A miRNA-based strategy to impulse regenerative medicine in Diabetes

A new therapeutic approach for regeneration

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Type 1 Diabetes is AN UNMET NEED

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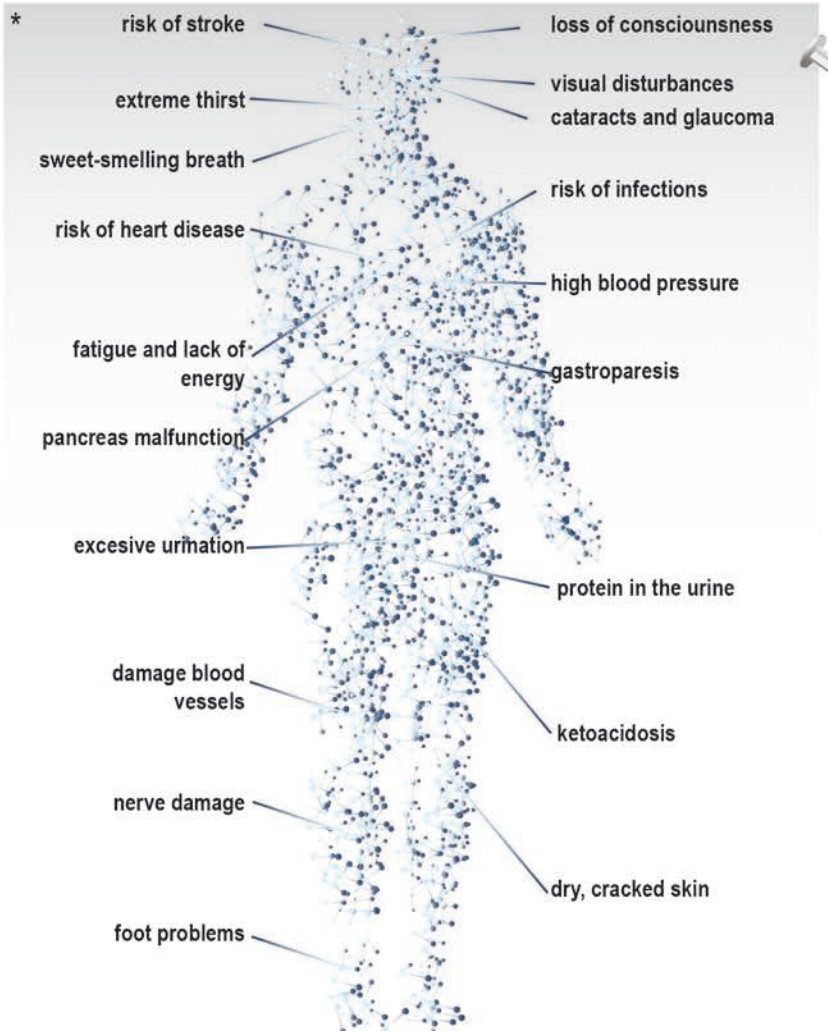
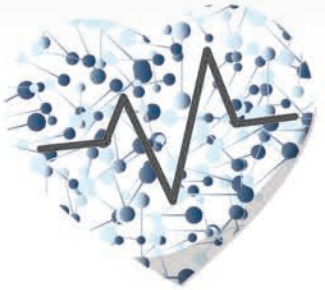
TYPE 1 DIABETES (T1D) is an autoimmune disease that destroys the beta cells, leading to high blood glucose levels and therefore, metabolic failure.**



