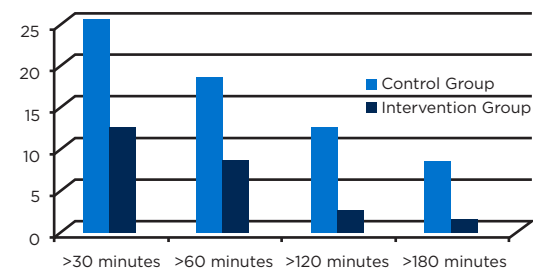
### Sleeping Without Fear

#### Study: Artificial pancreas systems with predictive low-glucose-suspend help reduce overnight hypoglycemia in individuals with type 1 diabetes

Bedtime may soon be safer and a lot less anxiety filled for people with type 1 diabetes (T1D) thanks to software being developed as a next-step component for artificial pancreas systems. Called predictive low-glucose-suspend (pLGS), it interacts with a user's continuous glucose monitor (CGM) and insulin pump to predict when blood sugar is likely to reach a dangerously low threshold and reduce or stop insulin delivery ahead of time in order to prevent life-threatening hypoglycemic—or low blood sugar—episodes.

Predictive low-glucose-suspend software is expected to debut in next-generation artificial pancreas systems for sale in Europe later this year and possibly [in the United States by next year](#). In the meantime, researchers across the globe are developing and studying other versions of the technology that may also reach the marketplace, and their findings suggest pLGS-enabled artificial pancreas systems can substantially reduce overnight hypoglycemia. In a recent JDRF-funded home-based study, for example, Stanford University's Bruce Buckingham, M.D., and David Maahs, M.D., of the Barbara Davis Center for Childhood Diabetes tracked 45 individuals ages 15 to 45 with T1D who tested an investigational artificial pancreas system fitted with their novel pLGS software. Each participant was connected to the system for 42 nights, and investigators randomly activated the pLGS software so that an equal number of nights were spent with it switched on or off. In total the study evaluated 942 nights with the software turned on and 970 nights with it turned off. Participants didn't know on any given night whether it was switched on or off. Investigators found that participants had far fewer hypoglycemic episodes on nights when the software was active (intervention group) compared to nights when it was inactive (control group), according to [findings](#) published in the May 7th online version of Diabetes Care.

#### Differences in hypoglycemic episodes when trial participants slept without (control group) and with (intervention group) predictive low-glucose-suspend systems



The vertical axis reflects the percentage of nights that trial participants experienced glucose levels equal to or less than 60 mg/dL

The horizontal axis reflects the duration of sleep time that trial participants experienced glucose level less than or equal to 60 mg/dL

The study adds to a growing body of research showing that pLGS-enabled systems used during sleep are safe and effective, and the findings help bring people with T1D closer to having fully integrated artificial pancreas systems that offer 24-hour protection against life-threatening hypoglycemic episodes. Following the success of these studies, the researchers are now evaluating the effectiveness of the technology when used by children with T1D as young as three years old.

Artificial pancreas systems are one of JDRF's priority research areas, and they offer the most immediate promise for improved T1D treatment.

To learn more about or to support JDRF's Artificial Pancreas Program, click [here](#).

#### FAQS

##### Does use of pLGS technology completely prevent hypoglycemic episodes?

In the study, T1D patients experienced significantly fewer episodes of hypoglycemia when they slept with pLGS-enabled artificial pancreas systems, but the condition was not completely eliminated. Future versions of these integrated software systems are expected to more tightly control blood glucose levels.

##### Does pLGS software live on a separate device than either the CGM or insulin pump?

Currently, pLGS technologies are experimental software systems that live on laptop or handheld computer devices and are wireless integrated with CGMs and insulin pumps. Market-ready versions of these early artificial pancreas systems will likely vary from one device maker to the next, but advanced artificial pancreas systems will endeavor to incorporate all the components into a single device.

##### When will pLGS-enabled systems be available for purchase?

Medtronic's MiniMed 640G is the first pLGS-enabled system being considered for market approval in Europe. If the device is approved, it will most likely be available in European Union countries later this year. Review of the device by the U.S. Food and Drug Administration will likely begin late this year and, if approved, made available in the United States in 2015.

<sup>1</sup> Diabetes Control and Complications Trial: Adverse events and their association with treatment regimens in the Diabetes Control and Complications Trial; Diabetes Care; 1995; 18:1415-1427

<sup>2</sup> Buckingham B, (et al); Diabetes Research in Children Network: Response to nocturnal alarms using a real-time glucose sensor; Diabetes Technol Ther; 2005; 7:440-447



## Restoration

# A Picture's Worth a Thousand Words

## JDRF-funded study shows new imaging technique can track beta cell status

For nearly 100 years, we have known that type 1 diabetes (T1D) is a disease fundamentally about the progressive loss of insulin-producing beta cells, but measuring that loss has continued to elude researchers—at least until now.

