PANCREATIC ISLET XENOTRANSPLANTATION AS A TREATMENT OF TYPE I DIABETES MELLITUS

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OBJECTIVES

- Assess the potential of pancreatic islet xenotransplantation as a treatment of type 1 Diabetes Mellitus (T1D).
- Summarize the genetic modifications that can be performed in pigs to overcome xenotransplantation main obstacles.
- Discuss the legal and social implications that are bind to xenotransplantation.

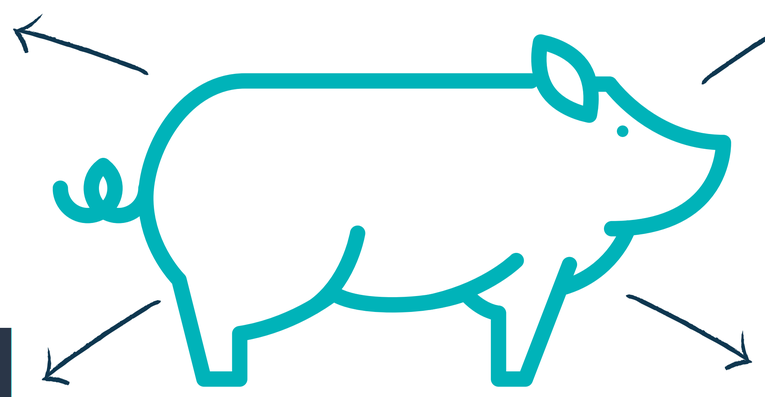
MAIN OBSTACLES

Hyperacute rejection

- Knock out key antigens → Gal, Neu5GC, Sda
- Add a human CRP, e.g. CD46

Coagulative dysregulation

- Add human thrombomodulin



Adaptative immune response

- Give anti-CD40mAb as immuno-suppressive

Transmission of infectious diseases

- Inactive PERVs from pig genome
- House the source-pigs in pathogen-free conditions

ISLET TRANSPLANTATION

Between humans → Normoglycaemia mantained 2 years in 40% of pacients

Pigs to non human primates → Normoglycaemia mantained more than 6 months in 4 out of 5 pacients

Obtain various pancreases

Add fresh collagenase

Centrifuge the filtrate (x3)

Incubate at 37°C

If there's no immune isolation, the islets are infunded in the portal vein or the omentum

IImmune isolated islets can be implanted in the peritoneum, the subcapsular kidney space or subcutaneously

Figure 1: Neonatal islets xenotransplantation procedure

CONCLUSIONS

- Pancreatic islet xenotransplantation to reach normoglycaemia in T1D patients is the one with the greater potential.
- Clinical trials are being held but the ideal protocols to perform it are yet to be found.
- New approaches are being studied to be able to reach a broad clinical application in the near future.
- Regulations concerning xenotransplantation should be internationally harmonized.
- Public opinion about the potential risks associated with xenotransplantation should be explored, coupled with efforts to educate society about the procedure.