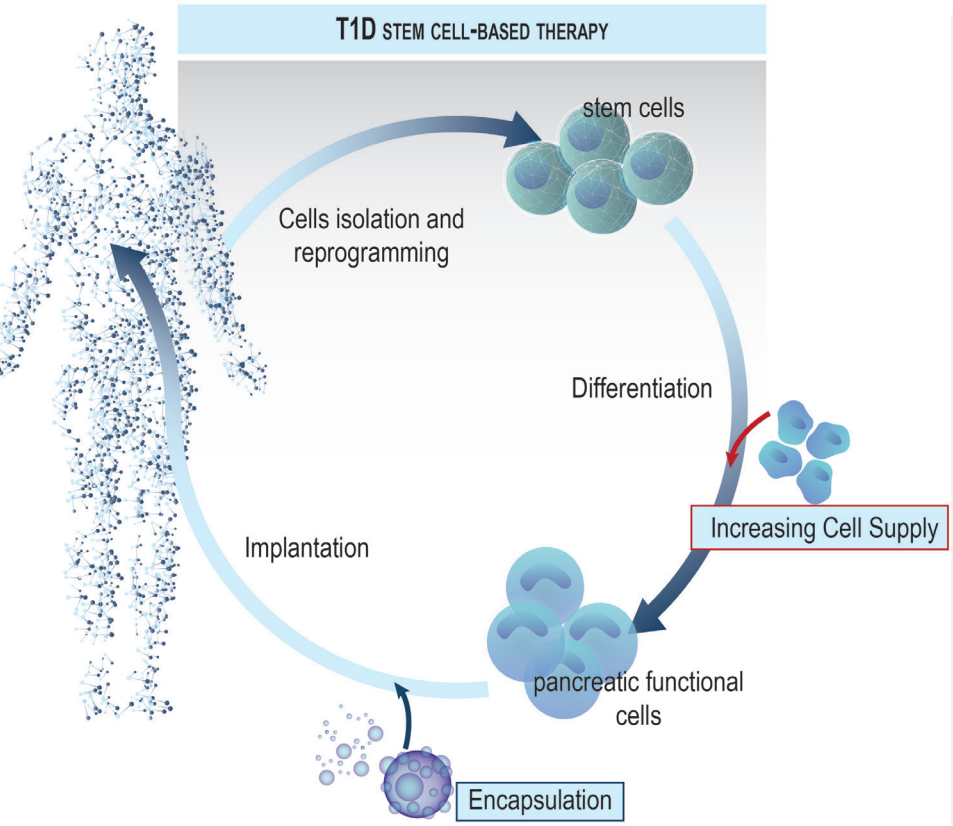
miRNA-BASED STRATEGY TO EXPAND REGENERATIVE THERAPIES IN DIABETES

EXECUTIVE SUMMARY

Type I diabetes (T1D) has no cure and is managed using lifelong insulin injections. Although promising, Regenerative Therapies are still showing a number of limitations, specially related to the maturity and survival of the obtained pancreatic cells. Using our novel microRNA-based technology, we generate **MImoPancreas**: pancreatic organoids able to efficiently produce insulin and with high survival rates. This strategy may represent an encouraging solution to revolutionize the current state-of-the-art for pancreatic cell replacement.



- The market size in Diabetes is outstanding and the expected growth is about 4% CAGR in the next few years. As a promise for the near future, Advanced Regenerative Therapies for T1D are currently under development by several companies.
- Current competitive market is trying to develop the technology for pancreatic cell replacement: (i) starting from pluripotent stem cells, (ESCs, iPSCs); (ii) differentiating them to pancreatic cells; (iii) including them in a particular device that allows free traffic of glucose/insulin but does not permit the entry of immune cells (thus avoiding the immune attack).
- Nevertheless, the success is still limited by the insufficient potential of stem cells to (i) survive under challenging conditions; (ii) differentiate and maturate to be functional; (iii) maintain those properties in the long-term.