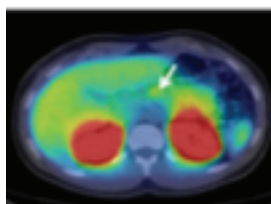
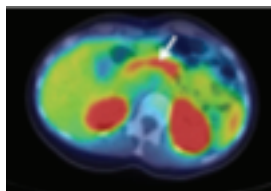
In a recent scientific [publication](#), JDRF-funded researchers used a radiotracer or marker and PET (Positron Emission Tomography) scanning as a non-invasive technique to follow changes in how many active beta cells a person has. Dr. Olle Korsgren and his colleagues at the University of Uppsala in Sweden used the technique in a clinical study of 10 people with T1D and nine without the disease to compare the amount of beta cells in each group. They found the amount or volume of active beta cells was significantly lower in the group with T1D compared to those without T1D, and the reduction was close to what researchers predicted given a loss of the majority of beta cells in the pancreas in T1D. In another study of people with type 2 diabetes, the researchers were able to use the technique to detect a progressive loss of the amount of beta cells in one person imaged repeatedly over a two-year period.

The PET imaging technique is based on recently discovered biological processes that take place in the beta cell. One specific process in the beta cell causes the cells to take up a commonly used imaging radiotracer administered at the beginning of the procedure. The amount of the tracer that is deposited in the pancreas primarily depends on how many beta cells are alive and active. The PET scan can then detect the amount of radiotracer in the pancreas as an approximate measure of the overall amount or volume of beta cells present. The procedure takes only a few hours to complete.

This imaging technique will most likely have no role in diagnosing T1D because of the large variability of the number of beta cells among people with T1D and even among those without T1D. However, it could become a key tool for tracking the loss of beta cells in a person at risk of T1D and as a faster and more precise way to evaluate the benefit of novel beta cell survival and regeneration therapies. More human validation studies of this technique are needed before it can be used routinely.

For more information and to support JDRF's beta cell restoration research program, please click [here](#).

## PET Images of Human Pancreas



PET imaging of pancreas in a non-T1D (top) and a T1D (bottom) individual. Arrows mark the location of the pancreas. Red color indicates the highest concentration of the marker (red ovals show high marker levels in the kidneys in both individuals). [Reference](#)

### FAQS

#### Is the radiotracer used in this PET procedure dangerous?

The specific radiotracer used in this beta cell imaging procedure has been commonly used in a variety of medical imaging procedures for many years and has a long history of safe use. It dissipates quickly in the body and can no longer be detected several hours after it is injected.

#### Where will this technique be of most value in T1D?

Research has accelerated significantly over the past several years into beta cell replacement and regeneration therapies. Testing these novel therapies can take a long time to determine if they are working as hoped if insulin use or C-peptide levels are the yard sticks of success. This novel beta cell imaging technique might be more sensitive and provide faster answers to the value of such novel therapies, accelerating the whole development process for finding a cure.

#### When might this technique be ready for routine use?

The clinical results with this beta cell imaging technique are very encouraging and an important step. Multiple additional human studies, which will take years to complete, are needed to be able to better interpret the results from such images before this can be used routinely in following people with T1D or in clinical trials of novel T1D therapies.



## Restoration

# Specific Protein May Help Beta Cells Survive in Type 1 Diabetes

## JDRF-funded researchers find therapeutic potential of MANF protein to reduce beta cell stress in type 1 diabetes

In the healthy pancreas of someone without type 1 diabetes (T1D), the hormone insulin (essential for turning food into energy) is produced, stored, and released in a normal “factory-like” process within pancreatic beta cells in response to glucose in the diet. Early in the course of T1D, however, excessive or pathologic stress in beta cells compromises their ability to properly secrete insulin, triggering a cascade of events ultimately contributing to the beta cell death. Over the past several years, JDRF-funded researchers have found [evidence](#) that beta cell stress may play a role in the onset of T1D, and are exploring [possible ways to stop it](#) from occurring, thus potentially protecting beta cell health and maintaining normal beta cell function. In April, JDRF-funded researchers in Finland released [new findings in the journal \*CellPress\*](#) that add another piece to the puzzle of beta cell stress and T1D.

Led by Dr. Mart Saarma, Dr. Maria Lindahl, and Dr. Timo Otonkoski of the University of Helsinki, along with other investigators, the study showed that a protein called MANF (mesencephalic astrocyte-derived neurotrophic factor) may help protect beta cells from experiencing excessive or pathologic stress response. In the study, mice deficient in the protein developed rapid-onset of T1D due to a decrease in beta cell mass after birth. In contrast, overexpression of the MANF protein in mice resulted in increased beta cell regeneration and promoted beta cell survival in this mouse model of T1D. The study indicates that MANF protein may thwart beta cell stress, promoting the proliferation and survival of beta cells—information that could prove valuable in the translational development of beta cell survival therapies for humans with T1D in the future.