SOCIAL AND ECONOMIC COSTS

insulin injections
constant glucose control

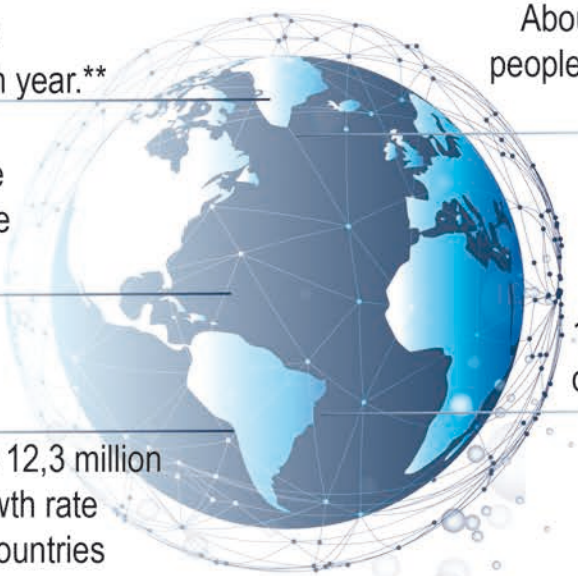
healthy diet and lifestyle



90,000 children diagnosed each year.**

About 10.2 million people diagnosed in 2018

>500,000 children are living with this disease globally**



14.9 billion USD only in US

By 2025, there will be 12,3 million – with the annual growth rate higher in developed countries (Spain leading this list)**

* WHO reports https://www.who.int/news-room/fact-sheets/detail/diabetes

** Katsarou, A. et al. (2017) Nat. Rev. Dis. Primers doi:10.1038/nrdp.2017.16

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T1D Market Opportunity

Market size and expected growth

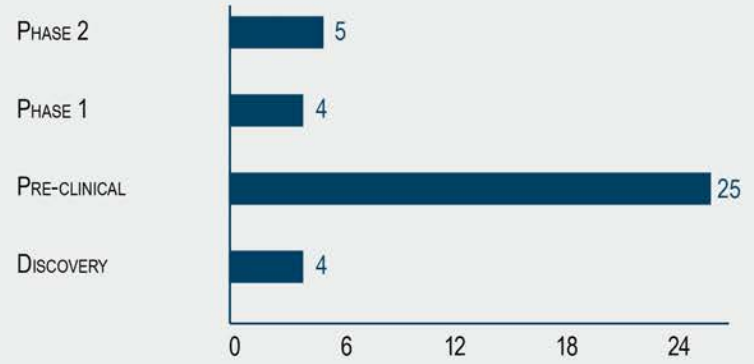
Most innovative drugs in the pipeline still in early stages of development – to be best-in-class.

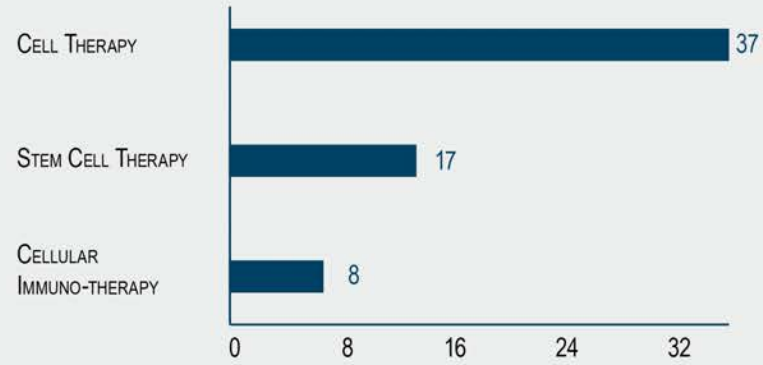
More competition in cell therapy approaches – to leverage investors interest in novel and more efficient approaches in cell therapy

