

## Nordic Pancreas and Islet Transplant group



**Date:** October 19<sup>th</sup> 2021

**Location:** Arlanda, Sweden Blue Radisson hotel

### Participants at Arlanda:

*Torbjörn Lundgren, Hanne Scholz, Maria Svenaeus Lundgren, Lydia Junebjörk, Karin Fransson, Tim Scholz, Torsten Eich, Monica Storö, Christina Andreasson, Paul Krohn, Bengt Gustafsson, Åsa Norén, Oleg Slivca, Marko Lempinen,*

**On ZOOM:** *Shinji Yamamoto, Olle Korsgren, Trond Geir Jensen, Marko Murruste, Anna Högvall, Maria Engman, Carola Shulman, Amir Sedigh, Morten Hagness*

### 1. Opening of the meeting

Torbjörn Lundgren welcomed 14 participants in the room and 9 participants digitally by Zoom. Torbjörn Lundgren was elected as chairman. Bengt von Zur-Mühlen was elected as secretary.

### 2. Approval of the agenda

The agenda was approved.

### 3. Minutes from last meeting 10<sup>th</sup> April 2018

All minutes are available on Scandiatransplant's homepage. Latest protocol from 4<sup>th</sup> February 2021 was approved [http://www.scandiatransplant.org/members/nordic-pancreas-group/MinutesNPITGzoom\\_04\\_feb\\_2021.pdf](http://www.scandiatransplant.org/members/nordic-pancreas-group/MinutesNPITGzoom_04_feb_2021.pdf)

Videos with patients receiving beta cell replacement therapy (one patient with islet transplantation and one patient with SPK) are in Swedish and available after contact with Tim Scholz: [tim.scholz@akademiska.se](mailto:tim.scholz@akademiska.se)

The traditional EPITA meeting in Igls, Austria has this year due to Covid been moved to Oslo in June 2022.

### 4. Islet specific meetings (protocols can be found on website)

**25<sup>th</sup> March 2021:** 12 participants on Zoom, previous islet specific meeting was in 2017.

- All centers had suffered of the corona pandemic with low activity.
- Increased auto interest.
- All centers had less referrals and one reason might be newer pumps with good control during the night but still daytime variability.

- To reach out better to the diabetologists better study endpoint i.e. in range measurements and QoL- data rather than c-peptide levels.
- Anti-CD40 by Novartis was discussed
- Also combined islets and T-reg/stromal cell therapies.
- Comparison of isolations of auto versus DBD/DCD.
- SOP are now fused in one document available at the Scandiatransplant homepage.
- The COBE used in islet isolation will not be available for service in Europe in a couple of years. Olle Korsgren has been in contact with the US supplier.
- Increased interest in the importance of the alpha- cells and glucagon production

**5<sup>th</sup> October 2021:**

- COBE replacement discussion and invited guests from Leiden, doing 4-12 allo and auto yearly showed their newly developed equipment, a one-line system that can be run with less laboratory staff. The equipment is not CE marked but a common research project might solve that problem.

**5. Short report from centers regarding activities and how covid 19 has affected patients and production**

Center	Covid	Pancreas	Islets
<b>Stockholm</b>	2021 rather favourable donor situation. Still some restrictions	3 pancreas	1 allo, 2-3 auto
<b>Uppsala</b>		2 pancreas 11 on the waiting list	1 allo islet, 1 auto later this week 2 patients on the waitinglist
<b>Oslo</b>	Almost back to normal	4 SPK, 1 PA Few on the waiting list	No allo Immunizes pat on WL 3 auto (No 12 in total)
<b>Copenhagen</b>		5 SPK, 1 PAK	No islets
<b>Helsinki</b>	Covid turned red a week ago, previously very calm. Quite normal donor year.	22 SPK, 1 PA Two manageable leakages with reop after 2-4 weeks. No thrombotic events, some bleedings. 11 patients on the waiting list	No islets, but preparing restart. Waiting for hospital authorisation.

