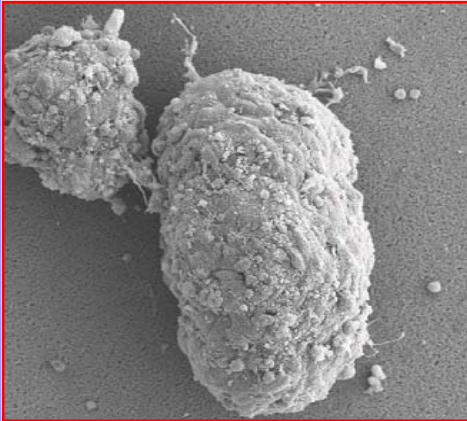


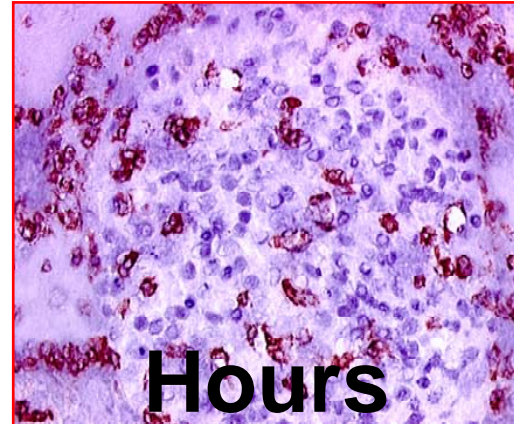
Insulin stimulation index

Olle Korsgren, MD, PhD
Uppsala University Hospital
Uppsala, Sweden

“the fate of an islet”



