2017 RESEARCH UPDATE

A Year of Scientific Progress

JDRF IMPROVING LIVES. CURING TYPE 1 DIABETES.

"First, we need basic scientific understanding.

Then we must translate that understanding into therapies that must then be tested and approved by regulators.

And then the therapies must be affordable and accessible.

And finally, clinicians must prescribe the therapies to people with T1D.

At JDRF, we know that if any part of the chain is broken people with T1D will not benefit and do better."

Aaron J. Kowalski, Ph.D.
Chief Mission Officer, JDRF

OUR VISION

A world without type 1 diabetes

OUR MISSION

Accelerating life-changing breakthroughs to cure, prevent and treat T1D and its complications

Dear JDRF Community,

At JDRF, we're fighting every day to create a world without T1D. In 2017, with your support, we deepened our impact and advanced our mission to accelerate breakthroughs to cure, prevent and treat T1D and its complications.

In the past 12 months, we pioneered new pathways to unlock the science around T1D. We augmented our understanding of the immune system as we worked to prevent the disease from ever touching another generation. And our efforts in 2017 resulted in real-world therapies that make T1D easier to manage so people can live healthier lives right now. We welcomed promising results from important human clinical trials—and showed the value of measuring the success of interventions beyond hemoglobin A1c.

I feel a true sense of optimism as we head into a new year.

Since our founding, JDRF has raised more than $2 billion to fund T1D research. But the enormity of the challenge means we also must advocate for additional funding from governments around the world, and from our academic and industry partners. For every dollar we invest in research, our research and advocacy efforts catalyze an additional $2.50 in investment into the fight against T1D—a disease that by 2050 is currently projected to affect more than five million Americans and millions more around the world.

We invite you to read more about our research highlights of 2017, a year of important innovation made possible by the passion and inspiration of our volunteers, donors, partners, advocates and the scientific community. With more than 500 active research grants, no organization is making a bigger impact in the fight against T1D than JDRF.

In 2018, we'll keep working to defeat this unforgiving disease and achieve our ultimate vision: a world without T1D. Thank you for joining JDRF in our mission.

Derek K. Rapp
JDRF President & CEO

"T1D parents created this community by founding JDRF, and we all are on this journey together. We will continue until we realize our vision of a world without T1D. I say this as CEO—and as a T1D dad."

Derek K. Rapp
JDRF President & CEO

Our Research Strategy

At JDRF, our ultimate goal is finding a cure for type 1 diabetes (T1D). We won't stop until we get there. Since our founding in 1970, we've also worked relentlessly to drive therapies and technologies that help people manage this disease—and stay as healthy as possible. To achieve our vision of a world without T1D, we drive multiple approaches to cure, prevent and treat T1D and its complications. Our scientific strategy is organized into six research areas.

RESEARCH PROGRAM AREAS

JDRF funds multiple therapeutic approaches to cure, prevent and treat T1D and its complications.

Artificial Pancreas
Systems that can automatically deliver more effective and precise insulin and multi-hormone therapy

Beta Cell Replacement
Cell replacement therapies in a protective device that can provide long-term relief from insulin therapy without the need for intensive immune suppression

Complications
Therapies that prevent or better treat T1D-related damage such as eye and kidney disease

Glucose Control
Treatments that will improve the body's glycemic balance through innovative and personalized therapies beyond the use of insulin alone

Prevention
Therapies that will keep individuals, especially those at higher risk, from ever developing T1D

Restoration
Stopping or reversing the autoimmune attack and restoring the body's ability to produce insulin, which would represent a biological cure for T1D

HOW JDRF FUNDS RESEARCH

Our research portfolio is overseen by internal and external experts whose charge is to ensure scientific integrity and strategic direction. JDRF's in-house team of Ph.D. and M.D. scientists possess vast experience in translating research in academia and industry.

