IBEC
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# Fellowships IBEC International PhD Programme

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## Biosensors for bioengineering group

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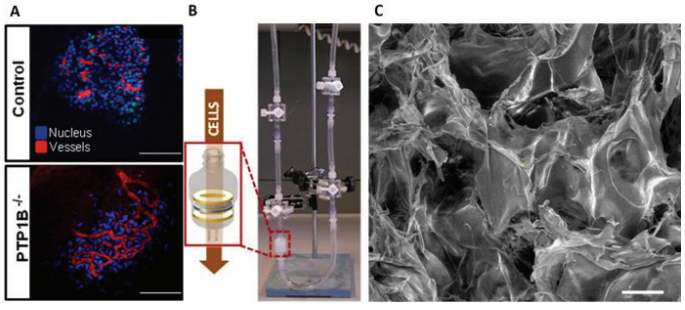
## Advancing in β-cell replacement therapy in type I diabetes: Novel scaffold designs for the improvement of islet graft revascularization and survival

This proposal constitutes a novel approach to developing an islet transplantation scaffold as a β-cell replacement therapy for type I diabetes, as it seeks to cover important gaps currently present in this area of research. Following transplantation, poor revascularization of the islet graft, or insufficient restoration of blood vessels in the transplanted islet, is one of the major causes of graft failure and death. To achieve long-term clinical success in islet transplantation, it is widely acknowledged that the revascularization of the pancreatic islet graft and transplant site must be promoted. Despite important improvements in clinical islet transplantation, poor revascularization remains a challenge to graft failure and loss, as it impairs oxygen, nutrient and hormone modulation delivery to graft cells. Our mission is to develop strategies for improving long-term clinical success in islet transplantation by combining the latest knowledge in islet revascularization with state-of-the-art technology in drug encapsulation and extracellular matrix mimicking scaffolds.

Here we propose to develop a scaffold capable of greatly promoting long-term islet graft and transplantation site revascularization, with a potentially significant impact on diabetes remission, as it will create an excellent environment fostering optimal spatial organization for vessel formation and also provide an optimized structure for diffusion of angiogenesis therapy to islets and adjacent tissue. We will create an innovative scaffold design for islet transplantation featuring a controlled-release drug delivery system and biomaterials that improve and mimic the extra-cellular matrix (ECM). Hydrogels are not biodegradable, which makes them ideal in a scaffold for use as an anchorage for drug delivery alginate microbeads and other materials like ECM-mimicking collagen, as the scaffold will be able to be safely retrieved following transplantation. Moreover, islet survival and insulin secretion in response to glucose stimulation in islets incorporated into the scaffold will be assessed. Furthermore, graft revascularization will be visualized periodically through angiography imaging using state-of-the-art infrared fluorescent technology. Finally, after scaffold retrieval, graft revascularization and survival will be assessed by high-resolution two photon microscopy.




*A) Graft Revascularization and survival. Islets isolated from PTP1B-/- and controls were transplanted into the anterior chamber of the eye of a DM1 mice model. In vivo revascularization was accessed using a two- photon microscopy after injection of dextran, where graft vascular density was measured. B) Perfusion loop with a peristaltic pump to introduce the pancreatic islets into through the Collagen foam. Two perfusion chambers will be connected to the loop. Inside the perfusion chambers, we will place the scaffolds, squeezing them at their edges with two silicone gaskets. C) Collagen foam micro-structure.*