- Donor related factors
- Preservation
- Isolation



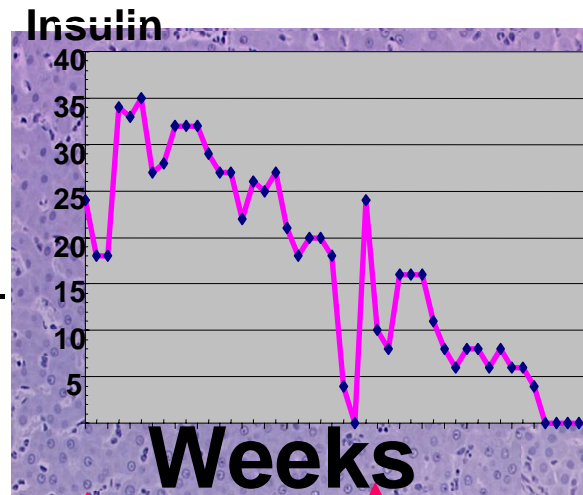
- Inflammation
- IBMIR

Hours



- Hypoxia
- Glucotoxicity
- Revascularization

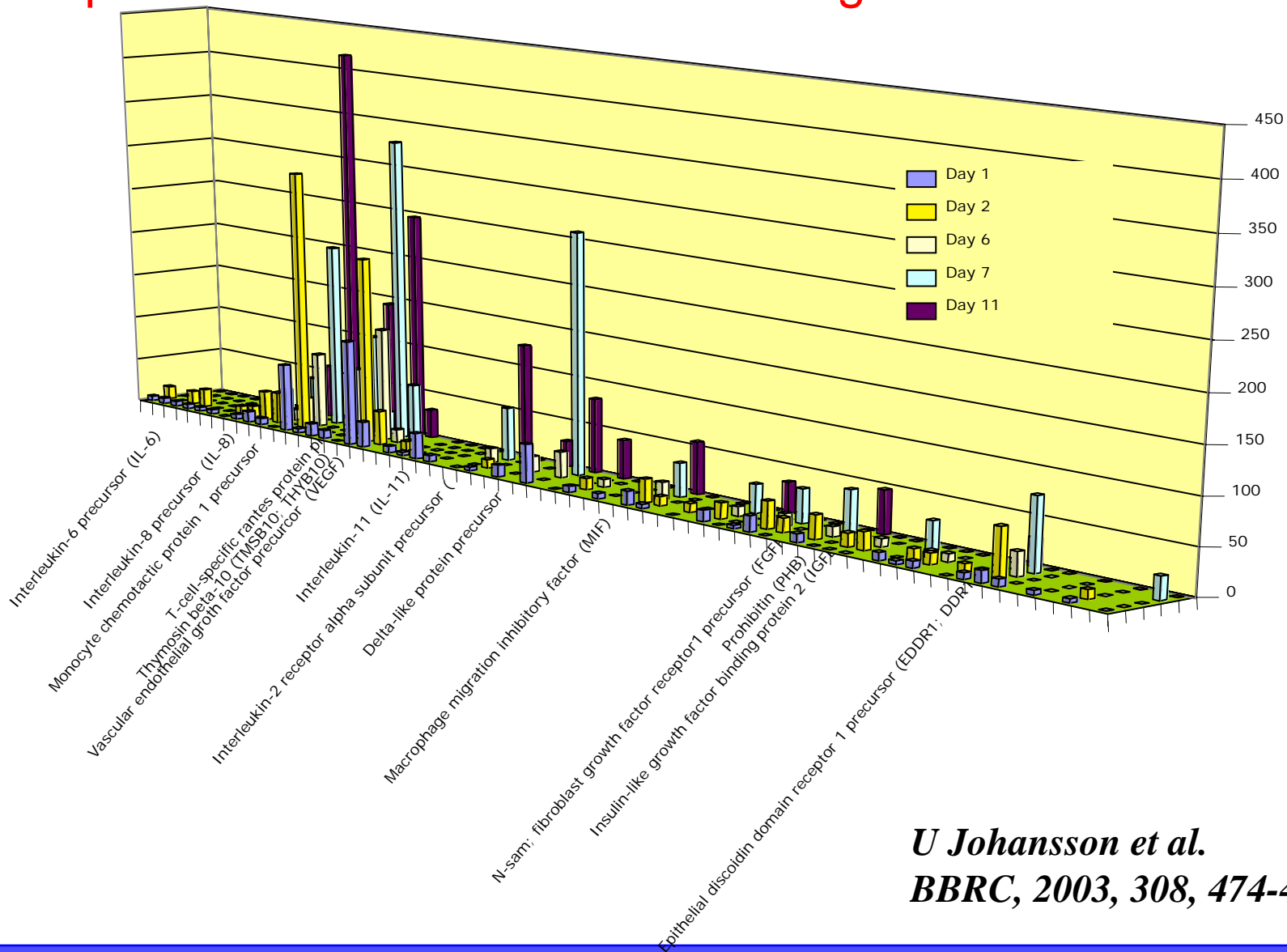
Days



- Rejection
- i.s. drugs

Weeks

Expression of inflammation-related genes in human islets



U Johansson et al.
BBRC, 2003, 308, 474-479

C-peptide/Creatinine at 2 weeks after Tx

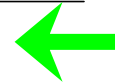
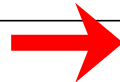
Variable	r	P
Age (years)	0.23	0.14
ICU length (days)	-0.21	0.17
Cause of death (Traumatic/Non-traumatic)	0.21	0.18
Body mass index (kg/m ²)	0.16	0.31
Weight of pancreas (g)	0.004	0.98
Minimal glucose (mmol/l)	0.29	0.08
Maximal ALAT (U/l)	-0.25	0.11
Maximal ASAT (U/l)	-0.20	0.25
Maximal amylase (U/l)	-0.20	0.29
Maximal ALP (U/l)	0.11	0.55
Maximal CRP (nmol/l)	-0.07	0.69
Maximal Creatinine (umol/l)	0.05	0.74
Maximal r-GT (U/l)	-0.005	0.98
Treatment with furosemide	0.20	0.20
Treatment with mannitol	0.12	0.45
Treatment with pitressin	0.08	0.62
Treatment with steroid	-0.01	0.97
Treatment with catecholamine	-0.002	0.99
TF expression in pancreas biopsy	-0.48	0.005
Procurement team (center 'X'/others)	0.35	0.01
Warm ischemia time (min)	-0.29	0.09
Cold ischemia time (min)	-0.23	0.14
Organ perfusion volume (aorta/portal)	0.06	0.72
Procurement team (local/distant)	0.04	0.81
TNFA expression in pancreas biopsy	0.32	0.08
IL-8 expression in pancreas biopsy	-0.23	0.21
ICAM-1 expression in pancreas biopsy	-0.26	0.23
IP-10 expression in pancreas biopsy	-0.24	0.28
MCP-1 expression in pancreas biopsy	-0.20	0.29
RANTES expression in pancreas biopsy	-0.21	0.34
TGF-b1 expression in pancreas biopsy	-0.19	0.39
IL-6 expression in pancreas biopsy	-0.07	0.75
IL-1b expression in pancreas biopsy	0.02	0.92
Harvest starting time (min)	-0.31	0.04
Transplanted islet equivalents (IEQs)	0.19	0.23
Liberase lot (efficient/non-efficient)	-0.14	0.42
Isolation method (old/new)	0.13	0.42
Harvest time (min)	-0.11	0.53
Mean purity of transplanted islets (%)	-0.11	0.54
Stimulation index <i>in vitro</i> test	0.05	0.79
Liberase amount per g of pancreas (mg/g)	0.01	0.95
Dissection time (min)	0.03	0.87
Maximal TAT (ug/ml)	-0.38	0.01
Volume of transplanted grafts (mL)	0.20	0.25
Transplanted centers (local/distant)	-0.15	0.31

Donor related variables

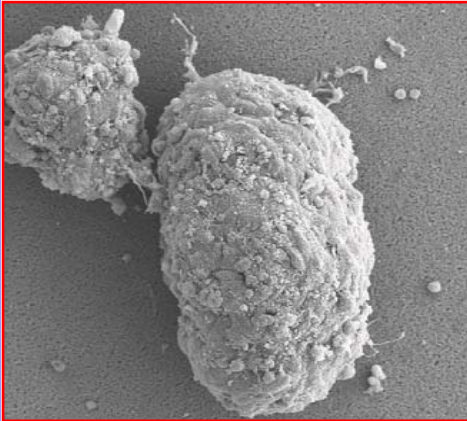
Organ procurement variables

Islet isolation variables

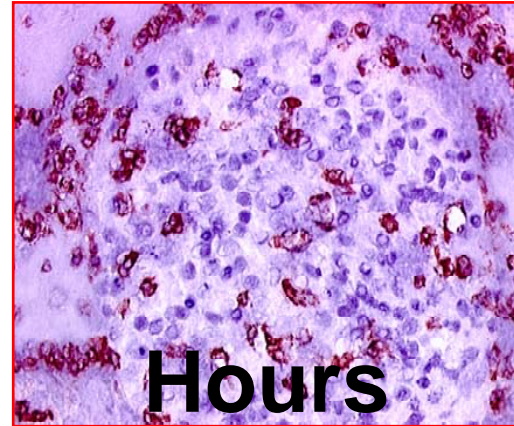
Tx related variables



“the fate of an islet”



