

Nordic Pancreas and Islet Transplant group



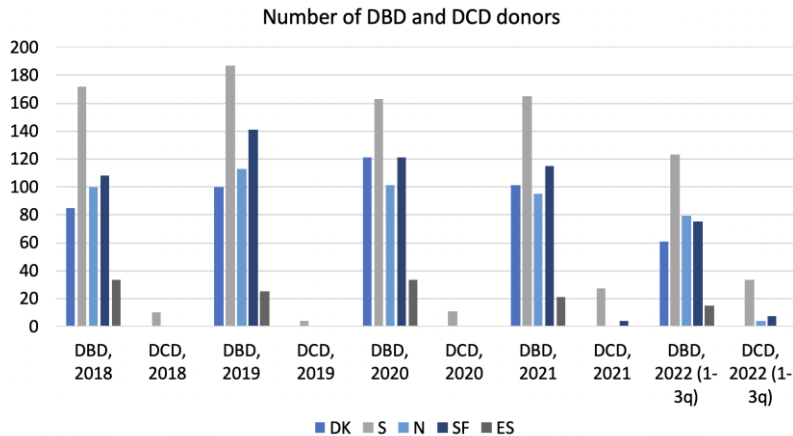
Date: 25th October 2022

Location: Clarion Arlanda (Meeting Room - Madrid Barajas) or Zoom Link

Participants:

*Amir Sedigh, Bengt von Zur-Mühlen, Karin Lindh Tx coordinator Uppsala,
Lydia Junebjörk, Anna Högvall Research nurse Uppsala
Alireza Biglarnia, Oleg Slivca Malmö
Anne Ørskov, Ilse Weinreich Scandiatransplant
Olle Korsgren, Torsten Eich Isletlab Uppsala
Paul Suno Krohn Copenhagen,
Torbjörn Lundgren Stockholm,
Alexandra Thorsell, Karin Fransson Research nurses Stockholm
Marko Lempinen, Kaisa Ahopelto Helsinki,
Bengt Gustavsson Gothenburg
Monica Storö, Tx coordinator Oslo, Kristine Fasting, Oslo
Hanne Scholz Isletlab Oslo*

1. Hanne Scholz welcomed present and online participants and was elected chairperson for the meeting. Bengt von Zur-Mühlen was elected secretary until lunch and Torbjörn Lundgren after lunch.
2. Introduction of participants
3. Agenda was approved, no additions.
4. Minutes from last meeting 7th April 2022, Online meeting. The minutes were approved.
5. Short report from centers regarding activities. General discussion of direct and secondary effects of Covid. After the introduction of DCD an initial decrease in DBD has been seen in Sweden. There is a general increasing mean age of donors. The current age limit is 65 for islets. Discussion of reported experiences in the UK and US of pancreas and islet transplantation in type 2 diabetes and the wide range of different types. 2022, so far



- a. Oslo: 2 SPK uncomplicated, 1 IAK went well but complicated with bleeding that needed laparoscopy, 3 auto-islets
 - b. Gothenburg: 3 SPK/PAK, 2 patients on the islet waiting list for islets and at the end of the year hopefully 6 patients on the islet waiting list. New head of the department Niklas Kvarnström.
 - c. Uppsala: 2 SPK uncomplicated, no islets, 7 patients on the pancreas list (4 PA), 2 auto-islets Umeå
 - d. Copenhagen: 3 SPK, one removed due to severe bleeding, 5 on SPK waiting list
 - e. Helsinki: 18 SPK normal degree of complications but also a few late complications (1 case after severe diarrhea/dehydration, 1 nonadherence), 1 auto-islet
 - f. Stockholm: 4 SPK (1 DCD NRP), 1 IA, 1 islet on the waiting list and 2 in pipeline, 1 auto-islets
 - g. Malmö: 3 SPK, 1 complicated with severe myocardial infarction and pancreas was lost, patient had ok cardiac investigations only months before the procedure. 1 lost pancreas due to unknown severe morphine addiction leading to enormous problems. 5 on the pancreas waiting list.
6. The Helmsley Charitable trust- type 1 diabetic pancreas organ donors.

T1D donors traditionally were not accepted for kidney-Tx, although there has been an increase in recent years. There is a huge need for research on islets from Type donors, including the function and importance of the alpha-cells. The network has so far sent 1 pancreas for isolation within this project. The coordinators don't think that we have missed harvesting a pancreas for islet isolation. There is a need for the approval of research purposes. The program is well-funded. The funds are there to promote general organ donation to that way find more T1D donors. Ilse Weinrich

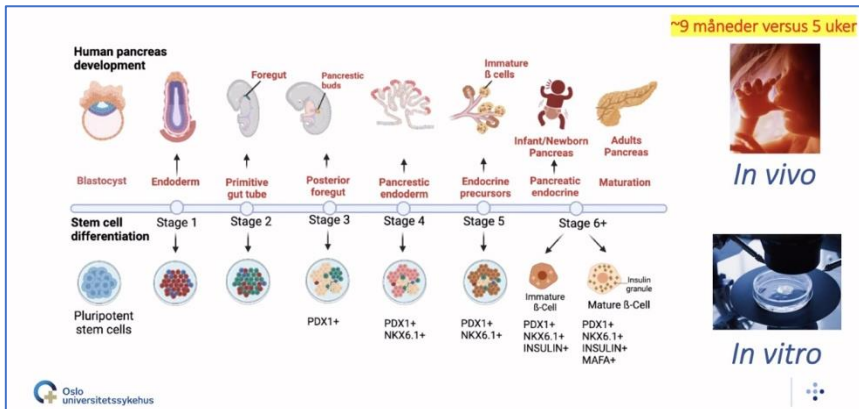
checked in the ScandiTransplant registry how many T1D donors there have been (see below). Apply to Olle if you have a project that you think would fit.

