JDRF Research Update

November 2006

The JDRF Diabetes Research portfolio of funded science is among the largest in the world focused on cures and treatments for diabetes and its complications. Exceeding $122 million last year and representing over 500 projects, JDRF science revolves around a set of targeted areas of research. JDRF calls these areas Cure Therapeutics, because they are targeted at moving scientific discoveries in each discipline into products, drugs, and treatments for people with diabetes.

AUTOIMMUNITY

A large concentration of research that JDRF funds is focused on stopping or reversing the immune-mediated mechanisms that result in the body attacking the insulin producing beta cells within the pancreas

FY 2006 funding: $41 million

Recent Progress/Advances:

Steady progress has been made in understanding how the body attacks insulin-producing beta cells, eventually killing off the majority of those cells to cause type 1 diabetes. Last year's big news in immune research was a clinical trial that dramatically slowed the progression of diabetes in newly diagnosed patients by using anti-CD3 antibodies. Short-term treatment with these antibodies preserved beta cell function for up to 18 months, significantly reducing insulin requirements and helping maintain good blood glucose control. The research has progressed to the point that several biotechnology companies, including TolerRx in Massachusetts and Macrogenics in Maryland, will be launching pivotal phase III registration clinical trials to seek regulatory approval.

Current notable projects:

- The continuation of clinical trials using anti-CD3 antibodies to stop the autoimmune attack and activate immunoregulation to preserve beta cell function in new onset type 1 diabetes.
- A Center for Immunological Tolerance at Harvard Medical School investigating how immune system failures lead to type 1 diabetes, and how to re-establish "tolerance" in order to prevent or cure the disease.
- The first-ever diabetes vaccine trial, using an insulin peptide to train the immune system to tolerate beta cells rather than attack them, led by investigators at King's College and Bristol University in the U.K.

COMPLICATIONS

Diabetes-related complications such as retinopathy (eye disease), neuropathy (nerve damage), nephropathy (kidney disease), hypoglycemia (low blood sugar), and heart disease and stroke, are devastating to health and create an enormous economic burden on society. JDRF's leadership in funding innovative complications research is focused on enabling people with diabetes to live longer, healthier lives.

FY 2006 funding: $26 million

Recent Progress/Advances:

In the last year, there were important basic discoveries, and promising drugs advanced along the development pipeline. Researchers at Johns Hopkins University demonstrated that intraocular injection of an antibody directed at vascular endothelial growth factor (VEGF), can treat diabetic macular edema. This antibody is already FDA approved for a non-diabetes eye disease. Investigators at Albert Einstein College of Medicine discovered that high blood sugar causes the abnormal buildup of a molecule called MG in the body's cells, starting a chain of events that leads to the onset of several complications, including retinopathy and nerve and kidney damage. Penn State researchers found that minocycline, an antibiotic already approved by the FDA as an acne treatment, significantly reduced retinal damage in animals.

Current notable projects:

- The progression from phase I to Phase II clinical trials of VEGF inhibitors to treat diabetic macular edema.
- Investigations at the JDRF Center for Mechanisms and Intervention of Diabetic Retinopathy at Pennsylvania State University Hershey Medical Center that focus on the early stages of damage to the retina that leads to diabetic retinopathy.
- The Center for the Study of Hypoglycemia at Yale University probing causes of hypoglycemia and identifying therapeutic targets for drugs that could help prevent the dangerous complication or mitigate its damaging effects.

REGENERATION

Among the fastest-growing areas JDRF supports is research aimed at regenerating insulin-producing cells in individuals with established type 1 diabetes (without transplanting cells from human donors or animal sources). Regenerated beta cells will still likely be susceptible to autoimmune attack, which will need to be addressed, but will not require the immunosuppressive drugs used to prevent foreign tissue rejection as used in islet transplantation.

FY 2006 funding: $8 million

Recent Progress/Advances:

JDRF has made significant strides in regeneration in the last year. Rockefeller University scientists identified a protein that regulates cell growth specifically in pancreatic islets. The Regeneration of Beta Cell Function team screened a massive library of existing clinical compounds that might expand beta cells, and identified five with relevant activities.

Current notable projects:

- The JDRF Regeneration of Beta Cell Function program, involving 16 scientists from five countries working to prove within two years that therapeutics can help restore or regenerate human beta cell function.
- A partnership with Transition Therapeutics, based in Toronto, to support a clinical development plan for a diabetes regenerative product called GLP1-I.N.T.™ JDRF will provide milestone-driven payments of up to $4 million to the project over two years, to push this diabetes regenerative product into Phase II clinical trials in type 1 diabetes patients.

METABOLIC CONTROL

An ideal treatment for people with diabetes would continually monitor the body's glucose levels and respond with correct doses of insulin. Such a device would be constructed as a "closed loop" system, functioning as an artificial pancreas. An artificial pancreas would link two existing technologies: an insulin pump and continuous glucose monitors.

FY 2006 funding: $6 million

Recent Progress/Advances:

Using a working prototype of a complete closed loop artificial pancreas, researchers at the JDRF Center for the Study of Hypoglycemia at Yale University were able to maintain normal insulin levels throughout the night in teenagers with type 1 diabetes.

Current notable projects:

The JDRF Artificial Pancreas Project, a multi-year initiative that aggressively combines research and advocacy to speed the development, approval and availability of devices that enable people with diabetes to better maintain normal glucose levels. It currently consists of:

- A large, one-year, multi-site clinical trial including researchers at nine institutions comparing the health outcomes of people who use continuous glucose sensors with those who do not to quantify the benefits of these devices.
- A multi-site scientific consortium, including scientists at Yale, Stanford and Cambridge, working collaboratively to research potential algorithms for a closed-loop system that links continuous glucose sensors and insulin pumps to automatically dispense insulin to patients with type 1 diabetes.

REPLACING ISLETS

Islet replacement therapies represented the largest total among the Cure Therapeutics areas. Ever since pioneering islet cell transplantation research in the 1970s, we have been pursuing novel transplantation technologies to replace lost islets with functioning ones—just like a heart or kidney transplant restores the function of those organs. However, we face a severe islet shortage in the U.S., to satisfy the transplant needs of people with type 1 diabetes. Consequently, JDRF is also focusing its research on expanding the supply of islets through stem cell research, animal sources, converting other cells to become insulin-secreting cells, and the expansion of available human islets through regeneration.

FY 2006 funding: $21 million (Transplantation)
$20 million (Renewable Cell Source)

Recent Progress/Advances:

JDRF research centers continue to develop new and potentially more effective transplant sites in the body, using new drug combinations that people can better tolerate. To pursue new sources of islets, JDRF funded over $10 million in adult and embryonic stem cell research projects in 12 countries, in many cases using its funds to leverage matching grants from local governments. During that period, a number of researchers successfully discovered new protocols to generate definitive endoderm, the first step in differentiating embryonic stem cells into functioning beta cells.

Current notable projects:

- A project at City of Hope National Medical Center in Los Angeles investigating ways to stimulate islet expansion with growth factors.
- Programs at the University of Minnesota and Emory University investigating the use of transplanted pig islets to reverse diabetes.
- A project in Sweden investigating how environmental cues from the embryo guide embryonic stem cells into becoming mature cells that resemble pancreatic beta cells.
- A project at Sheba Medical Center in Tel Hashomer, Israel exploring the use of gene therapy to stimulate human adult liver cells to produce insulin and alleviate symptoms of diabetes.

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