

PANCREAS ORGANOIDS FOR TYPE I DIABETES MELLITUS – IS IT FEASIBLE AS A CELL THERAPY?

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Human pancreas organoids are a promising cell therapy candidate for Type I Diabetes Mellitus (T1DM). T1DM is a disabling chronic disease with a juvenile onset. Auto-immune destruction of pancreatic beta cells results in insufficient insulin production to manage blood glucose. This can lead, on the long-term, to serious complications, such as hypoglycemic episodes, neuropathy, retinopathy, and renal failure. The current standard of care is insulin therapy. However this cannot fully prevent long-term complications from arising, especially in patients suffering from uncontrolled T1DM with severe hypoglycemic episodes. Restoration of the natural blood glucose management can prevent complications, for instance by restoring the beta cell population with a cell therapy. Organoids, proclaimed by the journal Nature as “Method of the year 2017”, are 3D structures that can be generated from progenitor cells of many different organs, such as pancreas, liver, brain, lung, and heart. These miniature organs, when differentiated to produce insulin, can be a 3D cell therapy for T1DM. In case of the pancreas, these can be generated from adult-derived progenitor cells, which have a safer profile than ESC or iPSC based cell therapies for T1DM.

Lonza Netherlands is a partner within the LSFM4LIFE project: a European consortium of universities and industrial partners that aims to produce a GMP batch of human pancreas organoids. To reach this goal, two milestones need to be achieved. First, to transfer the research process of organoid production into GMP. Specific challenges are a scalable GMP compliant platform for 3D culture and replacing research materials (e.g. complex media formulations and culture substrates) with GMP compliant substitutes. Additionally in process controls and QC assays are in its infancy for organoids and need to be developed. The second milestone is to develop a strategy for commercialization of this therapy, for which a number of analyses have been performed. A market and SWOT analysis have been performed (Figure 1). A clinical strategy is proposed to first access the market with an introduction into a small patient cohort and then to stay on the market by reaching all T1DM patients. An assessment of the manufacturing cost of goods is made for the current process, as well as how it could be envisioned in a commercial setting. From these costs, the cost-effectiveness compared to insulin therapy and islet of Langerhans transplantation is evaluated [1]. In conclusion, while the potential for organoids as a cellular therapy is considerable, this paper addresses the progress so far and the major challenges ahead.

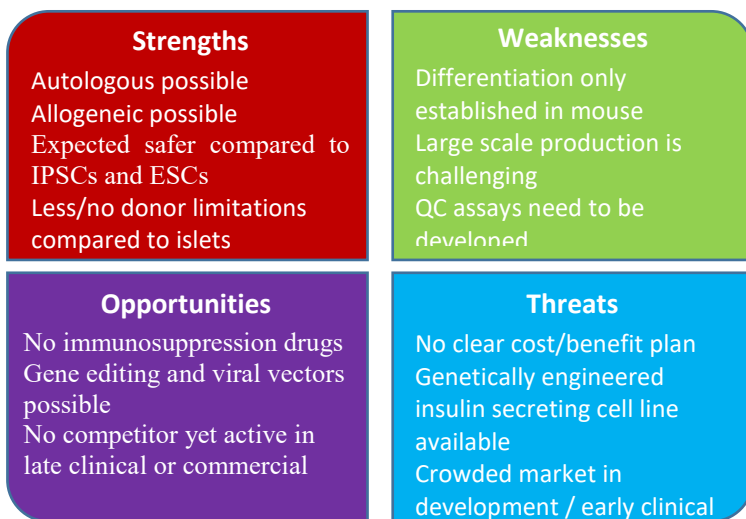


Figure 1 – Strengths Weaknesses Opportunities Threats (SWOT) analysis on pancreas organoid cell therapy.

The unique aspect of this paper is that it describes the commercialization of an early stage 3D cell therapy. Organoids could be envisioned as an autologous ex vivo gene therapy for a subset of T1DM patients, or a donor-matched allogeneic treatment, but could finally be used as an allogeneic treatment. Additionally, the assessments on this therapy are applicable in a broader sense to other therapeutic areas of organoids and to other 3D cell therapies. For some cell therapy applications, 3D structures could be essential to their success (e.g. cardiovascular, organ function replacement) and could be the next generation of cell therapies.

The paper is relevant for the sections “Advances in cell processing: New Techniques for new therapies” and potentially for “Bioprocess modeling for successful commercialization of advanced therapies”

[1] Beckwith, et al (2012). A health economic analysis of clinical islet transplantation. *Clinical transplantation*, 26(1), 23-33.