Inflammatory cytokines in the acute and subacute phases of islet engraftment after total pancreatectomy and islet autotransplantation (TPIAT).

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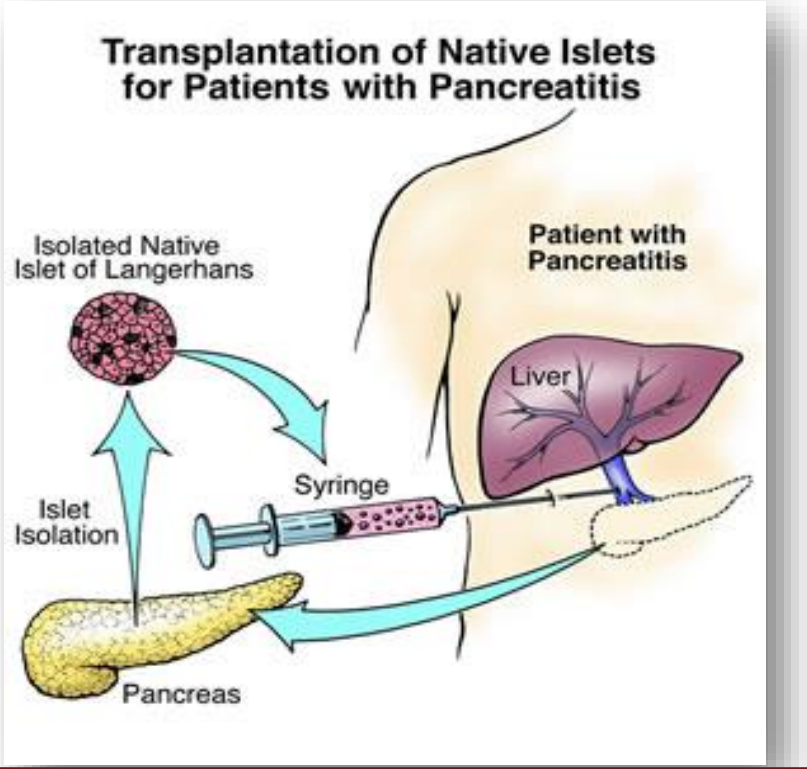
COI

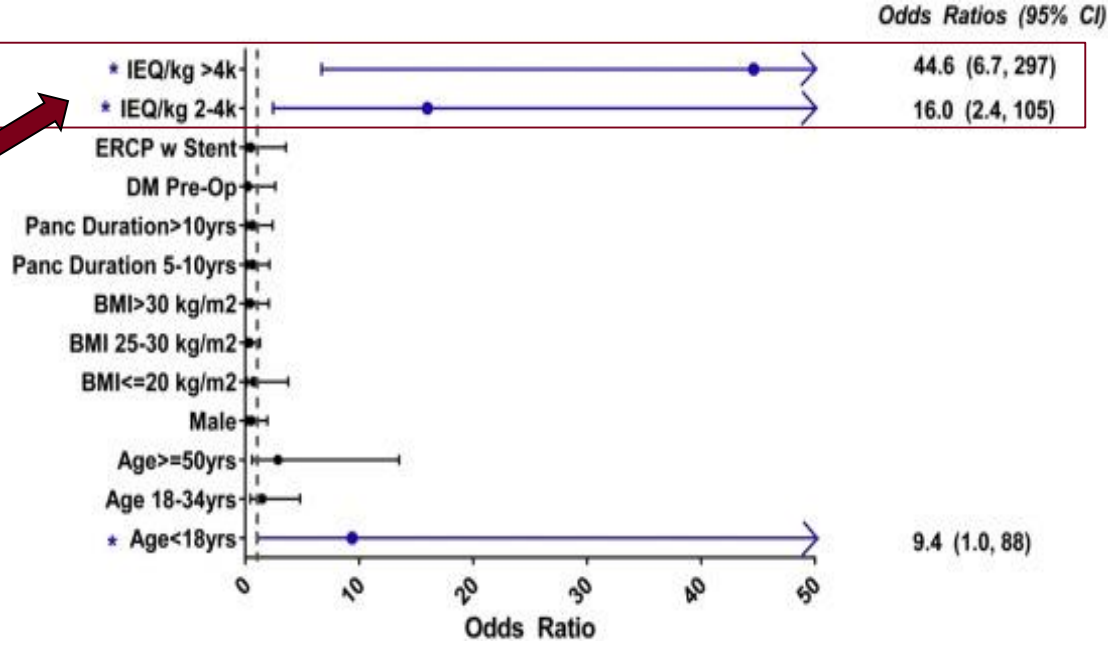
- Research support from Dexcom
  - Not applicable to the content of this talk