- Donor related factors
- Preservation
- Isolation



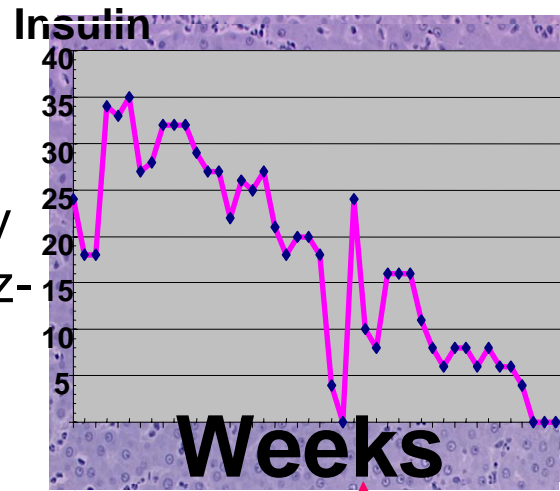
- Inflammation
- IBMIR

Hours



- Hypoxia
- Glucotoxicity
- Revascularization

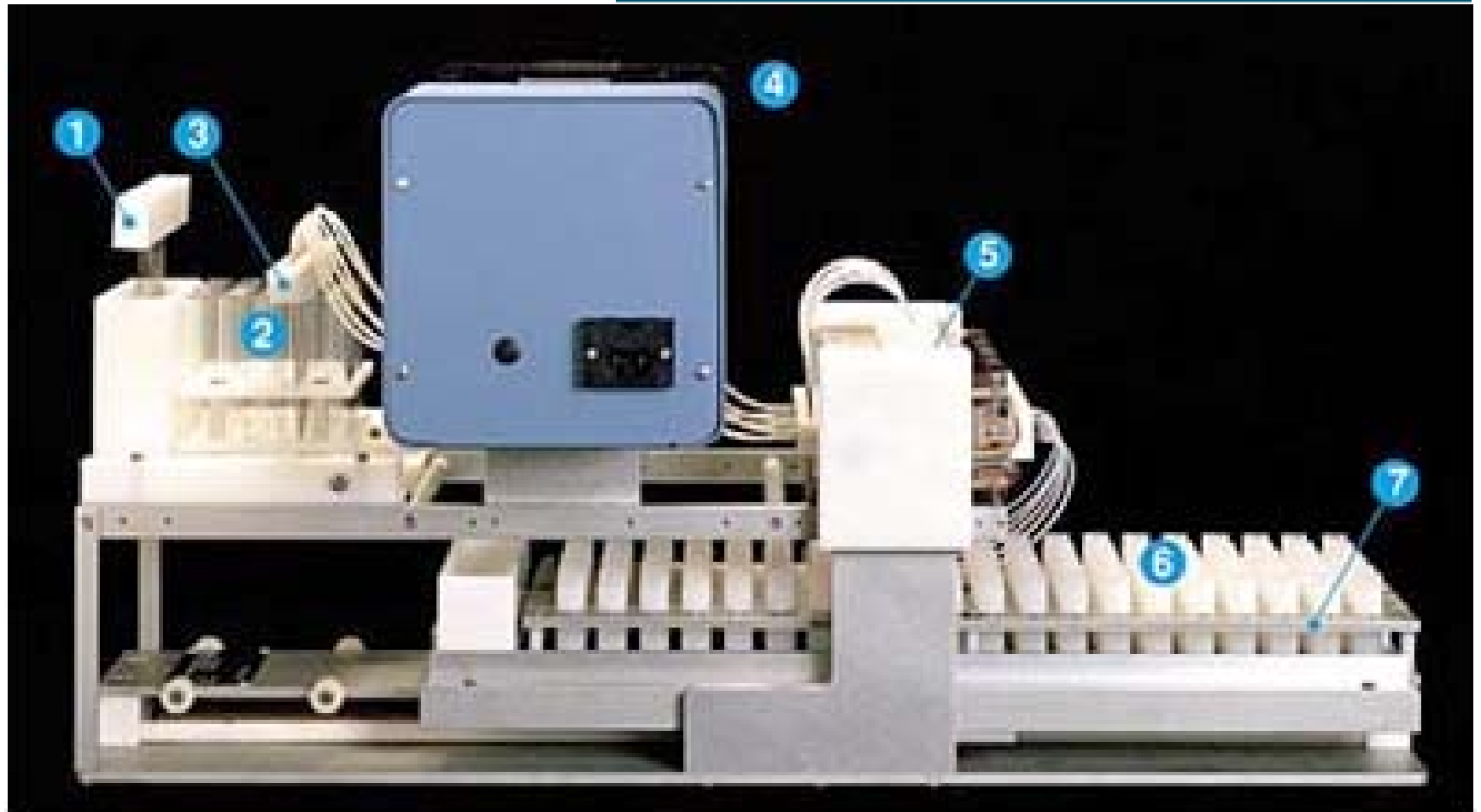
Days

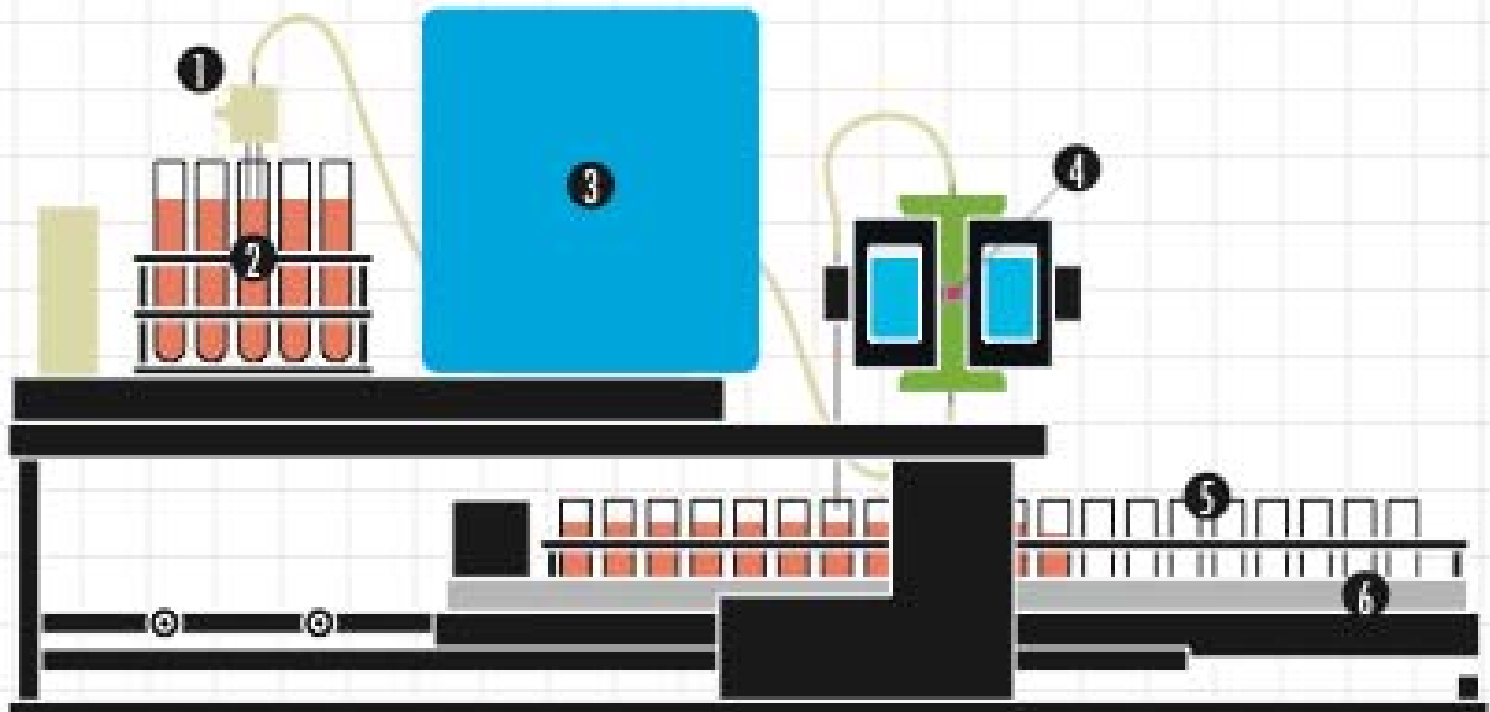


Weeks

- Rejection
- i.s. drugs

SUPRAFUSION SYSTEMS





1. Gassing probe
2. Test tubes
3. Peristaltic pump
4. Reaction chambers