OUR MISION

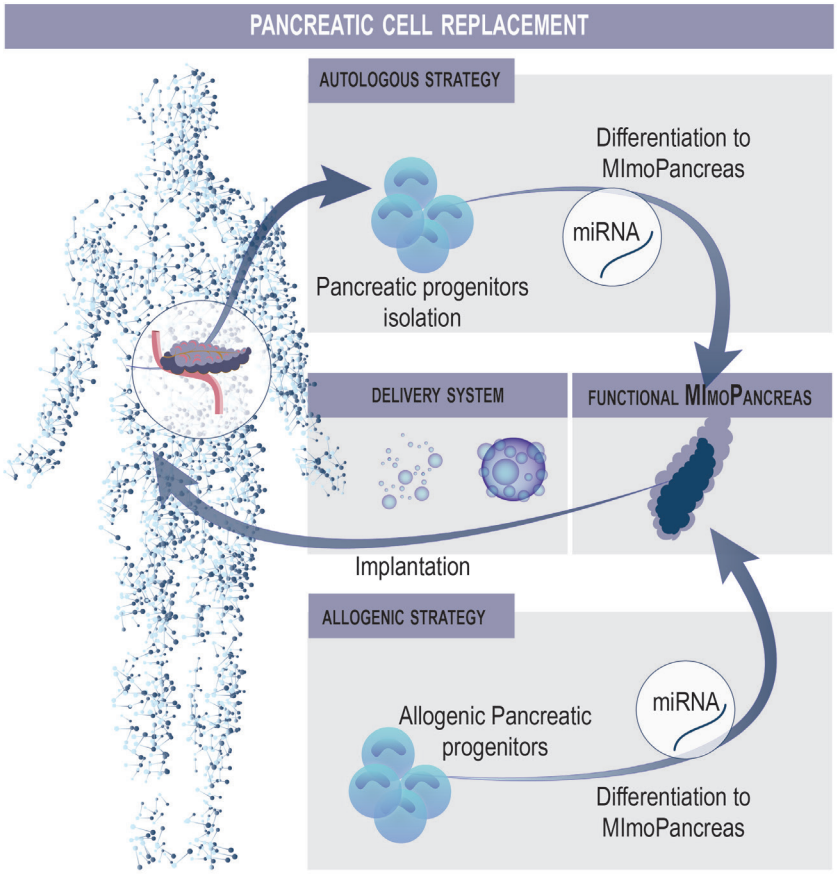
IMPROVED REGENERATIVE THERAPY IN DIABETES. GET CLOSER TO THE DEFINITIVE CURE.

Our technology will overcome the current issues related to beta cell maturation, functionality and stability. We offer a suitable methodology to significantly improve the **stem potential** of the initial material, their **survival** and their capacity to specialize into p**ancreatic mature and functional cells.**

Our mission is improving the technology for pancreatic cell replacement, bringing a definitive cure for Type I diabetes one step closer. The advantage of this protocol is getting pancreatic organoids (i) more mature, (ii) more efficient on insulin production and (iii) more stable in time, compared to the previous published strategies aimed to obtain beta cells in vitro for pancreatic cell replacement. Being organoids, they also include a subpopulation of inmortal pancreatic progenitors, which allow the self-renewal of these structures, their freezing and storage during several months and efficient thaw afterwards, conserving their properties.

María Salazar Roa, PhD. Project Lead
mariasalazarroa@ucm.es
Complutense University , Spain

PROJECT DESCRIPTION



We are **intended to be not only better but different:**

▪ Our novel product, **MImoPancreas**, is much more than a cluster of cells, but a **self-organized** tridimensional structure that accomplishes **different pancreatic cell types together**, working together for a more efficient outcome.
▪ **MImoPancreas** are created from **pancreatic progenitors** (avoiding concerns about pluripotency of ESCs/iPSCs).
▪ Starting from progenitors and following our miR-based strategy adapted to published protocols for organoids generation and maintenance, we generate *in vitro* MImoPancreas: self-organized tridimensional structures that include not only homogeneous and mature beta cells producers of insulin, but also other pancreatic cells (mainly alpha cells, producers of glucagon) working all together for a better control of glucose homeostasis. The miR-based technology makes them **mature, functional and stable.**
▪ The microRNA-based new protocol, transiently applied to **patient-derived or allogenic pancreatic progenitors**, will make them more proficient to differentiate *in vitro*, therefore developing the autologous or allogenic MImoPancreas to be implanted for cell replacement.
▪ **Our miR-based technology has been successfully tested** (i) in multiple applications and (ii) by several collaborators all over the world for several years.
▪ The mechanism of action is epigenetic. The miRNA erases transiently and reversibly the DNA methylation, in a manageable way, to promote better differentiation outcomes afterwards.

MILESTONES

▪ Q1: complete characterization of MImoPancreas *in vitro*.
▪ Q2-Q3: complete dossier of *in vivo* approaches with mouse MImoPancreas: proven efficacy and functionality of the transplanted MImoPancreas in diabetic mice.
▪ Q3: first Innovation Task Force (ITF) meeting with EMA.
▪ Q3-Q4: complete dossier of human settings optimization *in vitro*. miR-based strategy to produce human MImoPancreas properly developed.
▪ Q3-Q4: new patent for MImoPancreas IP protection ready for application. Freedom to Operate (FTO) analysis performed.
▪ Q4-Q5: successful approach to partners for co-developing the encapsulation of MImoPancreas.
▪ Q6-Q7: Development of encapsulated MImoPancreas and first functionality tests.

Q= QUARTER YEAR

We aim to establish **strategic alliances** with companies or lead laboratories on the field, devoted to improve regenerative medicine in T1D. We believe those alliances will definitely reinforce our technology.

María Salazar Roa, PhD. Project Lead
mariasalazarroa@ucm.es
Complutense University , Spain