GlobalData from Pharma Intelligence Center Datamonitor Healthcare

CAGR – compound annual growth rate

T1D Pipeline for advanced therapies





THE PROBLEM : regenerative therapies in Type 1 Diabetes show limited success

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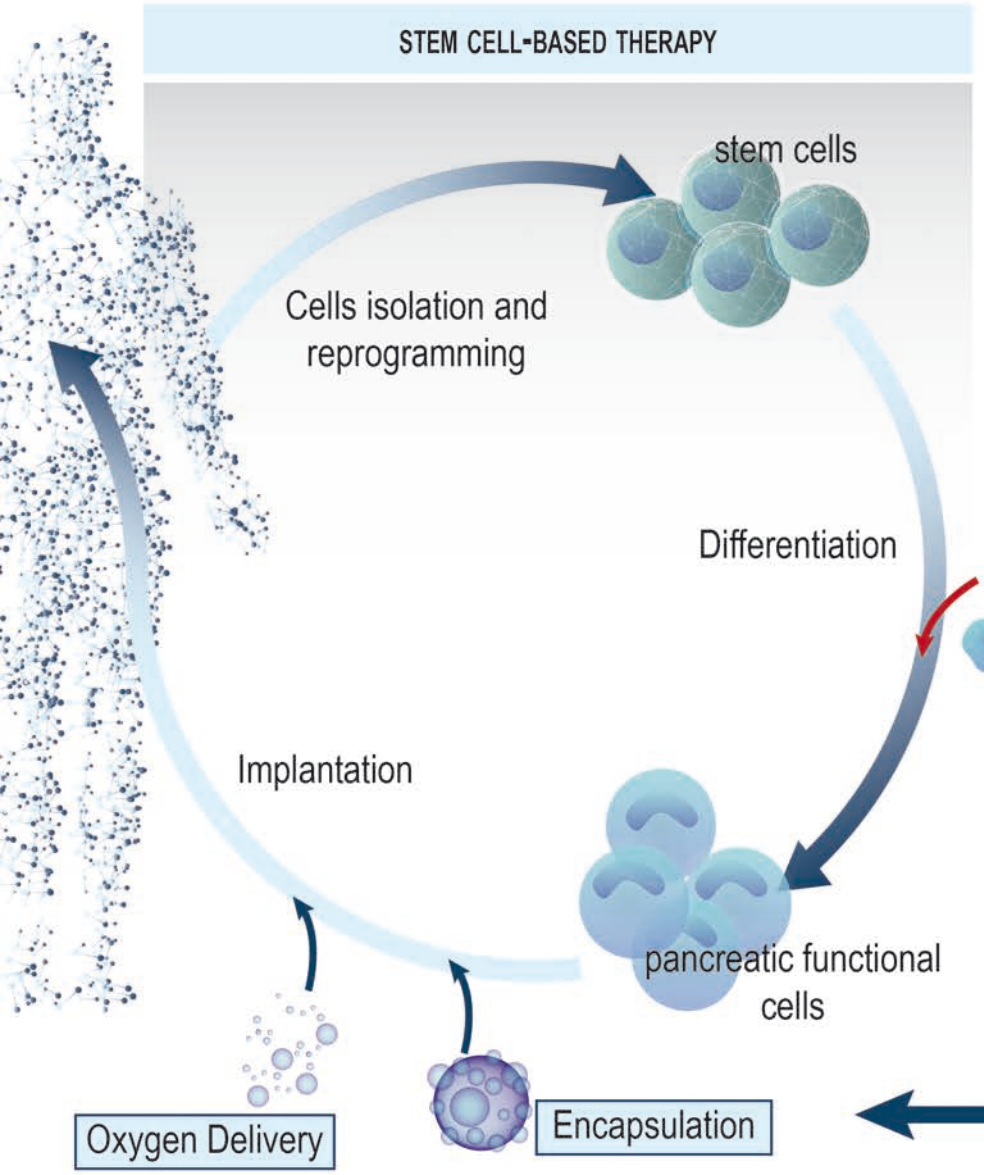

LIMITATIONS

low reprogramming efficiency
poor quality of pluripotent cells
loss of the pluripotent state
poor differentiation potential
lack of maturation properties and funtionality of the generated cells

Possible competitors

Increasing Cell Supply

Identifying, developing and/or regenerating a limitless supply of cells to sense glocuse levels and producing insuline.

Possible partners

Encapsulation

Protective barriers that conforms to the individual size and shape of each islet and allow the free flow of nutrients, glucose and insuline while screening out harmful immune system cells.

Oxygen Delivery

Oxygen generating materials provide the critical oxygen needed until new blood vessels grow.