Update on Artificial Pancreas Systems

REDUCING THE BURDEN OF LIVING WITH T1D

T1D is a disease that must be managed every hour of every day. To ease the burden, we're driving new technologies that allow people to more easily control their glucose levels. The JDRF Artificial Pancreas Project (AP), created in 2006, brought together researchers and scientists from around the world to develop and commercialize devices to monitor glucose levels—and then automatically provide the right amount of insulin.

Ten years later, the U.S. Food and Drug Administration approved the system that automatically doses insulin based upon a sensor reading. The system began reaching people and transforming lives in 2017. Around the same time, some people with T1D turned to do-it-yourself approaches that give them real-time access to Continuous Glucose Monitor (CGM) data on their websites, cell phones or smart watches. In such systems, online applications display CGM data and also control insulin delivery. To support these approaches, JDRF announced its Open Protocol Automated Insulin Delivery Initiative. The initiative will work with industry stakeholders to make devices compatible and to set industry standards. It will also work to make sure these approaches are safe and the pathway to regulatory approval is clear.

We'll continue to support the development and commercialization of increasingly sophisticated AP systems. The T1D community wants—and deserves—devices that are smaller, easier to use, and highly effective—devices good enough to let people forget they have T1D for a while.

In our early days, people with T1D often were told they should not exercise. Even today, myths and confusion surround T1D and exercise. That's why JDRF's T1D Performance in Exercise and Knowledge (PEAK) program established the first published guidelines to help people with T1D exercise safely.

Furthering Beta Cell Replacement

PIONEERING RESEARCH MOVES FORWARD

We've seen people with transplanted beta cells achieve normalized blood-glucose control for 10 years or even longer. But widespread use of transplants is not possible for two reasons: not enough islets, or clusters of cells, are available; and transplant recipients must take powerful immunosuppressive drugs to prevent the immune system from destroying the newly transplanted cells.

JDRF is working with scientists to overcome these obstacles. Our efforts have resulted in techniques to scale up production of implantable cells in the laboratory. At the same time, we're supporting the development of beta cell replacement materials that show promise in blocking an immune system attack. Human clinical trials have begun to test the safety and efficacy of these therapies.

PROGRESS CONTINUED IN 2017

semma THERAPEUTICS

Semma Therapeutics, a biopharmaceutical company developing stem-cell derived islet therapy, received funding from the JDRF T1D Fund. The fund is exclusively devoted to finding and funding the best early-stage T1D commercial opportunities. The Cambridge, Massachusetts, biopharmaceutical company focuses on developing transformative therapies for T1D patients and was founded by Harvard University Professor Douglas Melton, whose groundbreaking work led to the discovery of a method to generate billions of functional, insulin-producing beta cells in the laboratory.

Massachusetts Institute of Technology

Boston Children's Hospital
Until every child is well™

Researchers at MIT and Boston Children's Hospital conducted and published research that helps scientists more clearly understand the body's immune responses to the materials used in implanted medical devices. The findings could have a significant impact on the ability to prevent immune rejection of cell encapsulation and transplantation devices. The study was funded through collaboration between JDRF and The Leona M. and Harry B. Helmsley Charitable Trust.

VIACYTE

ViaCyte launched a trial to assess the safety and efficacy of a device known as PEC-Direct™, which uses the same transplanted cells as ViaCyte's original device, PEC-Encap™, but places them in a so-called "scaffold" that is more open to and interactive with the recipient's body. The PEC-Direct device is designed for use by people with severe hypoglycemic unawareness, preferably those who have already had kidney or pancreas transplants, as the device requires the use of broad-scale immunosuppression. It is hoped that the PEC-Direct device will address some challenges that the original device encountered during clinical trials. Insights gained from the new trial will influence the design and development of future encapsulation products.