5. Collection vials
6. Collection rack

Upper Probe

Platinum Wire *

Electrical Contact *

Reaction Chamber Block

Wire Raceway

Water Cavity

Platinum Screen *

Tissue Support

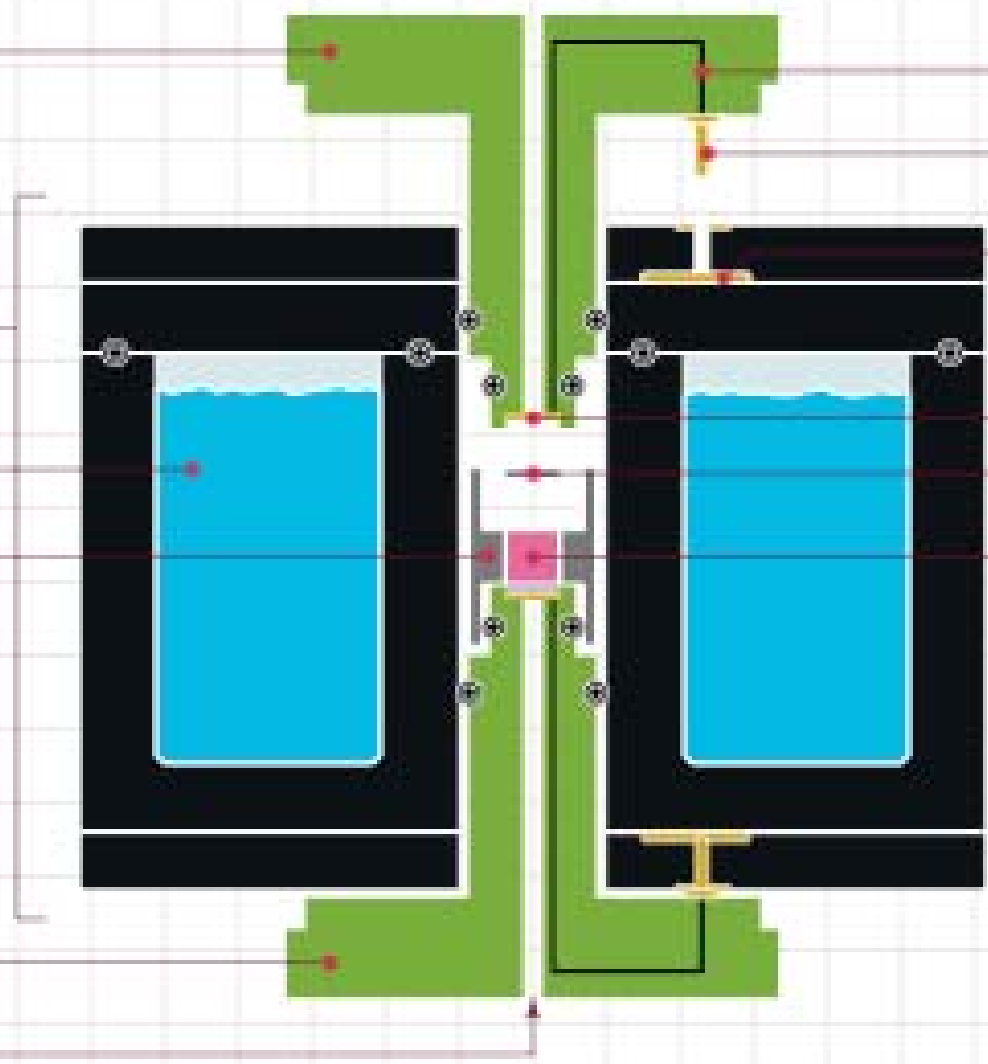
Reaction Chamber

Tissue Chamber

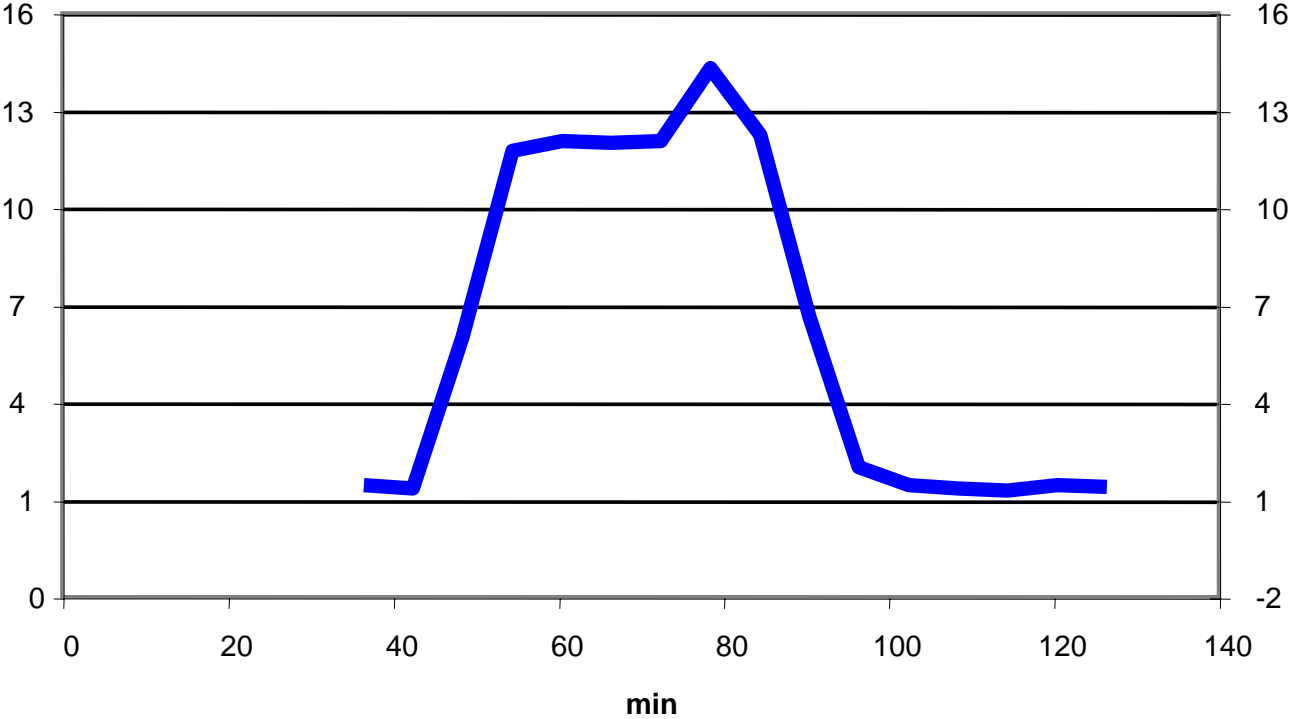
Lower Probe

Flow

* Electrical Probes Only

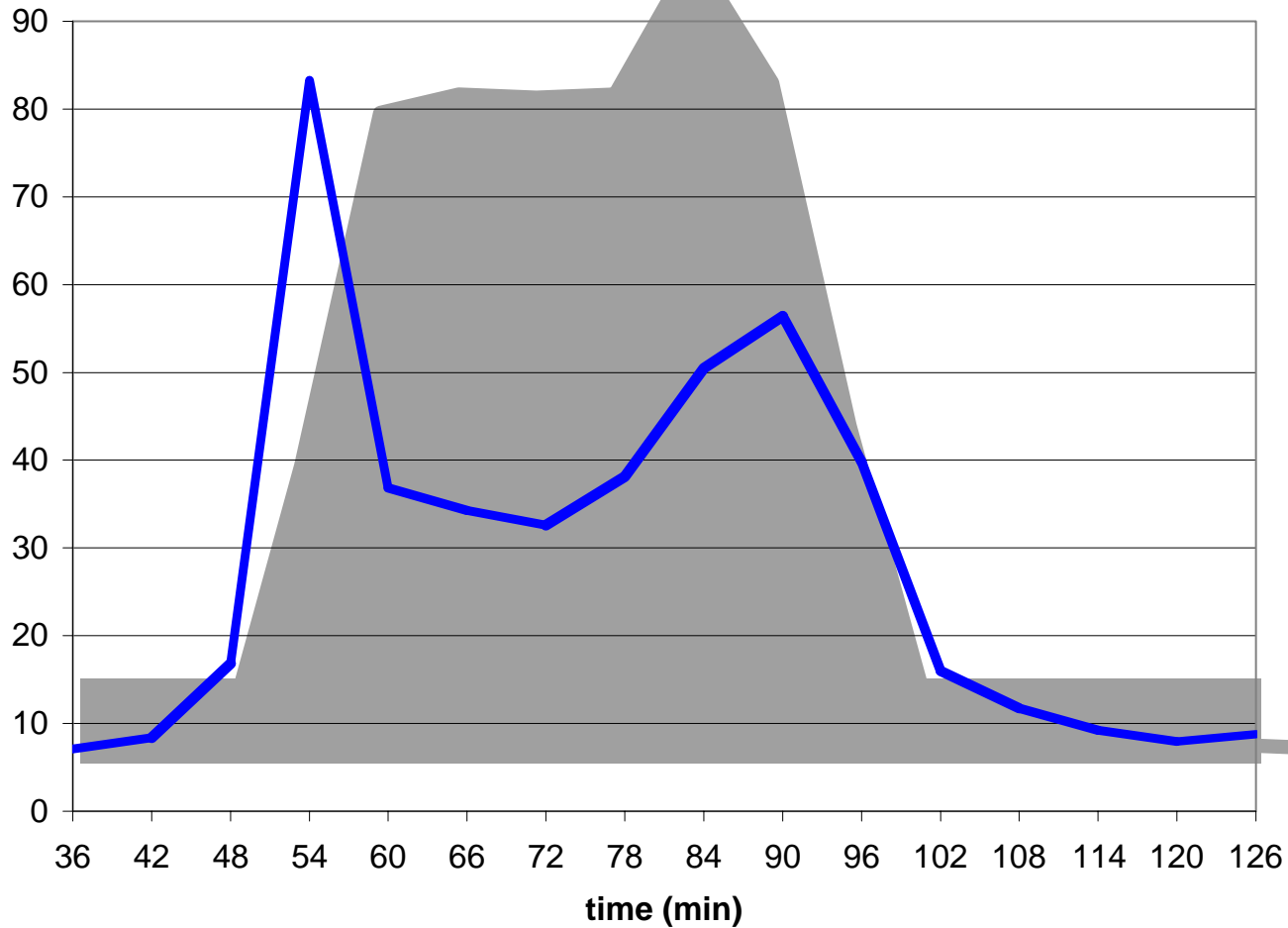


Glucose (mM)



