JUVENILE DIABETES RESEARCH FOUNDATION INTERNATIONAL

Emerging Technologies IN DIABETES RESEARCH

The JDRF Emerging Technologies E-Newsletter No. 6 January 2008

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BILLING CODES ISSUED FOR COVERAGE OF CONTINUOUS GLUCOSE MONITORS

The Centers for Medicare and Medicaid Services (CMS) announced late last year that it is issuing billing codes for continuous glucose monitoring technology. The codes, which took effect on January 1, 2008, are used by public and private health insurance plans to process payments for these devices. Separate billing codes are being issued for each component of a continuous glucose monitoring system. The codes are: A9276 for the sensor, A9277 for the transmitter, and A9278 for the receiver.

The new billing codes should make it easier for health plans to process payment for continuous glucose monitors (CGM). While most health plans are waiting for the results of studies like JDRF's CGM clinical trial before making a formal decision to cover the technology, many are paying for CGM on a case by case basis for some individuals, and the codes will help facilitate that process. JDRF has prepared tips to help those seeking case by case coverage, which are posted at www.jdrf.org/cgmcoverage.

JDRF began advocating for billing codes more than a year and a half ago. The foundation's actions included:

• Testifying at CMS public hearings and submitting formal comments from JDRF about how the granting of codes would help people with diabetes; and

• Working with Congress, device manufacturers, and private health plans to share information with CMS about the importance of the billing codes.

JDRF has launched the Artificial Pancreas Project to accelerate the availability of an artificial pancreas to people with diabetes, one of the foundation's cure therapeutic pathways. The overall goal of the project is to accelerate the development, regulatory approval, health insurance coverage, and clinical acceptance of continuous glucose monitoring and artificial pancreas technology.

The long term goal is for broad patient access and a thriving competitive market for these devices and products.

For regular updates to the Artificial Pancreas Project, please visit www.jdrf.org/artificialpancreas.

RENOWNED BIOMATERIALS GROUP TACKLES ISLET ENCAPSULATION TECHNOLOGY

JDRF is funding acclaimed laboratories at the Massachusetts Institute of Technology (MIT) and Children's Hospital Boston of Harvard Medical School to develop synthetic materials for the protective encapsulation of islets prior to transplantation. If successful, the project could greatly improve the success of human islet transplants, and open the door to the successful use of islets from pigs or human stem cells. Islets are clusters of cells in the pancreas including beta cells, which are the insulin-producing cells that are destroyed by the immune system in the attack that causes type 1 diabetes. An islet cell transplant replaces these insulin-producing cells with functioning ones from a donor.

The three-year, $4.3 million initiative will seek to identify the best materials for shielding islets from immune attack while allowing them to secrete insulin normally. The work will be conducted by Robert S. Langer, an internationally renowned researcher at MIT's Center for Cancer Research with expertise in biotechnology and materials science. Working with Dr. Langer will be MIT's Daniel Anderson, Gordon Weir, M.D., a JDRF researcher at Joslin Diabetes Center, and Daniel S. Kohane, at Children's Hospital.

"Although islet encapsulation is currently being tested by a number of labs, novel synthetic biomaterials may possess properties superior to commonly used materials to enable effective beta cell replacement," said JDRF Replacement Therapeutic Program Director Julia Greenstein. "This program has the potential to elevate the field to another level."

Researchers have long been interested in encapsulating islets before transplantation, which could remove the need for immune-suppressing drugs, which can be toxic. There were tantalizing achievements in animals more than 20 years ago, when encapsulated islets corrected diabetes in rats and in several non-human primates. However, the field has not lived up to expectations, as scientists have not been able to reproduce that initial success consistently and long-term in studies on monkeys and humans.

One reason for this difficulty is the fragility of islets. Although encapsulation works well for certain uses—such as the slow, steady release of a drug into the body—it is much harder to encase living cells and ensure they will survive and function over long periods. Scientists have so far failed to develop a semi-permeable material that effectively allows the transport of glucose and insulin while completely blocking the attack from immune cells. The limitation may be due to using materials that had already been successful in other systems—but that weren't developed with islets in mind.

In the last year, however, there have been signs that the field is progressing rapidly. In consultation with researchers, JDRF determined that there have been significant advances in the chemical purity of encapsulation materials, leading to promising results in preliminary tests. At the same time, it became clear that the encapsulation field was suffering from a lack of academic and corporate support.

In one approach to fill this gap, JDRF turned to Drs. Langer and Anderson. Dr. Langer is a world-famous expert in biomaterials, especially focusing on the use of polymers (synthetic materials) to deliver drugs continuously at controlled rates for prolonged periods. He has received more than 150 major awards and has more than 600 issued or pending patents. In 2001, *Time* magazine and CNN named Dr. Langer one of the 100 most important people in America and one of the 18 top people in science or medicine. Dr. Langer was a recipient of a National Medal of Science in 2006 for his revolutionary discoveries in the areas of polymeric controlled-release systems and tissue engineering and synthesis of new materials that have led to new medical treatments that have profoundly affected the well-being of mankind.