Reducing Complications

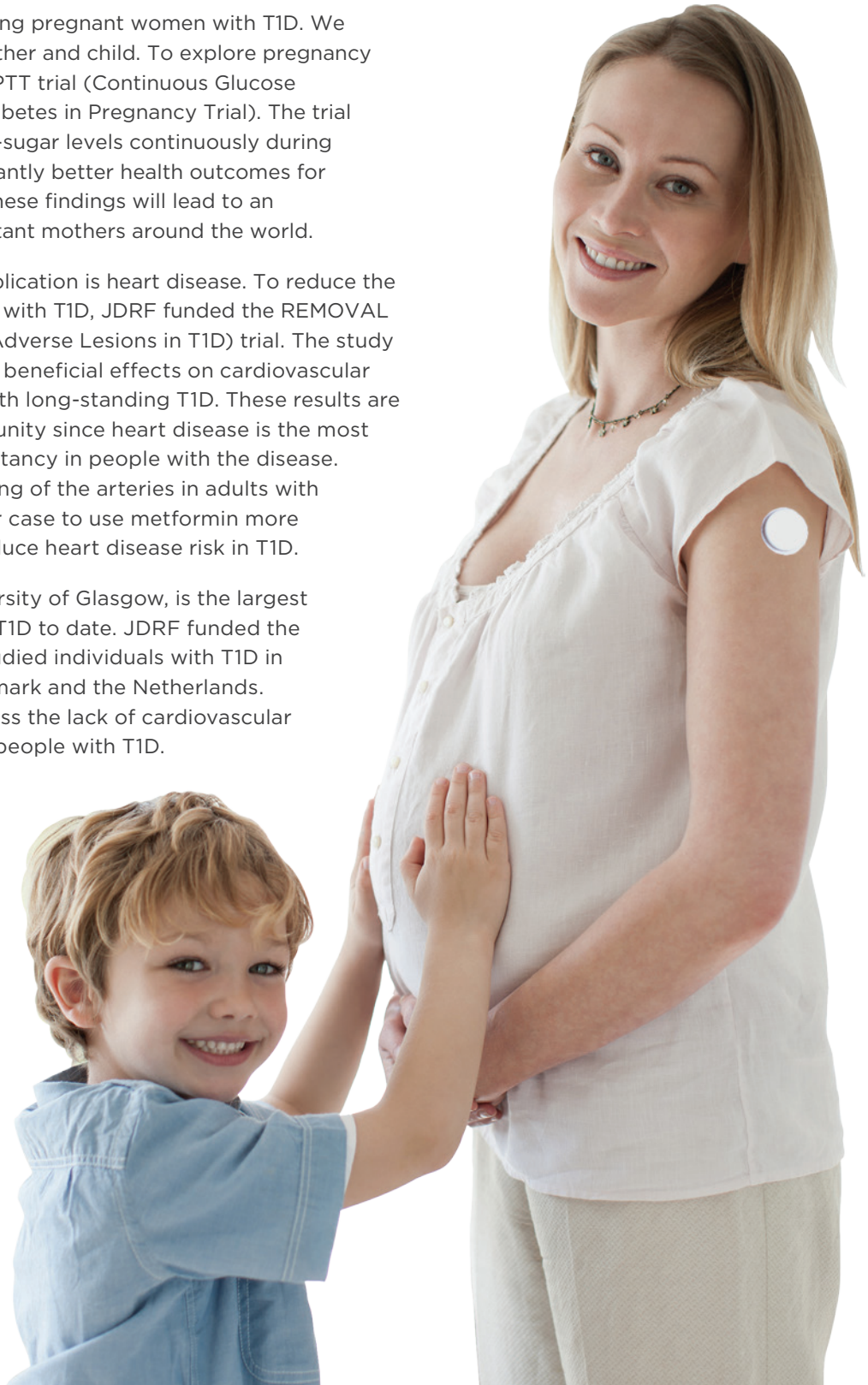
MAINTAINING HEALTH AND WELLNESS

Even with close and careful monitoring of glucose levels, many people with T1D experience complications that can range from eye disease to heart and kidney disease. These complications can have devastating effects on the lives of people with T1D.