<b>Gothenburg</b>	1 late loss (7 years) of a SPK after Covid vaccination	3 SPK, 1 was lost due to hypoxia/vasopressants?	Planning to put the first patient on the waiting list and quite a few in pipe-line.
<b>Tartu</b>	Covid situation has been deteriorating and elective surgery has been stopped	No pancreas One pancreas sent to Finland	No islets
<b>Malmö</b>	Oleg Slivca was trained in Minnesota	2-3 SPK	No islets

**6. Helmsley Charitable trust <https://helmsleytrust.org/our-grants/>**

The importance of glucagon has been ignored historically. Alpha cell project – glucagon and exploring problems such as hypoglycemia and decreasing awareness. Trying to find treatments to improve/restore alpha cell function.

New project aiming at isolation of islets from type 1 diabetic deceased donors for research (duration of illness > 5 years). Funding from Helmsley Charitable Trust. Until now donors from Sweden and Norway have been identified to be able to join the project. In Finland pancreas may not be able to export organs for research, but maybe it is possible if there is an ethical approval. Denmark cannot export organs for research purposes.

Funding is 400 000 USD for the first year, and if good results similar funding is possible in the future. Everything that enables pancreas procurement can be funded.

**Decision:** Tx coordinator in Sweden and Norway works together to help secure that T1D donors with research consent are sent to Rudbeck Lab in Uppsala for isolation.


**7. Lithuania in collaboration**

Marius Miglinas (nephrologist) and colleagues from Vilnius in Lithuania have been preparing a program for allo islet transplantation since 2016.


A national registry is now ready to register patients for islet transplantation. In recent years (before Covid) 0-4 yearly SPK have been performed.

All donors will be assessed for procurement of pancreas for either SPK or islet after kidney on collaboration with the Nordic network. Next steps are licensing and logistical arrangements. Start possible from December 2021. Discussion if 7 hours retrieval of pancreas before scheduled flight is suitable. A representative from the Lithuanian National Transplant Bureau (NTB) confirmed that they are prepared and need no further information.


**From pancreas to islet transplantation**



All potential donors will be assessed for procurement of pancreas for either simultaneous pancreas-kidney or islet after kidney transplantation



If no contraindications are found coordinator from Nephrology department will contact ☎ Transplant Coordinator at Akademiska sjukhuset regarding potential islet isolation



Nephrology department in VUH SK

**Decision:** Uppsala/Stockholm have already agreement to receive pancreas for isolation and will help with Islet Tx in Lithuania. Ongoing discussions to join Scandiatransplant will continue.

Information about the EPITA and islet isolation working group. The meeting will be four days in Oslo in June 2022 (moved from Igls) - <https://esot.org/epita/>

**Decision:** Oslo (Hanne) will send email with save the dates as soon as they are been confirmed by EPITA

## 8. Studies and *Better end points*

Miscommunication between the transplant area and the diabetologic area. Can a new islet transplantation project focusing on end points from current diabetological research improve our interaction with diabetologists? Olle Korsgren has been in contact with professor Marcus Lind in Uddevalla and Bengt Gustafsson Gothenburg and there is a IAK study protocol developed. Focus on QoL – type 1 diabetes patients have to live with their disease 24/7 planning treatment, exercise and calorie intake. What variables are most important for the patient in contrast to c-peptide levels. We should also invite diabetologists as authors/coauthors. Torbjörn Lundgren will share the study protocol draft with NIPTG members – comments are welcome.

**Decision:** A group will be formed to take this project forward. Torbjörn Lundgren, Olle Korsgren, Bengt Gustafsson, Trond Geir Jensen will join to start with. Kaisa Ahopelto from Helsinki will also be asked. Paul Krohn tries to find a danish representative.

Trond Geir Jensen emphasized that nephrologists have experience in managing immunosuppression in organ transplantation, unlike most diabetologists. We need to address the perceived obstacle with immunosuppressive therapy, which is why Islet after kidney (IAK) is a good starting point. Ongoing discussion how to recruit patients.

A challenge is to change and/or reduce the need of immunosuppression. Anti CD40 has been discussed, but one kidney study in de novo kidney transplantation (CIRRUS-1) was halted September 3<sup>d</sup>.