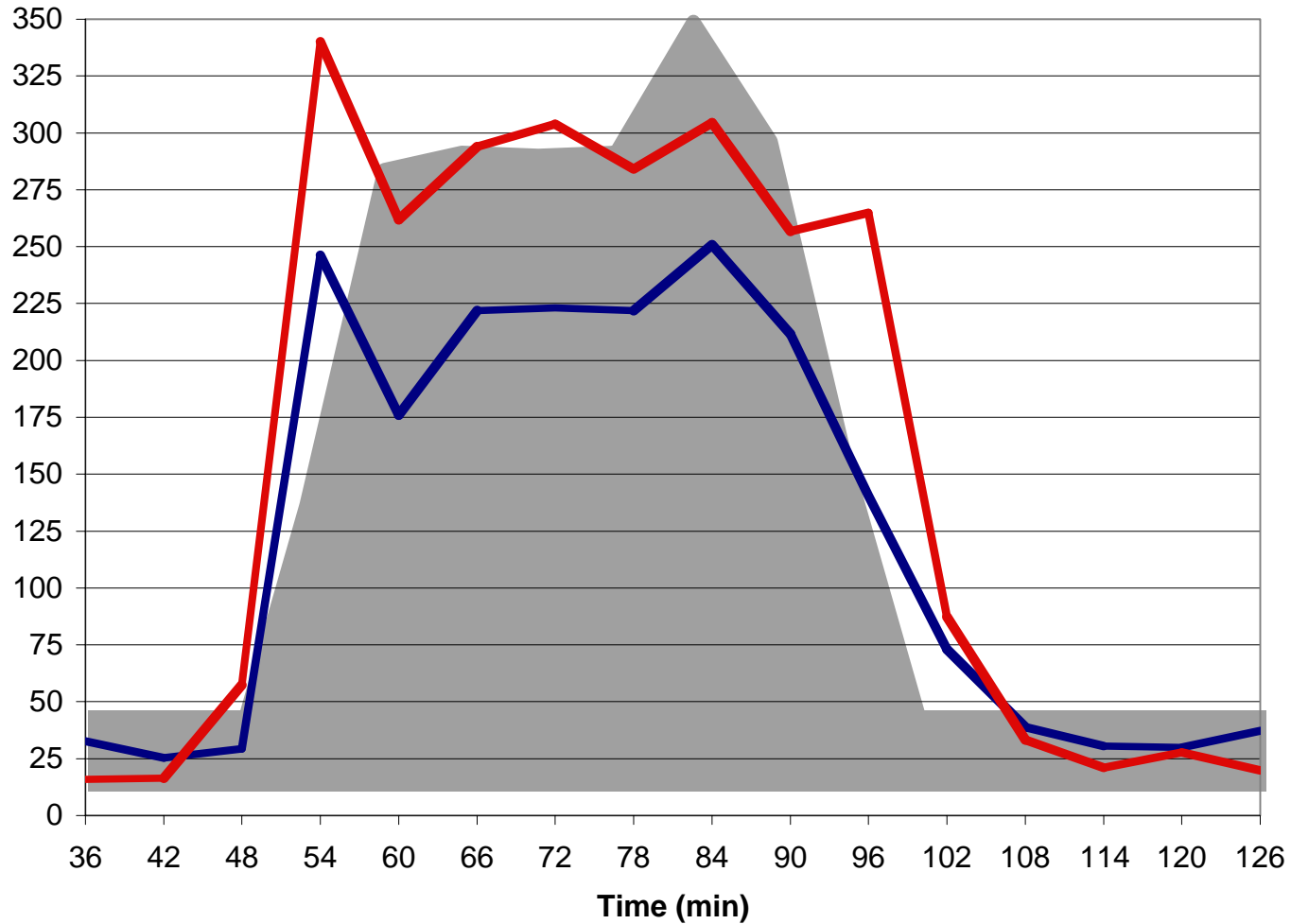
Insulin Release vs Glucose Challenge

Normal Functioning Islets



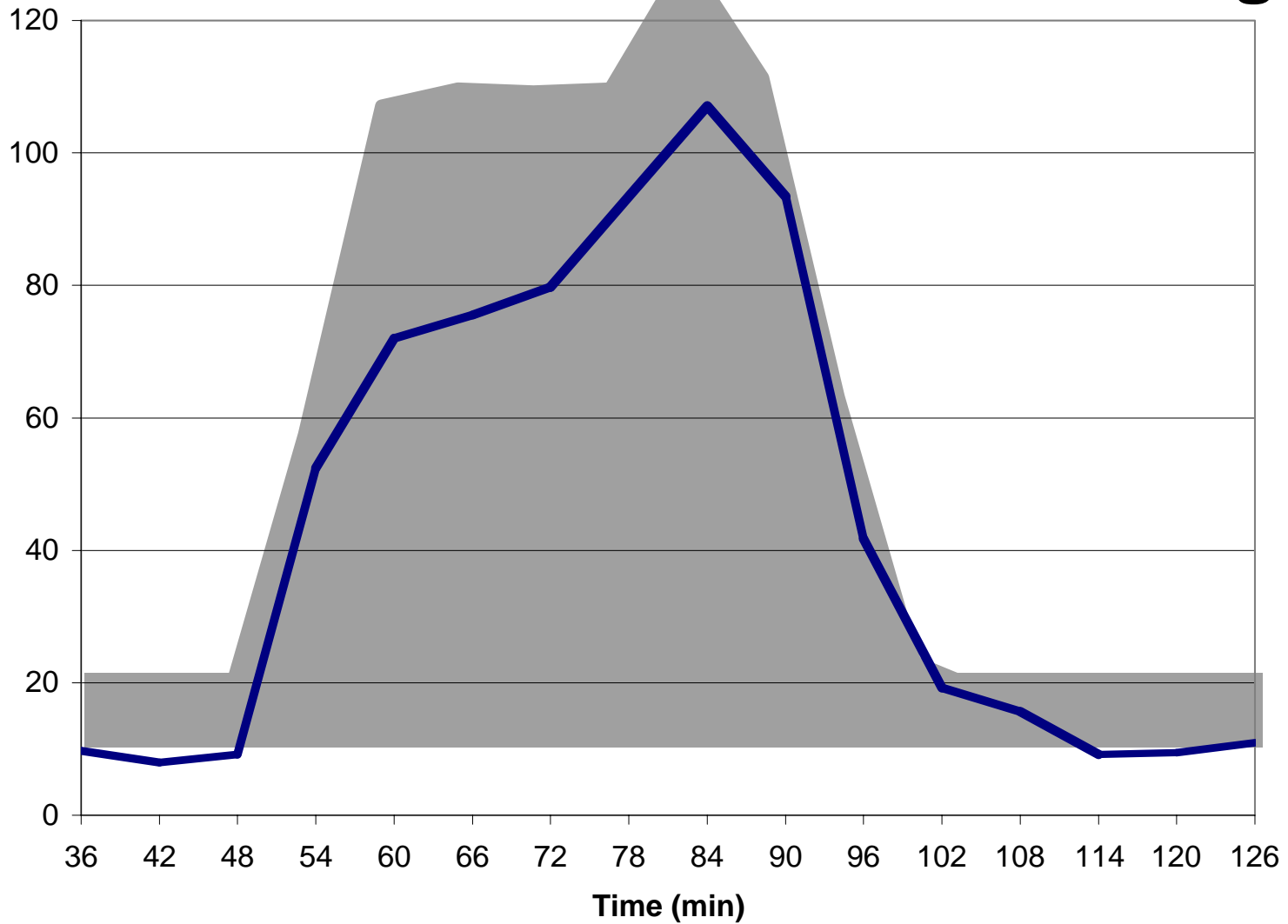
Insulin Release vs Glucose Challenge

Reproducible results after day 1 & 2 in culture



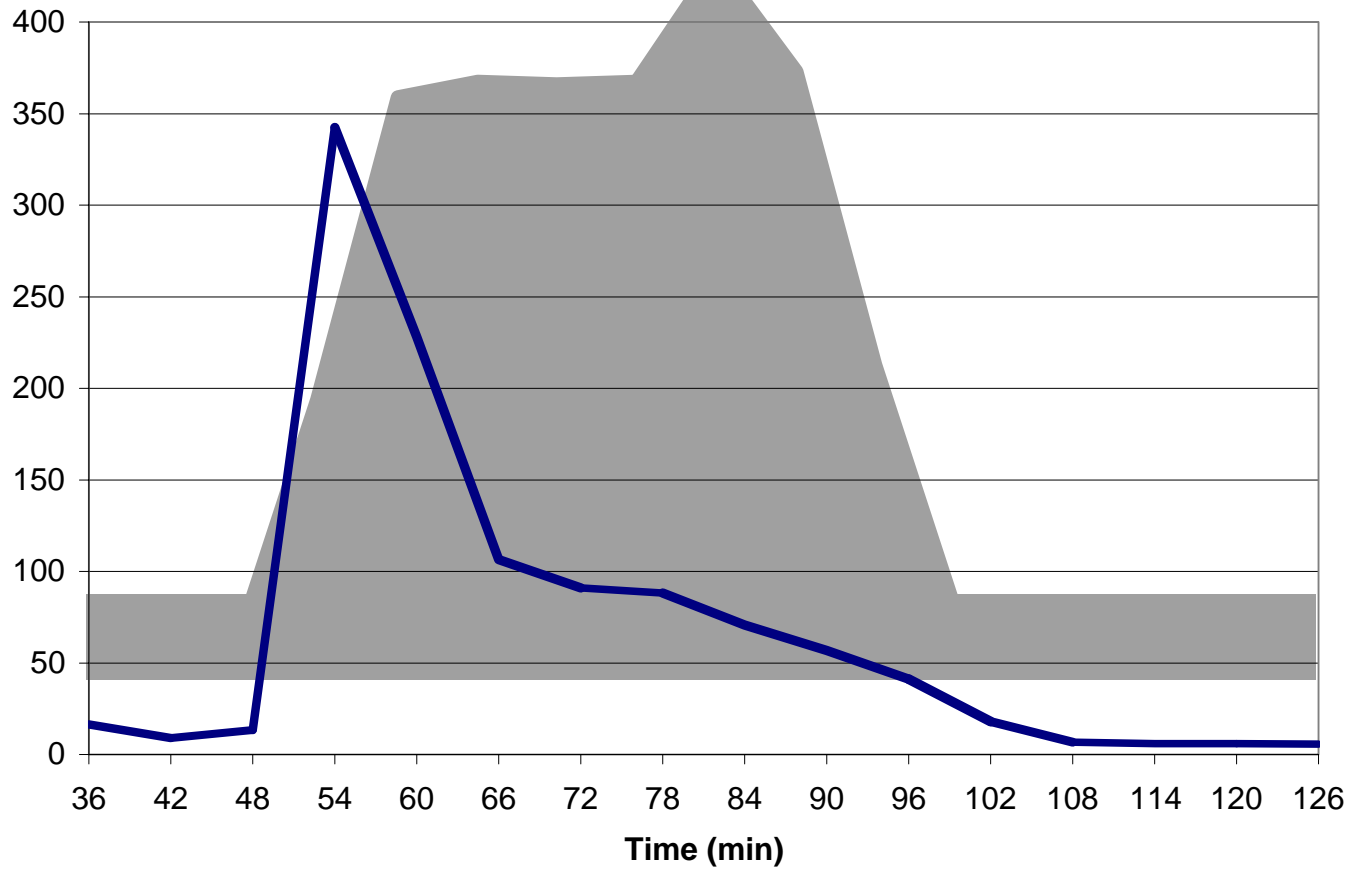
Damaged Islets

Phase One Insulin Release Missing



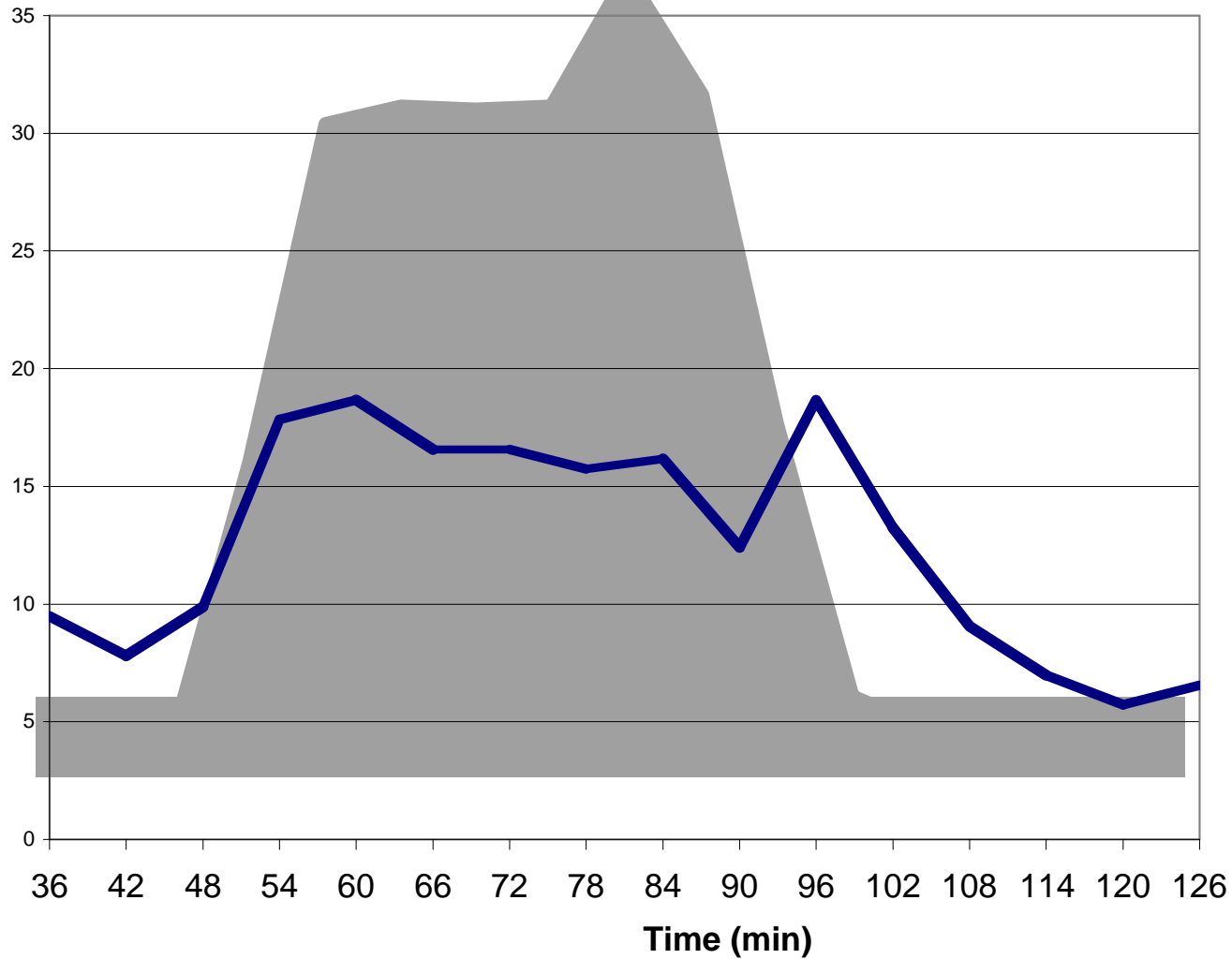