One area of deep concern is supporting pregnant women with T1D. We want the best outcomes for both mother and child. To explore pregnancy outcomes, JDRF-funded the CONCEPTT trial (Continuous Glucose Monitoring in Women with Type 1 Diabetes in Pregnancy Trial). The trial demonstrated that monitoring blood-sugar levels continuously during pregnancy with a CGM led to significantly better health outcomes for mothers with T1D and their babies. These findings will lead to an improved standard of care for expectant mothers around the world.

Another potentially life-altering complication is heart disease. To reduce the impact of heart issues among people with T1D, JDRF funded the REMOVAL (Reducing with Metformin Vascular Adverse Lesions in T1D) trial. The study showed that the drug metformin has beneficial effects on cardiovascular and metabolic outcomes in adults with long-standing T1D. These results are extremely relevant to the T1D community since heart disease is the most common cause of reduced life expectancy in people with the disease. The results showed reduced thickening of the arteries in adults with T1D, meaning there is now a stronger case to use metformin more widely as a long-term strategy to reduce heart disease risk in T1D.

The REMOVAL trial, led by the University of Glasgow, is the largest clinical trial of metformin therapy in T1D to date. JDRF funded the five-year international trial, which studied individuals with T1D in the UK, U.S., Australia, Canada, Denmark and the Netherlands. The multi-center trial aimed to address the lack of cardiovascular data in the area of metformin use in people with T1D.



Maintaining Glucose Control

FINDING BETTER WAYS TO MANAGE T1D

At JDRF, we know that managing blood sugar should be much easier, and that's why we're committed to driving new approaches. One is the development of glucose-responsive insulin that would circulate through the bloodstream, turning on when it's needed and turning off when blood sugar starts to go low. A successful glucose-responsive insulin would keep tight control over blood sugar and reduce the need for glucose monitoring and likely require fewer doses to maintain control throughout the day. JDRF also funds research into other medications that could significantly improve blood-sugar management when taken along with insulin.

PROGRESS INCLUDES:

Results of ongoing clinical trials of Lexicon's dual SGLT inhibitor sotagliflozin, a type of drug that helps users avoid high blood-sugar levels by increasing excretion of glucose via urine. The findings of the trials showed that sotagliflozin not only reduced HbA1c in adults with T1D but also improved other key health measures, such as time in range, body weight and blood pressure, without increasing hypoglycemia. Tighter glucose control reduces the risks of complications and so we're committed to funding trials that explore new ways to make it easier to manage T1D.

Unlocking Prevention

UNRAVELING THE PROGRESSION OF T1D

Unfortunately, there is a genetic component to T1D; and family members and next generations of people with T1D are at increased risk of developing the disease. JDRF is committed to preventing T1D in those at risk and in future generations. We now know that T1D begins well before symptoms appear, and progresses through distinct stages. By screening people at risk of developing T1D, researchers can monitor the disease from its earliest stages. The information obtained is helping researchers understand how the disease develops—and how it might be stopped.

JDRF began an exciting collaboration with IBM to develop and apply machine-learning methods to identify factors leading to the onset of T1D in children. With the advanced computing power of IBM, for the first time we'll be able to comprehensively analyze data sets from research from around the world. The aim is to better understand the risk factors and progression of T1D—and to find ways to prevent the disease entirely.

Never before has JDRF been able to analyze the wealth of data so comprehensively to determine why some children who are at risk develop T1D and others do not. That knowledge could also contribute to finding a cure for people who already have T1D.

