 DRIVE Report Summary

Project ID: 645991
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Periodic Reporting for period 1 - DRIVE (Diabetes Reversing Implants with enhanced Viability and long-term Efficacy)

Reporting period: 2015-06-01 to 2016-11-30

Summary of the context and overall objectives of the project

THE PROBLEM: Diabetes mellitus is a chronic disease characterised by high blood sugar due to a shortage of insulin that affects 415 million people worldwide. Pancreatic islet transplant therapy is an extremely promising cell therapy, with the potential to cure insulin-dependent diabetes. Transplant of the islands of insulin-producing cells found in the pancreas restores tight natural control of blood sugar, eliminating the need for multiple daily injections of insulin, constant blood glucose monitoring and the risk of dangerous hypoglycaemic (low blood sugar) episodes or “hypos”, all of which greatly affects diabetes patients’ quality of life. Islet transplant therapy involves purifying pancreatic islets from donor pancreases and infusing them into the patient’s liver via intra-venous catheter. Current limitations of the therapy include:

(1) poor survival and engraftment of transplanted islets in the hostile liver environment
(2) a shortage of donor pancreases
(3) the need for the patient to take lifelong immune suppressive therapy, which increases the risk of serious infections and cancer

Therefore this therapy is currently limited to a small percentage of “brittle” type 1 diabetes patients prone to “hypos” for which daily insulin injections are not sufficient to control their diabetes.

DRIVE’S SOLUTION: The DRIVE project aims to enable diabetes-reversing islet transplant therapy for all insulin-dependent diabetes patients through the development of smart biocompatible material (biomaterial) implants and enabling technologies. We aim to develop three components (the β-Gel, the β-Shell, and the β-Cath) which will be used to enable delivery and engraftment of functional pancreatic islets to a more suitable body site of the patient using a minimally invasive laparoscopic procedure. β-Gel will be delivered in a minimally-invasive fashion to an immune-protective capsule β-Shell using a specialised delivery catheter β-Cath.

The β-Gel can be delivered as a liquid and will form a solid gel at the delivery site that mimics the native pancreas environment. It provides an optimal support matrix to the islets and supplies them with nutrients after engraftment, when they are most vulnerable.

β-Shell will be a biocompatible capsule for the protection of islets in β-Gel from destruction by the body’s immune and inflammatory response. It will contain smart drug delivery systems to enhance bio-integration for optimal function of the islet graft.
β-Cath will be a custom delivery catheter that will enable the minimally invasive delivery of β-Gel and β-Shell.

Other enabling technologies under development in the DRIVE project include:

i. Localised immunosuppression to prevent graft rejection without systemic side effects
ii. Adult stem cell sources of insulin producing β-cells as renewable sources of insulin producing cells
iii. Bioengineered collagenase enzymes for optimal islet harvesting from donor pancreases
iv. Islet preservation, culture and storage systems to facilitate distribution of islets for transplant
v. Biodegradable drug microparticles for sustained release of drugs at targeted body sites
vi. 3D in vitro tissue model of the human pancreas for use as a lab-based test system reflective of the human body

**Work performed from the beginning of the project to the end of the period covered by the report and main results achieved so far**

During the first 18 months of the DRIVE project work has focused on developing and testing the β-Gel, β-Shell and enabling technologies in the lab. A formulation of β-Gel has been developed that is compatible with human islets. Initial laboratory tests suggest that β-Gel increases the survival and insulin secreting function of islets. Two prototypes for the β-Shell capsule have also been developed that are compatible with β-Gel. Both are made from materials previously used in FDA approved implants. The drug delivery systems to enhance bio-integration of the implant have also been developed and methods to combine them with the β-Shell are currently being explored. Drug delivery systems for the sustained local delivery of the immunosuppressant drug cocktail at the transplant site have also been designed. Dose-response studies have been performed using human islets to calculate a suitable target dose for each of these drugs. Preclinical studies have been approved to test the DRIVE technologies. A standard protocol for islet harvesting from pancreases that uses bio-engineered collagenase enzymes has been developed and optimised in rodents. The enzymes have also been used successfully for human islet isolations. Further optimisation of the human islet isolation protocol with these enzymes is planned. Progress has also been made on the development of stem cell sources of insulin-producing cells. Preliminary R&D work on the β-Cath, the islet culture and storage systems and the 3D model has also taken place. DRIVE has also held a Patient Panel discussion event where clinical and scientific experts from the DRIVE Consortium met with diabetes patients and stakeholders to explain the technologies under development and get their opinion on how they could be improved.

**Progress beyond the state of the art and expected potential impact (including the socio-economic impact and the wider societal implications of the project so far)**

Over this first period a standardised protocol for harvesting pancreatic islets using bio-engineered collagenase enzymes was developed. This has the potential to impact greatly the availability of islets for transplantation by increasing the efficiency of donor islet isolation.