Damaged Islets

Second Phase Insulin Release Missing

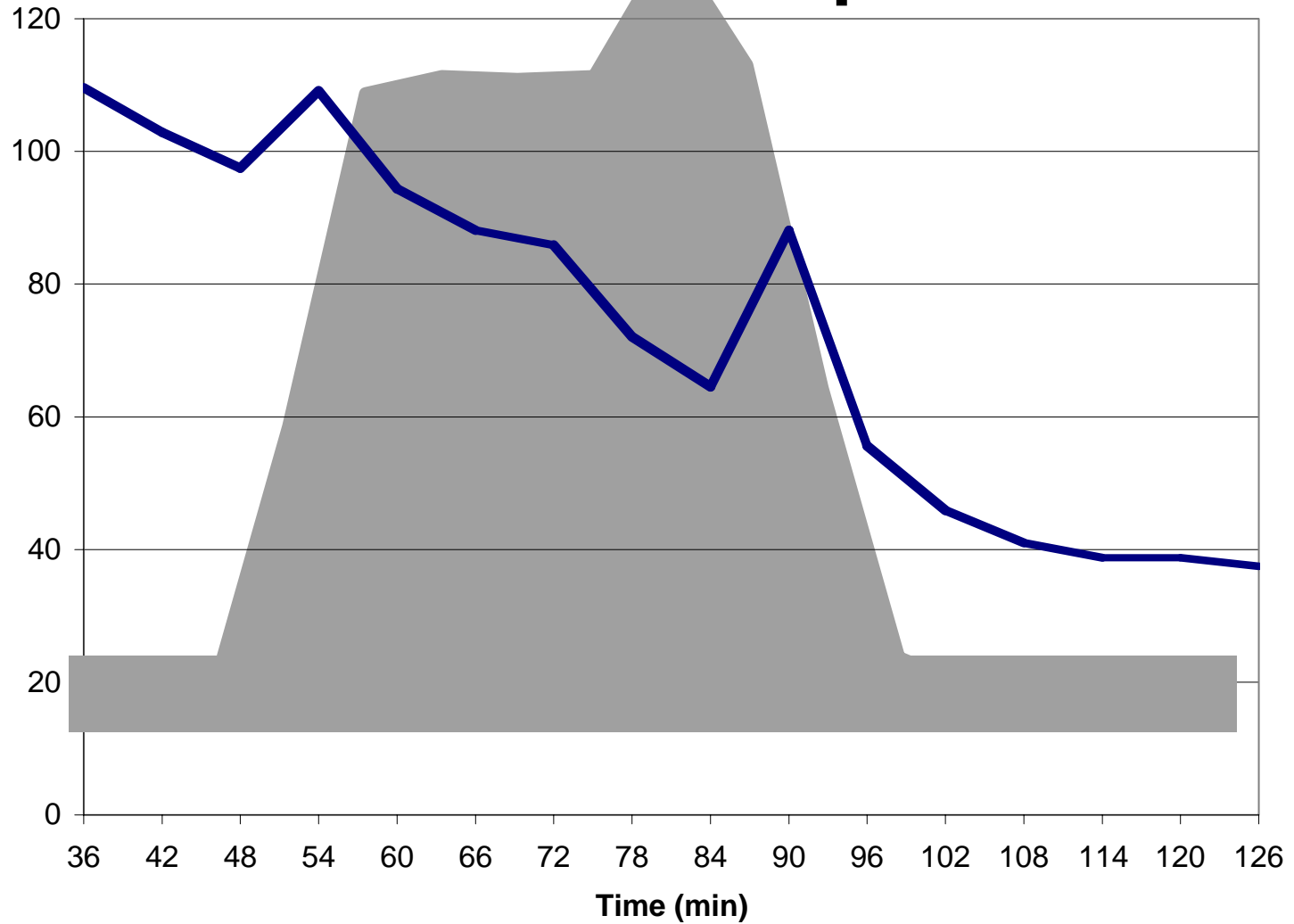


Damaged Islets

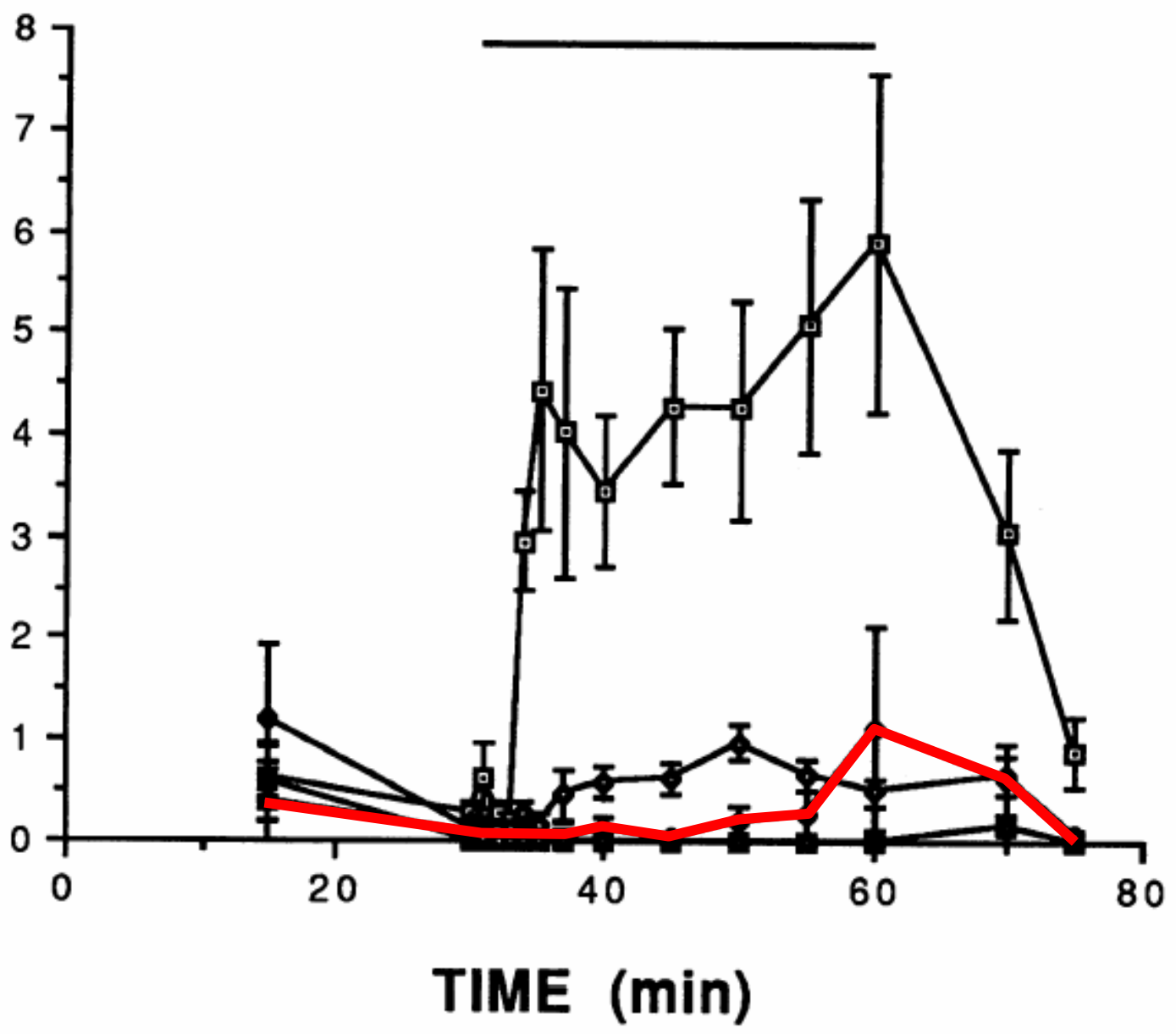
Poor Insulin Release



Non-responsive Islets Insulin Dump



**EFFLUENT INSULIN
(ng/min)**

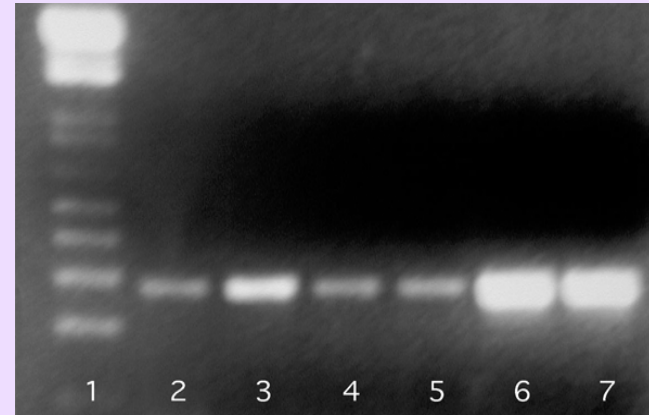
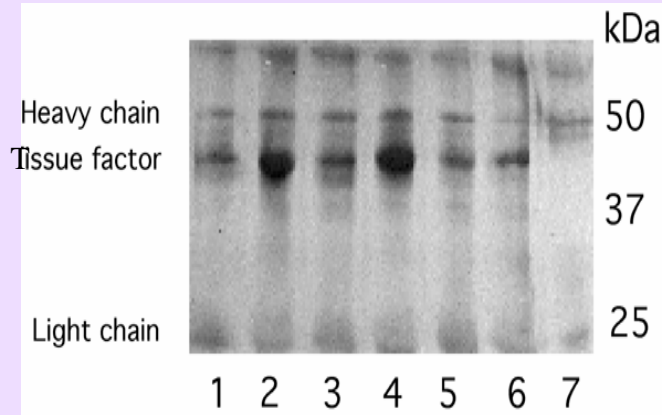
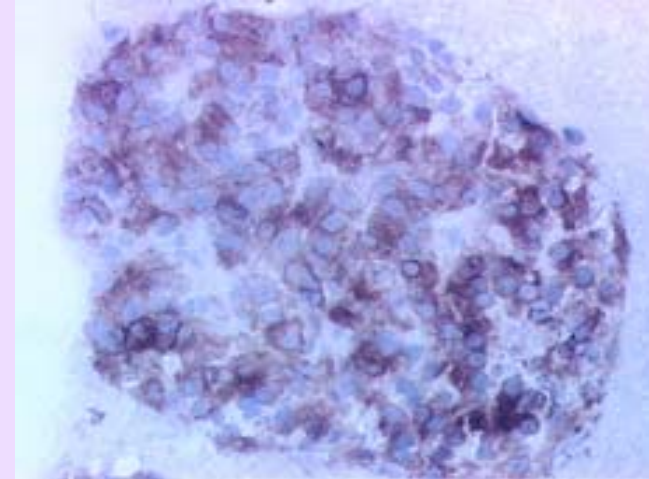
