Pump-Priming Grant

Report

Ann Ogbemudia

Title

Pancreagenesis: Incorporation of pancreatic islet cells into *ex situ* preserved skin flaps to create a transplantable endocrine allograft

Objective

The research objective was to investigate how *ex situ* machine preservation can be utilised to allow modification and assessment of non-transplanted tissue/organs to aid in beta cell replacement therapies for diabetes mellitus. Within this program of research, *ex situ* normothermic perfusion technology was used to provide long term preservation of skin flaps, as a modifiable biological scaffold to facilitate engraftment of pancreatic islets. This model can be translated as an attractive, alternative site to the liver for islet transplantation.

Method

A custom normothermic machine circuit was designed and constructed using similar principles used for extracorporeal life support in cardiothoracic medicine (figure 1). This circuit was then able to support 12 skin flaps donated from extraneous tissue from surgery or from deceased donors with the appropriate research consent. 2 of the 12 skin flaps had injection of allogenic human islets and were evaluated for viability and function by glucose challenges, histological assessment and adequate blood flow in the tissue was assessed by using a Microscan (figure 2).

The Microscan by Microvision medical (figure 2) uses side stream field (SDF) optics to visualise the microcirculation by using illumination by concentric lights emitting from a hand-held scanner. A functioning microcirculation is a prerequisite for tissue oxygenation, nutrition and exchange of metabolites; therefore an intact microcirculation is essential for life and being able to visualise it in *ex situ* preserved organs is potentially a good marker of viability.

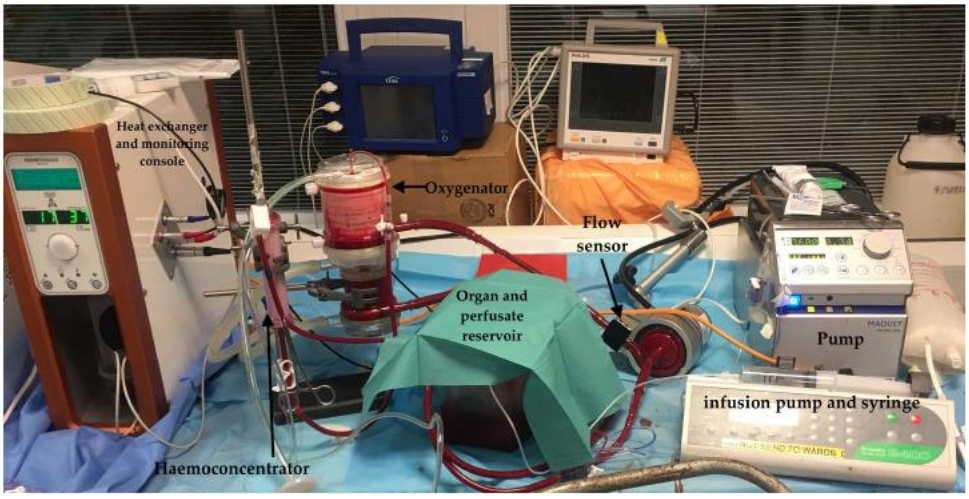

Figure 1: Normothermic perfusion circuit photograph

Figure 2: Using the MicroScan to visualise the skin microcirculation during normothermic machine perfusion

Results

Using the Microscan and its associated software, great video images (figure 3) were obtained and compared to my sublingual images as the positive control (figure 3, left image). Imaging was able to show viability during normothermic preservation of the skin flaps (figure 3, middle image) until tissue death (figure 3, right image).

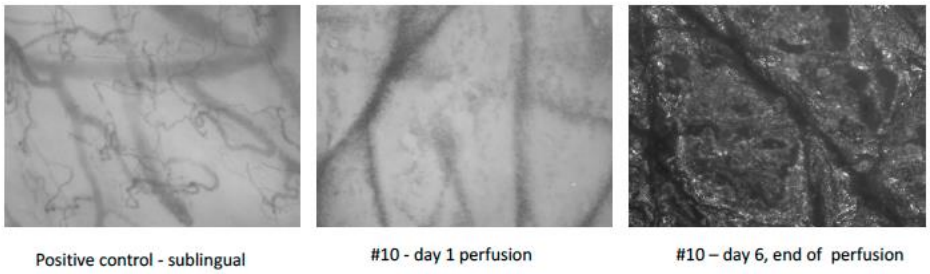

Figure 3: Microcirculation images of my sublingual area (left), Day 1 of perfusion of skin flap no 10 (middle) and at the end of the perfusion (right).

Histological assessment of 1 of the 2 skin flaps that had incorporated islets showed presence of the injected islets with surrounding endothelial cells suggestive of vascular 'sprouting' i.e. new blood vessel growth. In this early work, this was an encouraging finding implying that the islets might be engrafting into the tissue.

Outputs (publications/presentations)

The results of this work have led to

- A successful award of a bigger research grant from the Royal College of Surgeons Edinburgh
- Support from industry – Institut Georges Lopez, France have provided consumables to enable further preclinical work in pancreas machine perfusion

This work as part of allied research has led to one publication and has been presented (oral presentation) at numerous national and international conferences.

Publication

Development of *ex situ* normothermic reperfusion as an innovative method to assess pancreases after preservation. Ogbemudia et al. Transplantation International Sept 2021

Presentations

Feb 2021 - European pancreas and islet transplantation society (EPITA)

Feb 2021- British Transplant Society (BTS)

May 2021 - Societe Francophone de Transplantation (SFT)

Aug 2021- European Society of Transplantation (ESOT)

Next Steps (what is it leading to)

This work will be contributing to the achievement of my DPhil at the University of Oxford and the grant support provided by the Oxford Transplantation Foundation has being instrumental in allowing this happen. Additionally, the research will be continued by incoming research fellows and could potentially inform the design of a phase 1/early phase clinical trial in pancreas preservation for transplantation.