Total pancreatectomy with islet autotransplantation (TPIAT) for treatment of chronic pancreatitis



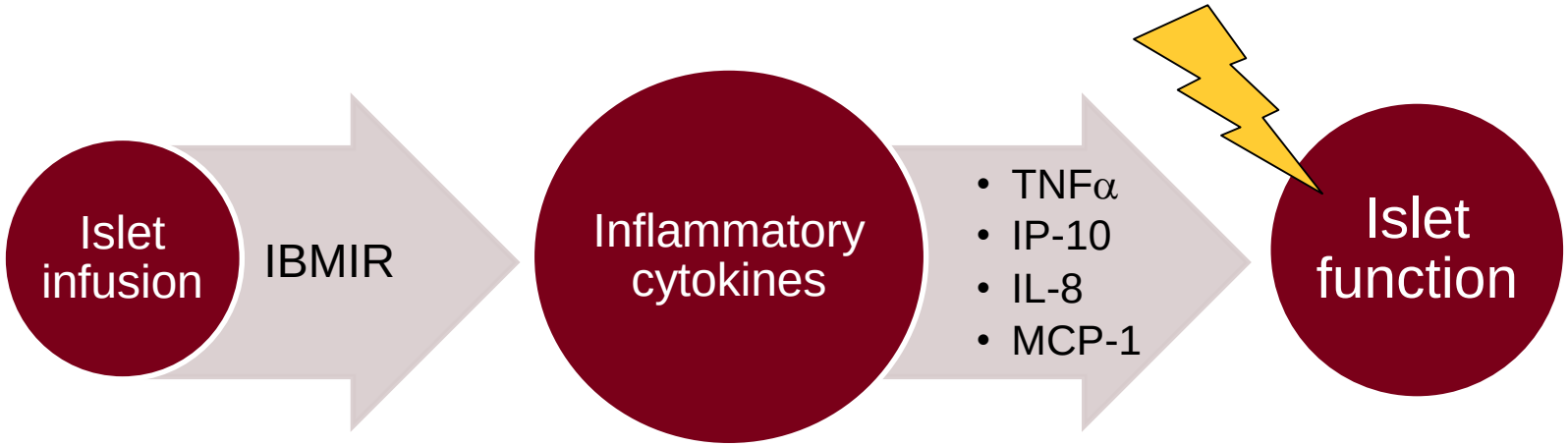
Insulin independence after TPIAT

- 30-40% of patients wean off insulin
- IEQ/kg = strongest predictor
- Islet engraftment limited in part by inflammatory & hypoxic insults