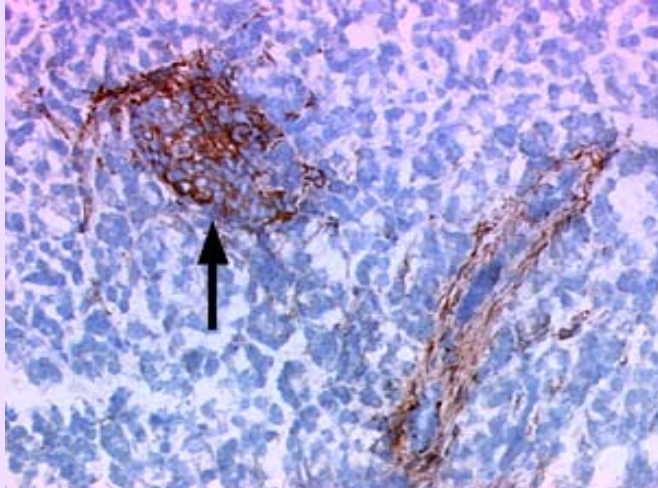


A microscopic image of an islet of Langerhans, a cluster of endocrine cells in the pancreas. The islet is a large, dark, irregularly shaped mass in the center, surrounded by a lighter, more granular background of exocrine tissue. The overall color palette is dominated by yellow, orange, and brown tones, with the central islet appearing in a darker, almost blackish-purple hue.