Because it is specifically focused on new biomaterials for islets, this project is unlike any encapsulation program to date. Drs. Langer and Anderson will develop new technology specifically aimed at using "high-throughput screening" to identify novel biomaterials suited to use with islets. High-throughput screening allows researchers to conduct millions of tests quickly to identify compounds that have the desired effect. In essence, it's a brute-force approach to collect a large amount of experimental data in a short time.

Their goal is to develop materials that work, but do not stimulate adverse reactions from the host. Implanted material tends to trigger a mild immune response that forms scar tissue. This build-up can choke off interaction with the surrounding cells, preventing the accurate reading of glucose levels and cutting off nutrients to the transplanted cells.

"There are a lot of requirements for this to happen," Dr. Anderson said. "The materials have to be both biocompatible to the host that you put the cells in, but also to the cells themselves. Ideally, you want them to live a long time so they don't need replacing often."

Dr. Anderson said there are several strategies for encapsulating islets. "You can do single cells, you can do little aggregates of cells, you can do larger colonies, you can do sheets. Whatever format you use, it's important that there's not a long diffusion time because you want your body to be able to react quickly to blood sugar."

The plan is to test encapsulation *in vitro* and then carry forward the most promising materials into animal tests—first rodents and then larger animals such as pigs. Dr. Weir, who has extensive experience in islet cell transplant, islet physiology, and clinical diabetes, will act as a collaborator on the project. He also will provide pig islet clusters for testing.

"This project reflects our interest in funding innovative, high-risk programs that have potential to transform the field," said JDRF executive vice president for research Richard Insel, M.D. "Attracting outstanding scientists to a diabetes-related challenge greatly increases prospects for achieving JDRF's goals."

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ARTIFICIAL PANCREAS CONSORTIUM MEETS TO UPDATE RESULTS AND REFINE GOALS

The JDRF-funded Artificial Pancreas Consortium held an all-day meeting late last year in San Francisco to discuss the latest research developments. The consortium, funded by JDRF, includes top diabetes researchers, mathematicians, and engineers at seven sites around the world who are developing and testing sophisticated computer programs that "close the loop" by linking continuous glucose monitors with insulin pumps to automatically control glucose levels in a variety of circumstances and types of people. Also included in the meeting were JDRF staff and lay volunteers as well as representatives from five diabetes device companies whose devices the consortium members are using to perform their studies.

Highlights of the meeting included:

• **Outcome Measures:** Researchers presented and discussed a set of outcome measures by which an artificial pancreas could be judged. The consortium would like to have agreement on which data should be used to evaluate an artificial pancreas's effectiveness.

• **Clinical Parameters:** Researchers presented and discussed proposals for key clinical data to be collected from each person participating in the artificial pancreas trials. In the current feasibility phase of the research, each site in the consortium is testing various versions of an artificial pancreas, but researchers believe having uniformity in certain data collection and safety parameters would be beneficial.

• **Results to date:** Each site presented a summary of results to date. While awaiting FDA approval for use of automated systems, many sites have refined their algorithms by manually controlling their closed-loop systems, where a doctor doses insulin based on the algorithm's recommendation.

• **FDA Issues:** Coordinators of the consortium are working with each site to help them submit information to the FDA quickly so the fully automated studies can start. The FDA has provided feedback on a computer simulation model that will enable researchers to test algorithms on 100 "virtual" patients (computer models) instead of on animals, as well as on the template the sites will use to share validation data on the closed-loop systems.

IN BRIEF: UPDATES FROM THE ARTIFICIAL PANCREAS PROJECT

Visit JDRF's Artificial Pancreas Project web site, www.jdrf.org/artificialpancreas for a wealth of articles and other updates about emerging technologies, including:

• **JDRF and The Endocrine Society Webcast Online:** JDRF has posted the webcast of the JDRF and the Endocrine Society session, "Using Continuous Glucose Monitors to Improve Diabetes Care: A Review of the Latest Research and Clinical Practice Strategies", which was held last year at the Endocrine Society annual meeting in Toronto. The session discusses the use of continuous glucose monitors in both adult and pediatric patients, including case studies of their use in clinical practice and a briefing on the state of artificial pancreas research.

To listen to the webcast, visit www.jdrf.org/endo2007.

• **JDRF and the American Association of Clinical Endocrinologists Webcast Online:** JDRF has posted the webcast of the JDRF and the American Association of Clinical Endocrinologists (AACE) session "Joint Scientific Forum to Explore New Frontiers in Diabetes Management and Emerging Technologies", which was held on April 13, 2007 at the AACE annual meeting in Seattle, Washington.

To watch the webcast, visit www.jdrf.org/aace2007.

• **Become an Advocate:** Join with others in becoming a JDRF advocate and help fight for CGM health insurance coverage and federal funding for diabetes research.

For more information, visit www.jdrf.org/advocacy.