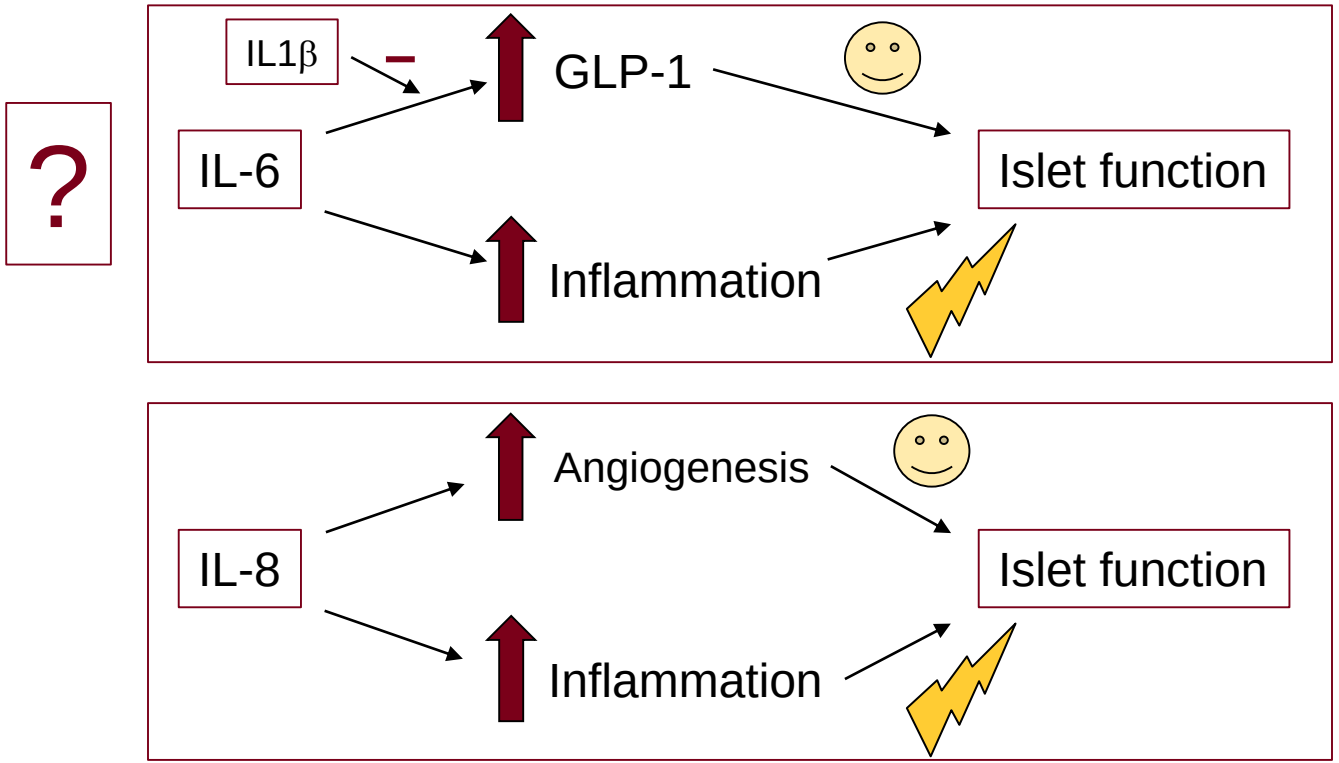


How Durable Is Total Pancreatectomy and Intraportal Islet Cell Transplantation for Treatment of Chronic Pancreatitis?
Bellin, Melena D., MD, Journal of the American College of Surgeons, Volume 228, Issue 4, 329-339

Inflammatory cytokines



Inflammatory cytokines



Hypothesis

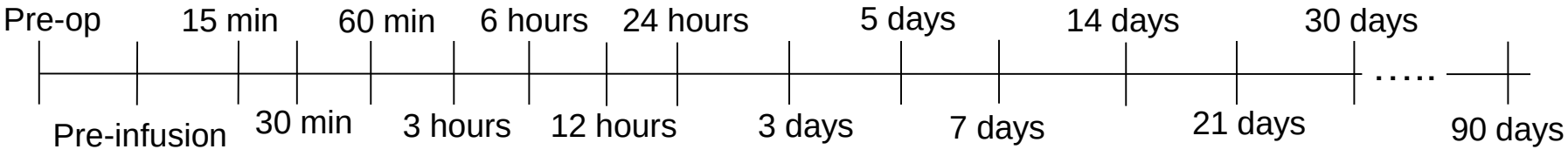
- Islet autotransplantation (IAT) may induce a unique inflammatory cytokine response, particularly early after transplant.
- Inflammation may lead to islet loss, and therefore cytokine levels would be inversely related with islet function after engraftment (90 days).

Objective

- To characterize the cytokine response profiles of TPIAT patients during the acute and subacute transplantation and engraftment phases.

Methods

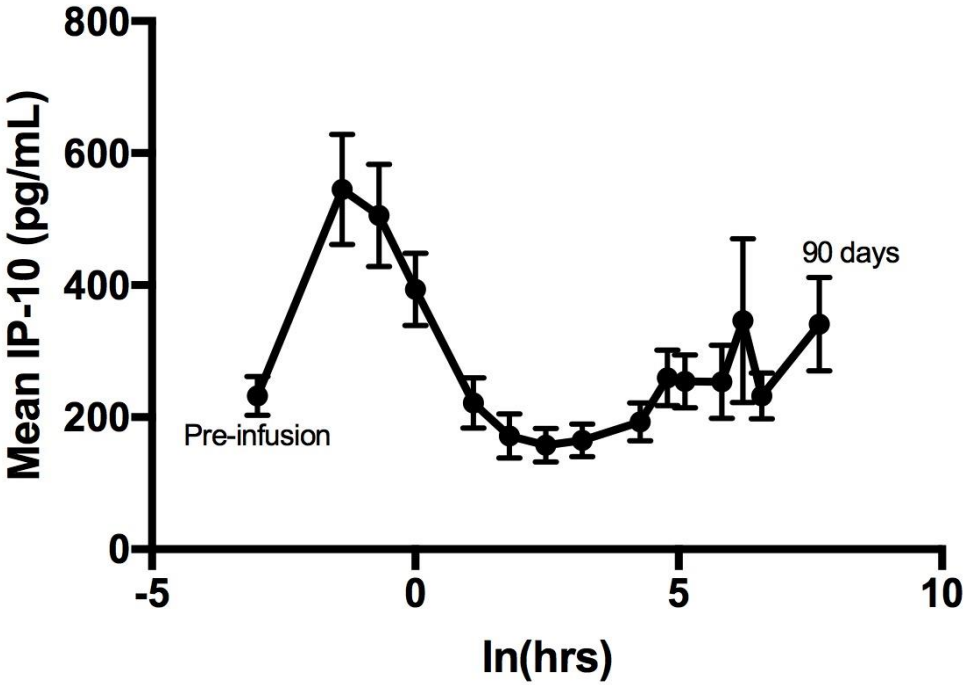
- 25 patients undergoing TPIAT
- Inflammatory cytokines characterized:
  - IL6, IL8, IP10, MCP1, TNFα
- Plasma levels collected:



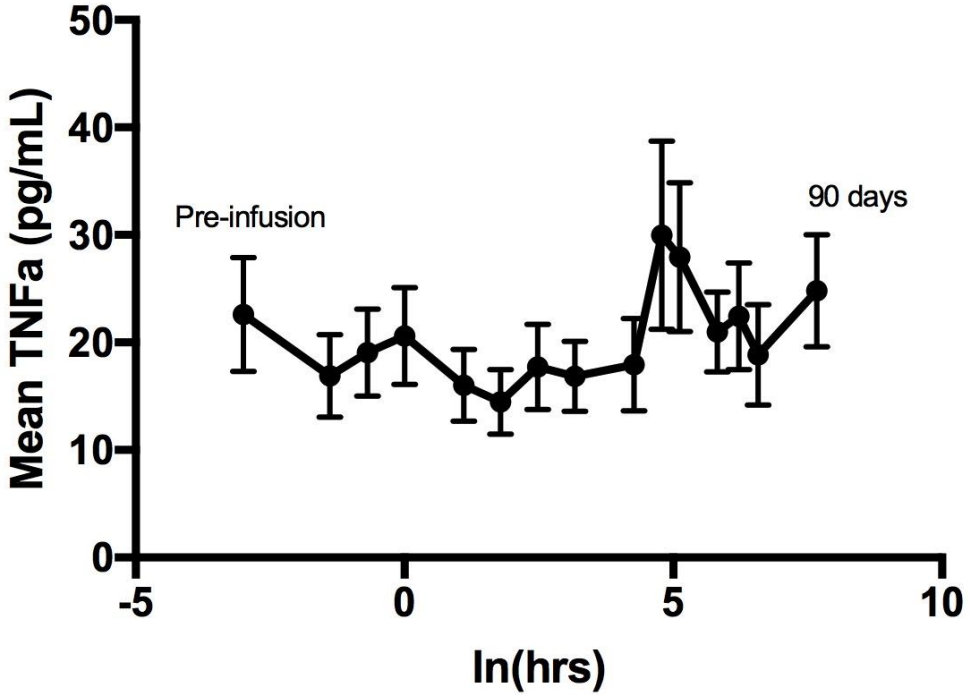
Methods cont’d

- 90-day islet function assessed by:
  - Amount of daily insulin needed
  - MMTT
  - IVGTT
  - Glucose-potentiated arginine stimulation test (AST)

Results: IP-10

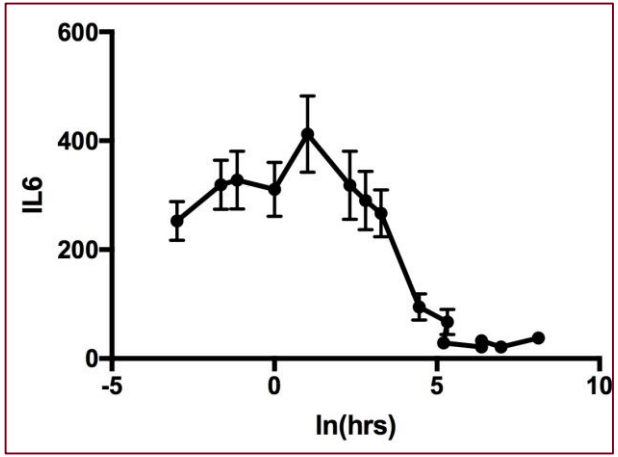


Results: TNFα

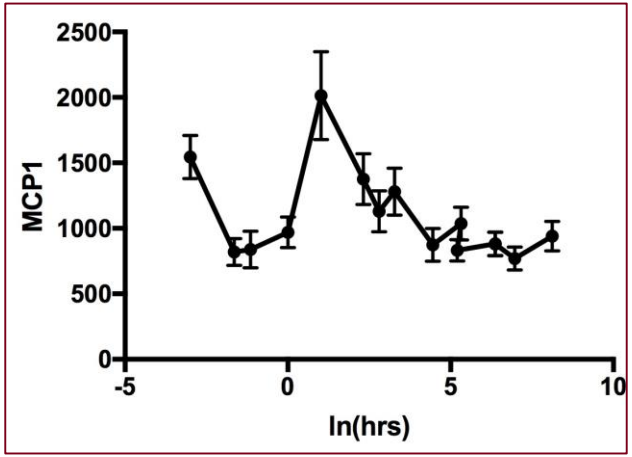


Results:

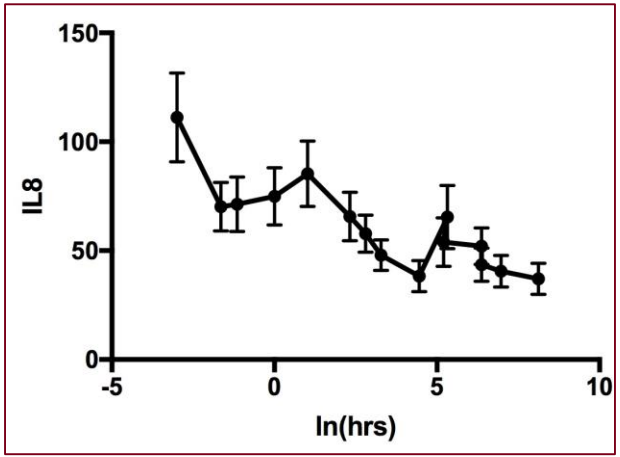
IL6



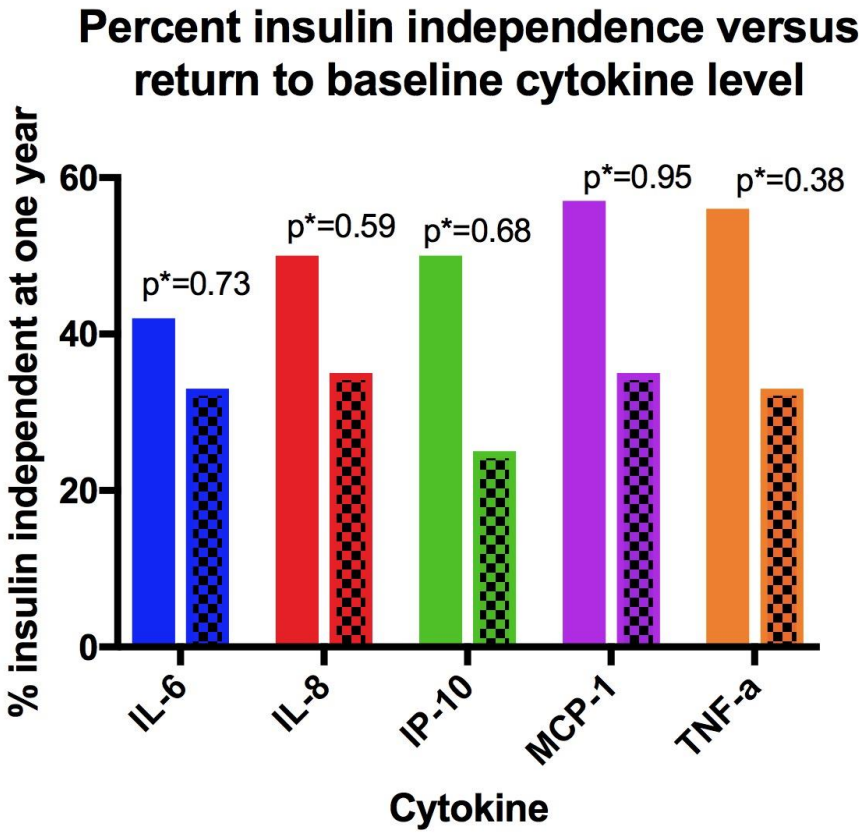
MCP1



IL8



Results



Checkered pattern represents the groups that did NOT return to baseline levels.

p* = adjusted for IEQ/kg transplanted

Results:

- Total area under the curve (AUC) of individual cytokine levels was not significantly associated with islet function (from MMTT, GPAIS, or IVGTT)*, insulin dose*, or IEQ transplanted.
- Persistently elevated cytokines at day 90 was not associated with islet function*.

*=adjusted for IEQ/kg

IP10, TNFα, IL6, and MCP1 are all increased from baseline after IAT, but at different time points and magnitudes.

IL8 levels show a general decline following IAT.

Inflammatory cytokines represent a potential target for therapeutic intervention in islet transplantation.

Acknowledgements

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