**T-regs and Quell:** A London based company, Quell: <https://quell-tx.com/> Quell is employing proprietary and innovative technologies to genetically enhance Tregs, to enable the targeting of Tregs in an antigen (Ag)-specific manner and directing them to particular targets within the body, i.e focusing their suppressive potential right where it is needed. Discussions are ongoing regarding using these in islet transplantation

**Melton lab:** Dough Melton <https://hscrb.harvard.edu/labs/melton-lab/research/> has developed methods to make hundreds of millions of beta cell like cells from human stem cells (ES or iPS cells). This allows us to pursue research that can lead to new treatments – or even a cure – for Type 1 diabetes. The substance has to follow all regulations for a drug. Yesterday the commercial company Vertex had a press release <https://investors.vrtx.com/news-releases/news-release-details/vertex-announces-positive-day-90-data-first-patient-phase-12>

*Vertex announced positive Day 90 data for the first patient from the Phase 1/2 clinical trial of VX-880, an investigational stem cell-derived, fully differentiated pancreatic islet cell replacement therapy for people with type 1 diabetes (T1D). This is the first demonstration of a patient with T1D achieving robust restoration of islet cell function from such a cell therapy.*

*The patient was treated with a single infusion of VX-880 at half the target dose in conjunction with immunosuppressive therapy. The patient achieved successful engraftment and demonstrated rapid and robust improvements in multiple measures, including increases in fasting and stimulated C-peptide, improvements in glycemic control, including HbA1c, and decreases in exogenous insulin requirement. VX-880 was generally well tolerated*

**Decision:** Olle Korsgren and Hanne Scholz can continue to develop collaboration with Melton/Vertex on behalf of the PI group.

## 9. Register status

- **Pancreas:** The registry is up and running but the frequency of registration is still low. It would be favourable if we could appoint a supervisor or if every center appoints a local supervisor. Even more important if our registry will be connected to a new European registry.

**Decision:** Every center reports how their registration is organised locally and how they use/interpretate the registration form + suggestions for improvement

- **Nordic islet registry (NIR):** Ongoing process to transfer the registry (Medscinet) to the Scandiatransplant system, delayed during the corona pandemic. Medscinet has been sold to a Norwegian company, but still all contracts are still valid.

Bengt Gustafsson has looked in his local register and noticed a number of leakages typically on day 4. Discussion at the meeting regarding how the bowel ends are closed and how the bowel/bowel anastomosis is performed. It's done more or less the same at all centers.

## 10. DCD

Donation after circulatory death (DCD) is rapidly increasing in Sweden. The islet labs need a decision if DCD pancreas can be used for islet isolation. But with the actual short waiting lists there is no shortage of pancreases for the moment. There have already been isolations in research projects and there are numerous reports in Europe and North America. Leiden has reported lower yields but good quality. Other groups have reported normal yields. Norway will restart their DCD program – normothermic approach.

**Decision:** Maria Svenaeus Lundgren will contact Ilse Duus at Scanditranplant so that both the pancreas and islet registries can report DBD or DCD donor.

## 11. Auto islets

Discussion of the importance to have good connections with GI surgeons. In chronic pancreatitis the results with auto will be less optimal if the pancreatectomy is done "too late". This will be discussed more in detail at the next meeting. Different strategies at all centers also in other aspects.

**Decision a):** Torbjörn Lundgren will contact the board of Scandiatransplant (Bo Göran Ericzon) and formally include autotransplantations in the Scandiatransplant registries.

**Decision b):** Morten Hagness (coordinator) Olle Korsgren, Hanne Scholz, Torbjörn Lundgren forms a working group. Maybe Poya Ghorbani (Stockholm), Ville Saminen (Helsinki) and gastrosurgeon Anne Waage (Oslo) can join. The group will work for collaboration, registries and common SOPs.

**12. Pancreas – lack of studies late outcomes (not surgical)**

General discussion regarding lack of studies. Small materials and low rate of long term metabolic follow up by the Tx-surgeons. Olle Korsgren proposes a working group, but no decisions were made in this regard.

**13. Next meeting**

**Decision:** Torbjörn Lundgren contacts Ilse Duus to coordinate the next meeting in 6 months.

**14. The meeting ended**

**Stockholm October 19th, 2021**

**Bengt von zur Mühlen**  
Secretary

**Torbjörn Lundgren**  
Chairman

**Hanne Scholz**  
Co chairman