The Nordic Network for Clinical Islet Transplantation

JDRF & NIH

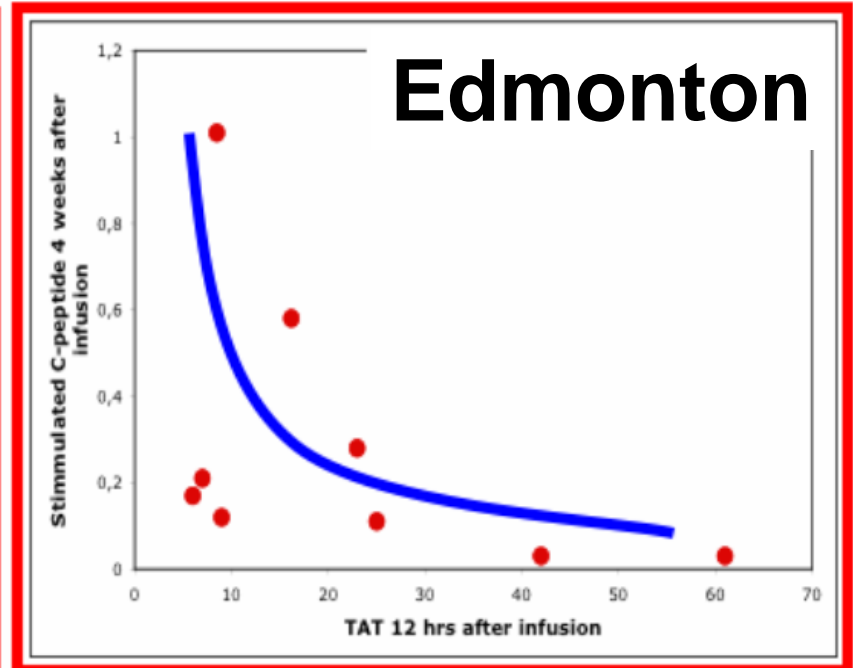
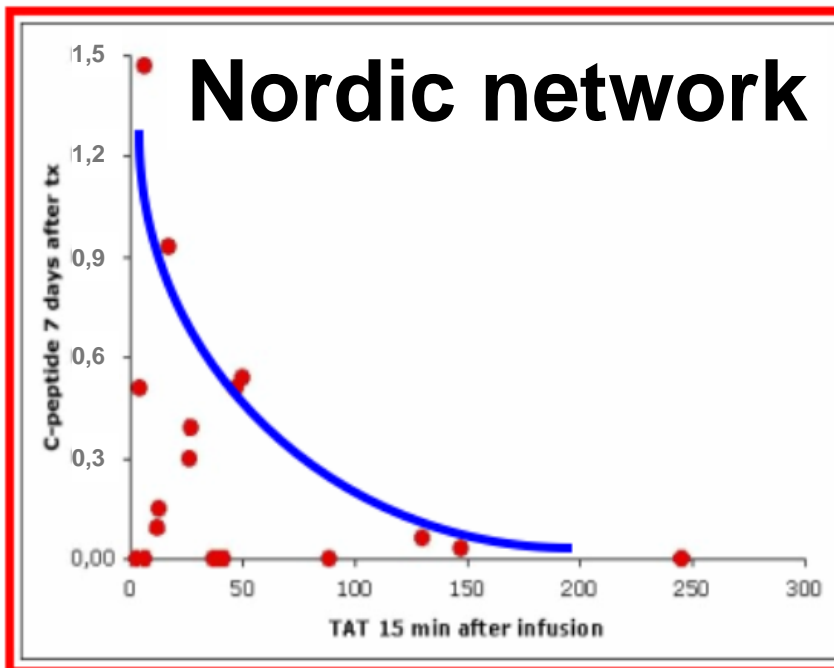
The presence of Tissue Factor in islet cells



Lisa Moberg 2002

IBMIR IN CLINICAL ISLET TRANSPLANTATION

No patients with both high C-peptide and TAT levels



Reaction Block Detail