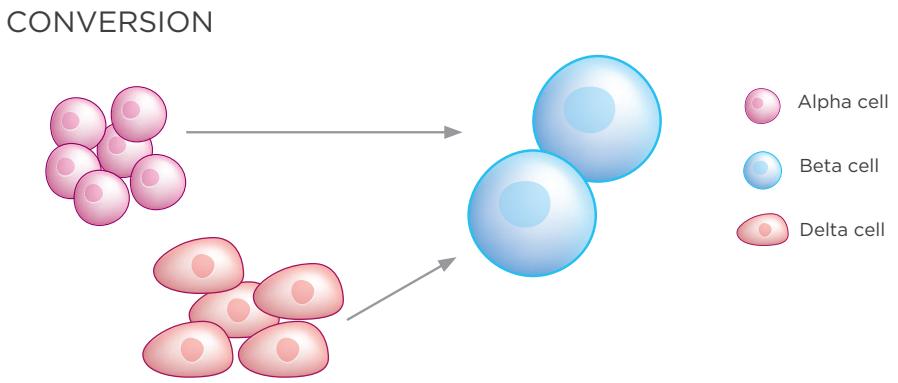
ALSO IN 2017

Another trial looked at the value of oral insulin to prevent the progression of T1D. The international Diabetes TrialNet Oral Insulin Prevention Trial, the largest and longest oral insulin prevention trial ever conducted, sought to answer whether treatment at early stages of disease can delay progression to clinical (stage 3) T1D. While there was not significant evidence of efficacy in the main group tested, in one of the predefined subgroups, characterized by specific biomarkers, oral insulin was able to delay the progression of T1D by 31 months on average.

Restoring Beta Cell Function

A CRITICAL STEP TOWARD A CURE

In T1D, the body's immune system attacks insulin-producing beta cells. JDRF drives innovative research to restore the body's ability to produce insulin by transplanting beta cells made in the laboratory into the pancreas. JDRF has also helped open new pathways for a cure: helping the body restore its own beta cells and blocking or retraining the immune system. JDRF's Beta Cell Restoration Program brings scientists from around the world together to collaborate on beta cell restoration.



The JDRF-funded investigator and French researcher Patrick Collombat, Ph.D., found that GABA, a naturally occurring chemical and common dietary supplement, triggers the conversion of mouse alpha cells into beta-like cells. Treating diabetic mice with GABA fully restored beta cell mass and reversed their diabetes, and human islets, or clusters of cells, transplanted into mice appeared to respond in the same way as the mouse islets.

Another JDRF-funded researcher, Stefan Kubicek, Ph.D., at the Austrian Academy of Sciences, achieved similar results using antimalarial drugs called artemisinins. The research suggests it may be possible to train alpha cells that survive in the pancreas of a person with T1D to become insulin-producing cells.

Especially significant is that both of these compounds already are approved and in use in humans. That means clinical trials could move forward quickly. Renewing the body's ability to produce insulin would be transformative for people with T1D and would reduce or eliminate the daily burden and hazards of managing blood-glucose levels. Even partial restoration or maintenance of beta cell function could offer significant benefits, such as slowing or preventing progression of the disease, reducing the need for insulin, improving glucose control and lowering the risks of complications.

We also fund research on specific drugs already in use to determine if they have value for people with T1D. Existing drugs can become available for people with T1D far more quickly than brand-new therapies never before on the market. One trial we launched tested the blockbuster cancer drug imatinib (brand name Gleevec®) and found that the drug slowed the progression of T1D and the loss of the body's own insulin production. On average, the people who got the medicine used less insulin and had higher beta cell function. The research also could help people with existing T1D. A biological cure will require new beta cells—from the laboratory or regenerated—and also new therapies to protect those cells from immune attack. As a result, clinical trials seeking to prevent the progression of T1D could benefit the entire T1D community.

ABOUT JDRF

JDRF is the leading global organization funding type 1 diabetes (T1D) research. Our mission is to accelerate life-changing breakthroughs to cure, prevent and treat T1D and its complications. To accomplish this, JDRF has invested more than $2 billion in research funding since our inception.

ABOUT JDRF IMPACT

JDRF has transformed scientific understanding of type 1 diabetes. Our deep knowledge of T1D's roots is leading the way to preventing future diagnoses of T1D—and one day stamping it out entirely. Our research investments deliver on the promise of making life with T1D better. We've championed technology with that goal in mind—from the first engineered insulin 25 years ago to recent breakthroughs like artificial pancreas systems and more. JDRF is the link between future research breakthroughs and the community living with T1D every day.

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