These findings come one year into a three-year research grant from JDRF to support the discovery and development of potential methods to protect and regenerate beta cells in people with T1D. Still, more research needs to be done in additional animal models of T1D, as one model alone does not precisely mimic the complex pathogenesis of T1D in humans. Additionally, preliminary findings will be validated with human beta cells. The growing knowledge of beta cell biology, thanks to studies like this one, helps to open multiple paths toward potentially preserving and restoring beta cell function in people with T1D.

For more information and to support JDRF’s beta cell restoration program, please click [here](#).

### FAQS

#### Why is JDRF supporting this research

This study is part of a three-year research grant from JDRF and supports JDRF’s beta cell restoration program, aimed at discovering and developing therapies that promote the protection and proliferation of insulin-producing beta cells.

#### What causes beta cell stress?

Researchers are still looking into the possible causes of beta cell stress, but this latest study shines light on the topic by showing the role of the MANF protein in protecting beta cells from this phenomenon. Continued research is needed into beta cell stress, its causes and ways to stop it.

#### What are the next steps?

More research needs to be done in additional animal models of T1D, as one model alone does not precisely mimic the complex pathogenesis of T1D in humans. Additionally, findings will be validated with human beta cells in order to determine therapeutic potential for people with T1D.



## Research Portfolio

# JDRF Ranked as Top Non-Governmental Diabetes Research Funder

## Independent analysis of key scientific literature found JDRF among the top organizations funding diabetes research globally

In a recent independent analysis of key diabetes-related scientific literature, JDRF was ranked as the third most frequently cited funder of diabetes research globally, behind only the U.S. National Institutes of Health and the National Natural Science Foundation of China. JDRF was the top ranked non-governmental or charitable funder of diabetes research. This [analysis](#) is a confirmation of the significant impact JDRF's strategic research plan is having on advancing diabetes research—made possible because of JDRF's generous supporters.

Thomson Reuters, a world leader supplying intelligent information for businesses and professionals, conducted the independent analysis of key scientific literature devoted to diabetes to determine the most common funders of diabetes-related research. Using their “[Web of Science](#)” database, they searched for publications between January 2008 and July 2013 on “diabetes” and related terms. From the roughly 200,000 publications and reports they identified, the organizations explicitly acknowledged as the funders of each were compiled and ranked by frequency of mentions. Using this unique database allowed funding acknowledgements to be linked with research publications. The analysis of such links is complicated for several reasons, but provides an independent view of the key funders in this field. Limitations of this analysis include the fact that authors may fail to mention multiple funders, different papers may acknowledge the same grant from the same funder, and authors may fail to mention funding sources. The “Web of Science” database upon which the analysis is based is a premier resource for research, its content used by more than 6,000 of the world's leading scholarly institutions responsible for scientific policy making.

This independent analysis shows the important impact JDRF is having on diabetes research and our goal of creating a world without type 1 diabetes (T1D). The top ranking of JDRF demonstrates not only the scope of the research plan JDRF is supporting, but also the quality of the research being funded toward turning Type One into Type None.

For more information and to support JDRF's T1D research program, please click [here](#).

## Funders of Diabetes Research

PROMINENT FUNDERS OF DIABETES RESEARCH (2008-2013)	
1	US National Institutes of Health
2	National Natural Science Foundation of China
3	JDRF
4	US National Institute of Diabetes and Digestive and Kidney Diseases
5	Canadian Institutes of Health Research

Ranked by number of diabetes-related publications in which funding entity is expressly acknowledged during January 2008 to July 2013.  
Source: [Thomson Reuters – Funding Diabetes Research](#)

### FAQS

#### Did JDRF commission this study?

No, this was an independent analysis undertaken by the Thomson Reuters organization. JDRF played no role in organizing or conducting the analysis.

#### Did the analysis examine only T1D-related scientific publications?

The analysis is based on a broad definition of diabetes research, not limited only to T1D. This makes JDRF's ranking even more impressive given all the other research being reported on type 2 diabetes and other forms of diabetes that JDRF is not focused on. JDRF's role in funding T1D-related research really stands out across all diabetes research.

#### How would JDRF rank if this was based on research funding

JDRF is a leading diabetes research funder by any measure. It is not clear where JDRF would rank by dollars funded among all organizations that fund diabetes research because not all these organizations report their research funding in this area as clearly as JDRF does. The impact JDRF is having on the scientific knowledge as shown in this recent analysis is perhaps a much more meaningful measure of the positive impact JDRF is having toward our goal than dollars alone.