

A new Horizon 2020-funded project, ISLET's kick-off meeting was held in Copenhagen on 5-6 March, 2020

Thursday 5th of March marked the official kick-off of “Advancing Innovative Stem Cell-based Therapy for Diabetes in Europe” (ISLET), a five-year, EU Horizon 2020-funded, project. Coordinated by the University of Copenhagen (UCPH), Denmark, the ISLET consortium also comprises seven other partners including in Belgium, the International Diabetes Federation Europe; in France, Institut National de la Santé et de la Recherche Médicale (INSERM); in Germany, Helmholtz Zentrum Muenchen Deutsches Forschungszentrum für Gesundheit und Umwelt Gmbh (HMGU), Klinikum Rechts der Isar Der technischen Universität München (TUM-MED) and Lipotype; and in the Netherlands, Academisch Ziekenhuis Leiden (LUMC).

Type 1 diabetes (T1D) represents a huge personal and societal challenge. According to the IDF Atlas, 9th edition, 1.1 million children and adolescents (0-19 years of age) live with T1D in the world including 296,500 in Europe. The number of newly-diagnosed children and adolescents in Europe each year is estimated to be around 31,000. Type 1 diabetes is an auto-immune condition in which the body's immune system attacks the insulin-producing beta cells of the pancreas, as a result of which the body produces little or no insulin. Type 1 diabetes most frequently develops in children and young adults and is one of the most common chronic diseases in childhood, although it can occur at any age. People living with T1D require daily insulin injections, without which they would die.

ISLET aims to build and implement a new and innovative programme for producing and marketing human pluripotent stem cell (hPSC)-derived advanced therapy medicinal products (ATMPs) for the treatment of people with T1D. It is envisaged that by the end of the project there will be:

- (i) A regulatory approved manufacturing process for production of hPSC-derived beta cells ready for use in a phase 1 human trials (First-generation ATMP)
- (ii) A new method for scaling up the engineering of a hPSC-derived product with increased therapeutic capacity. This product will be more alike the golden standard - the human islet – and composed of purified alpha and beta cells (Second Generation ATMP)
- (iii) An innovative process for predicting the therapeutic capacity of ATMPs, benefiting the whole field looking to bringing hPSC-derived ATMPs to the clinic.

The kick-off meeting started with project coordinator, Henrik Semb, from UCPH welcoming the participants and restating ISLET's main objectives. Next, Sabine Dupont from IDF Europe, introduced IDF Europe and explained the role that people living with a disease can play in the drug development continuum; starting with the early research phase to ensure any new development truly addresses unmet needs and meaningful outcomes.

One of IDF Europe's Youth Leadership Camp Alumni and current member of IDF Europe's youth network (YOURAH), Liv Olivia Fritzen, the president of the Youth Association of the Danish Diabetes Association, then went on to talk about the impact of diabetes on her daily life. Liv outlined the objectives and activities of the Danish Diabetes Association and then gave a powerful personal perspective on her condition, describing the constant attention it requires and the stress it can generate. She then explained the various treatment options available and demonstrated how to change an infusion set. Liv's talk was very engaging and provided strong, motivation to the scientists present of why their work is so important, and why engaging with the Diabetes community is essential for it to be impactful.

Liv's presentation triggered a lively discussion on the management of patient expectations and the potential benefits of the ATMPs to be developed by ISLET vs existing treatment options and new developments such as closed loop systems. The consensus was that it was critical to explain that the new research was at a very early stage, and that even if successful would only, at first, be deployed as a Phase I safety trial in a small group of patients.

The next presentation was from Cees Tack from Radboud University Medical Centre, one of the Scientific Advisory Board (SAB) Members, who presented the views and expectations of the ISLET project from a clinical perspective.

After lunch, the leaders of Work Packages 1 through to 5 outlined their specific goals and associated challenges. Led by HMGU, WP 1 will focus on establishing protocols and processes for the manufacture of clinical grade glucose-responsive beta cells from human embryonic stem cells (hESCs) that fulfil regulation for in-human use. This involves establishment of Master and Working Cell Banks from clinical grade hESCs and the manufacturing process to produce insulin-producing beta cells together with the necessary licence and product release.

LUMC will lead Work Package 2 which will look at defining a set of criteria for the characterisation and functionality of the cell products for future Phase I and II clinical testing, in particular relating to pre-clinical safety and efficacy. This will include creating the necessary platforms for in-depth testing of the cell aggregates at the cellular and molecular level and functionally *in vitro* and *in vivo*.

INSERM, meanwhile, which leads WP3, will examine the potential for upscaling production of functional human endocrine (alpha and beta) cells derived from hESCs for use in the second-generation ATMP. In particular ways of producing large numbers of these purified cells, so the second-generation ATMP can be available to a wider number of people living with Type 1 Diabetes.

WP4, led by HMGU will look at developing the second-generation ATMP which is planned to consist of clusters of alpha and beta cells, like the islets found in the pancreas (islet-like clusters), in contrast to beta cells alone in the first-generation ATMP. WP5, led by Lipotype and UCPH, will use multi-omics data to standardise and apply quantitative quality control criteria to predict the therapeutic capacity of the islet-like clusters.

The day concluded with a presentation by SAB-member, Andreas Kurtz, on HES cell therapy and ethics.

The second day of the meeting started with a presentation by SAB-member, Paula Salmikangas of NDA group, on the conditions, constraints and challenges associated with bringing ATMPs to market including obtaining both marketing authorisations and reimbursement.

The meeting continued with a presentation by Cathy Southworth on the objectives of the WP6 Dissemination and Communication components, a WP in which IDF Europe will be deeply involved. Among some of the tools and planned activities presented were the potential interaction between IDF Europe's YOURAH network and ISLET's researchers for a better mutual understanding of the research objectives and challenges and desired end points. An in-depth communication plan will be developed over the next few months as will a website and brand identity for the project. WP6, led by UCPH and Lipotype, will also look at the exploitation and commercialisation tasks for the ATMPs developed.

The meeting concluded with feedback from the Scientific Advisory Board to all consortium members.



All WPs are now set to start work on their deliverables, with updates provided to the consortium regularly over the next few months, and another face-to-face meeting of the entire consortium planned in a year's time.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement no. 874839.



Funded by
the European Union