NEXT - Nano engineering for Cross Tolerance: new approach for bioengineered, vascularised, chimeric islet transplantation in non-immunosuppressed hosts

PI Anna Casu, MD, Phd

Ente Finanziatore: Commissione Europea

Bando: FP7 HEALTH.2013.1.3-2 Innovative approaches to address adverse immune reactions to biomedical devices, implants and transplant tissues

Costo complessivo del progetto: euro 6.190.000,00

Contributo CE: euro 4.806,416,00

Budget ISMETT: euro 1.145.931,20

Coordinatore: University of Brighton (UK)

Partners: **ISMETT**, Explora s.r.l., Cellon SA, University of Geneva, AvantiCell Science Ltd

Durata: 48 mesi

Background

Diabetes is caused by insufficient or lack of insulin secretion by the specialized B cells of the pancreas and, if not treated adequately evolves into in complications which alter patients integrity and wellness. Treatment is based on lifetime drugs administration for blood glucose control or parenteral infusion of insulin to better control glucose levels and glycosylation of hemoglobin. Artificial pancreases are in development but still dependent by external energy sources and need permanent transcutaneous access to release the hormone. Pancreatic whole organ transplantation is a major intervention requiring selected recipient and matched cadaveric donor which keep numbers down. Islet of Langerhans transplantation is a non-invasive method for the treatment of type 1 diabetes but several questions remain and several issues have to be addressed in order to improve the method since islet engraftment is clearly suboptimal, as a result of pro-apoptotic and pro-inflammatory stimuli sustained during islet isolation and at the site of implantation, the long-term islet graft function drops to 15% with time, and the current systemic immunosuppressive regimen has several drawbacks in terms of side effects. Solution should be find to increase transplantation efficiency with an higher number of islet, eventually from animals, induce tolerance toward the graft, avoiding systemic, lifetime immunosuppression and, lowering a specific inflammatory reaction and enhancing graft micro vasculogenesis to improve islet nesting.

Innovazione e impatto

The main novelty of NEXT project is nanoengineering of pancreatic islet exploiting selfcamouflage by means of allo-antigens rather than interfering with integrity of potential T cell mediated anergy as traditional immunosuppressive drugs do.

NEXT provides a 360° solution to the pitfalls of current methodology for pancreatic islet

transplantation: i) Nano technologies, to engineer donor cell surfaces in order to derange recognition and suppress their rejection; ii) Advanced tissue engineering methods, to assemble bio synthetic islet, enriched by chimeric microvasculature; iii) Innovative double immune-suppressive strategy by graft - bound immunosuppressive nano peptides and shielded by self- vasculature.

Obiettivi del progetto

The NEXT project aims to develop nano-engineered pancreatic islets to investigate adverse immune reactions and develop immune-shielded pancreatic islets which could be transplanted in non-systemically immune-suppressed patients.

The concept beyond NEXT is to increase clinical efficacy and ensure permanent immune protection of pancreatic islets transplantation by means of self-camouflage of allo-antigens rather than interfering with integrity of potential T cell mediated anergy as traditional immunosuppressive drugs do. The objective of NEXT is to realize nano-engineered and immune-shielded pancreatic islet to be transplanted in non-immunosuppressed hosts.

In particular, NEXT will develop:

- Immunosuppressive mimetic peptides (ISP) engineered on the surface of donor Pancreatic β Cells and released locally
- Allogeneic β cells engineered by functionalising their glycocalyx
- Engineered chimeric islets (BioCHIP)
- BioCHIP functionalization for in vivo angiogenesis and local immunosuppression
- Inert biomaterials to prevent inflammatory reaction

Pubblicazioni/Risultati raggiunti

…….