Deceased donors - Treated diabetes in numbers

	Type 1	Type 2	Type 1+2	Unclassified	No diabetes	Missing info.
2017	5	34	2	5	381	100
2018	7	24	0	1	390	96
2019	5	43	1	1	449	78
2020	11	34	1	0	503	5
2021	4	35	1	1	497	1
2022 (25/10)	4	26	0	2	411	5

7. Stemcells (Vertex)

Hanne Scholz lecture about stem cells. In the Vertex study the stem cells are pluripotent from blastocytes from the embryo and are given specific factors to become insulin-producing tissue. The stem cell differentiation passes stages with a cocktail of signals that push them to the next stage. The development has improved the ability to produce islets. Vertex has developed an allogeneic cell product named VX 880, based on research at Harvard from Doug Melton’s group. The patient still needs immunosuppression, similar to allogeneic islet transplantation.



A clinical trial has started in USA and Canada, and the first patient enrolled was reported at EASD congress in Stockholm Sept 2022. The patient is 60 years, 40 years duration. insulin use 34U HbA1c 64 C-peptide negative. With one dose (half dose) injected to the liver achieved 99,9 in range and insulin independence at day 270. The second patient was presented at ADA congress 2022 followed for 150 days with less good result. The following 15 patients in the study will receive full dose (the study intend to include 17 patients). The cells implanted seems to be “fetal like” and it may therefore takes up to two months for them to mature. The development for such biological cell product is very expensive.

Oslo/The Nordic network is one of the approved trial sites and documents to the ethical committee and medical agency will be finalized in November. First patient planned for summer 2023. Study duration is 5 years (the patient will be followed for safety for up to 15 years).

8. News from The Islet Labs, Oslo and Uppsala

Oslo; The Nordic Network and hosted by the Oslo lab arranged a very well-attended EPITA islet workshop in June 2022. Participants from all major islet centers in Europe. Congratulations to Hanne and the Oslo isolation team for arranging this. Discussions on new equipment. Isolations for auto-transplantation is becoming a more prominent part of the activities.

Uppsala; 2 probable future studies were discussed. The first with a new group of patients with very high HbA1c where this could be considered a “medical emergency”. If these are well motivated and reasonable an islet transplantation aiming at lowering HbA1c and hopefully improving QoL could be motivated. Should be in close collaboration with diabetologists and preferably run by them. The second is a project aiming at avoiding T and NK cell interaction with the graft. This could have huge implications and hopefully more information can be given at the spring meeting

9. The EPITA Igls meeting Jan 22-24 2023. Abstracts? Participation?

Just a reminder of the meeting and a recommendation to go. Abstract deadline is Nov 9 (but is often extended a week or two)

10. Studies -ongoing, planned (NNCIT02, Pancreas studies?) NNCIT02 using LMW-DS is ongoing. 2/18 patients transplanted. More patients being put on the waiting list in the near future in Stockholm, Oslo and Gothenburg. Regarding pancreas transplantation Bengt G suggested that the group could/should put together a paper on the 100 latest pancreas transplantations. He was planned to take contact with all centers to check if they wanted to contribute. Registration in YASWA could be used as the source of data. A manuscript within a year and an abstract to Epita/Igls 2024 was proposed.

11. Report form the Working groups (progress on activities mentioned in previous minutes?)

- a. Auto islet transplantation. Morten, Torbjörn and Anne Waage arranged a meeting in Oslo in conjunction with the EPITA islet isolation workshop in June. It was well attended and with non-nordic guests as Paul Johnson fr Oxord, Francois Pattou fr Lille, and Thierry Berney fr Geneva. Anne had a good presentation of the subject in general and the results so far in Norway. The later has been published in a Norwegian surgical magazine. There was agreement around learning from each other and a new meeting more clearly

inviting the gastro surgeons involved from each center in the fall. Anne Waage was to take care of this (Hanne will check on progress). At the present meeting the topic of "non-allotransplantcenters" participating in this collaboration was discussed. No one suggested otherwise than that they can join. Known centers are Umeå (ongoing), Linköping (planned) and Tampere (planned). Scandiatransplant (YASWA) has been adapted to make it possible to include these transplants where donor and recipient are the same individual. How non-transplant hospitals shall enter data or registered patients there is not decided yet.

- b. Better end points. Trond Jensen could not attend the meeting but had sent a message in advance and is willing to join work regarding this. His thought was: "Hvilke målepunkter som skal legges inn i nye endpunkt må jeg tenke litt på. Eksempler kunne være:
 - i. - Sensor-assessed hypoglycemic events,
 - ii. - Insulin dose needed
 - iii. Fear of hypoglycemia scale (validated tools are available).

Impaired awareness should maybe be used instead of severe hypoglycemia as inclusion criteria. The background is that with the new sensor-pump system, the severe hypos are gone, but impaired awareness still appears in most cases."

- c. Patient recruitments. Close ties to b. and study mentioned under number 8. Apart from that there are patients coming onto the islet waitlist this year in Gothenburg, Finland and Stockholm. There have been few islet transplants in Malmö in recent years. Oleg thought there probably would be type 1 patients that had undergone kidney alone and might be interested in IAK. The group offered to help in any way they could.
- d. Pancreas – lack of studies late outcomes (not surgical). See 10. No discussions on late metabolic control was held

12. Any other business - None

13. Next meeting

Plans are to stick with the format of full online meetings in the spring and a face to face/hybrid meeting in the fall. Next meeting was set for March 29 2023, 13 00 – 16 00 online. Ilse to make a calendar booking now.