OUR SOLUTION : A microRNA-based strategy to enhance Stem Cells differentiation potential

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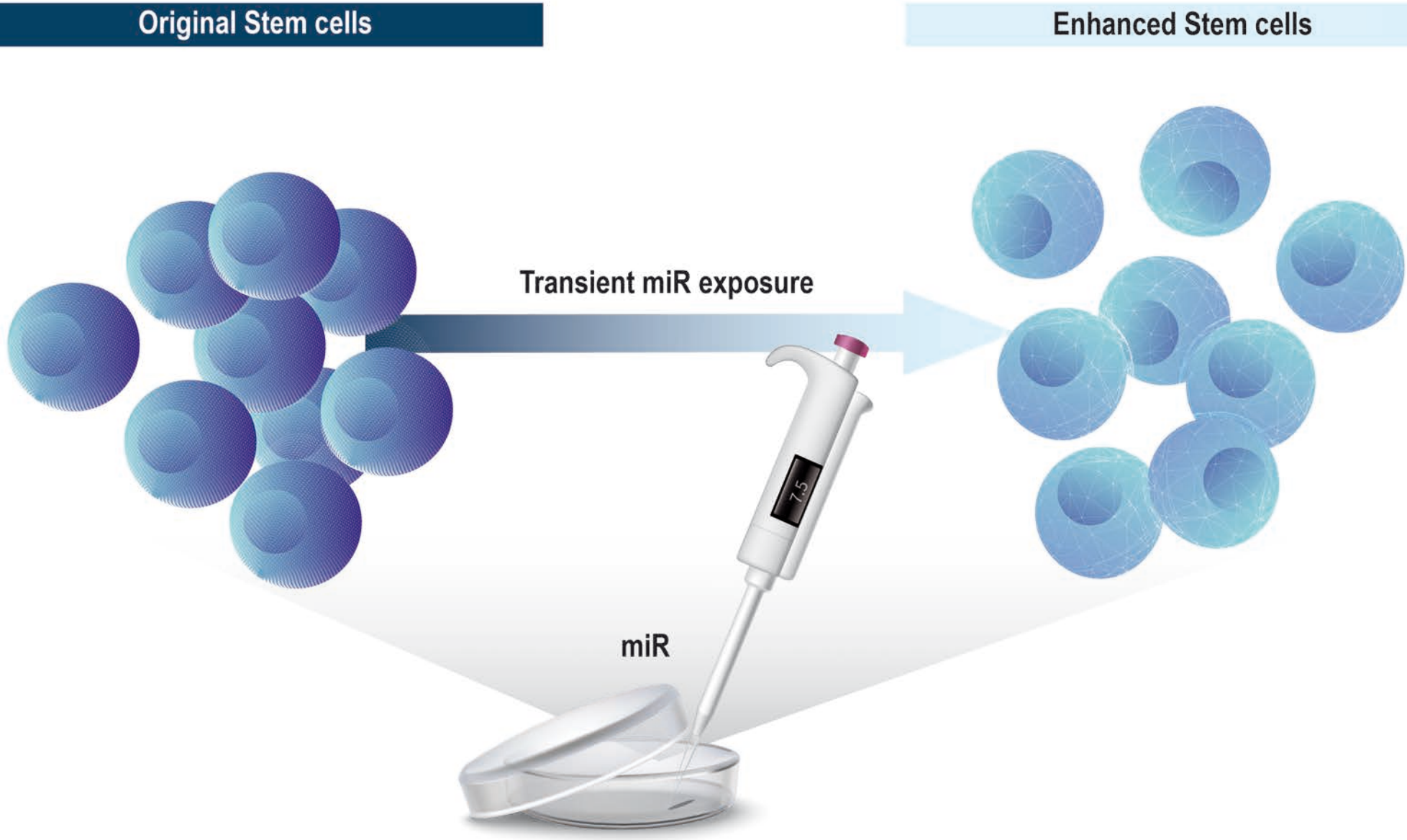
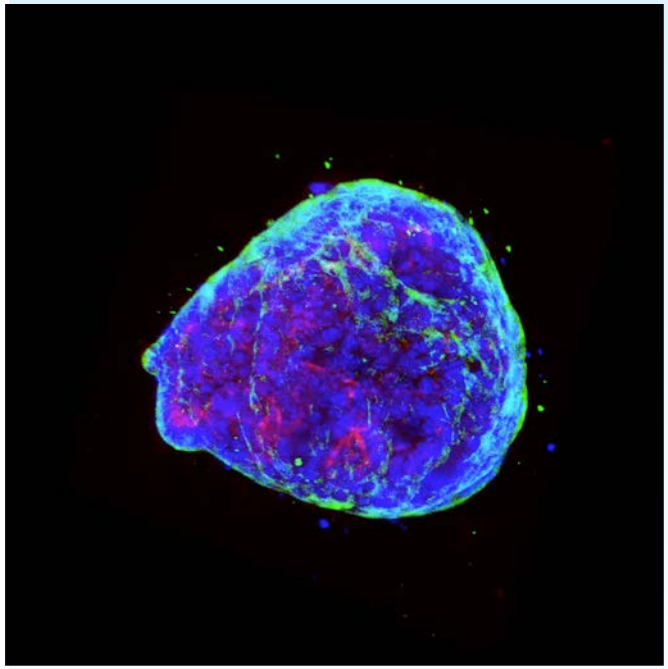
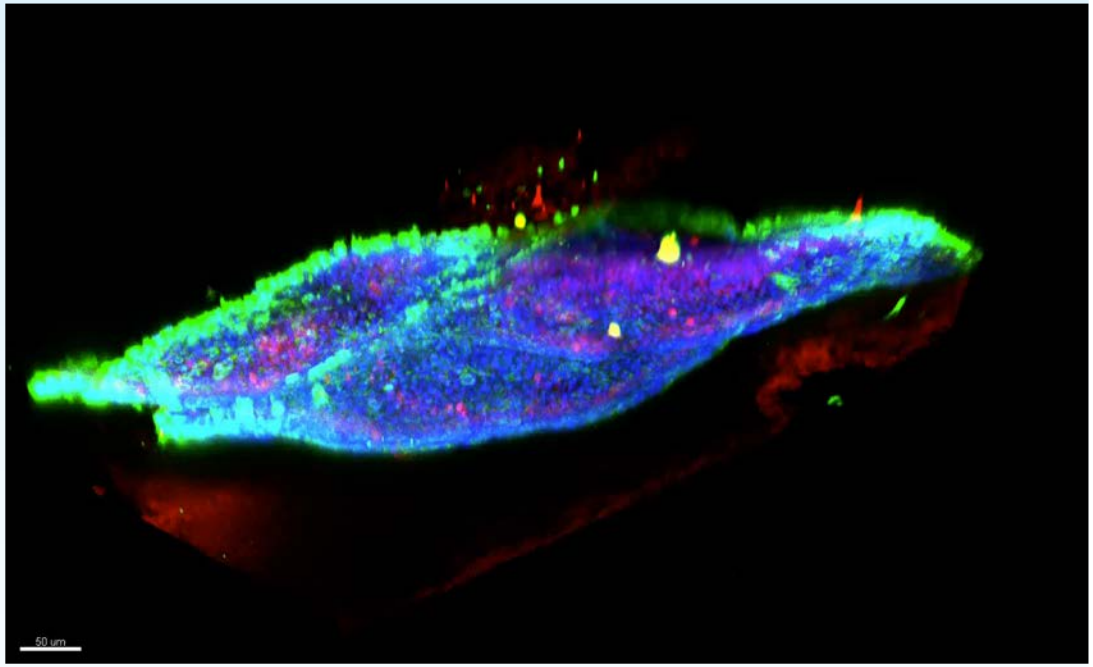


THE PRODUCT : MImoPancreas capable of producing insulin

Our vision: Long-life restoration of blood glucose control



50μm



50μm

Insulin (green); mucin1 (red); nuclei (blue)

• We are intended to be **not only better but different** from our competitors: 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.
Interestingly enough, MimoPancreas are **created from pancreatic progenitors** (avoiding concerns about pluripotency of ESCs/IPSCs).

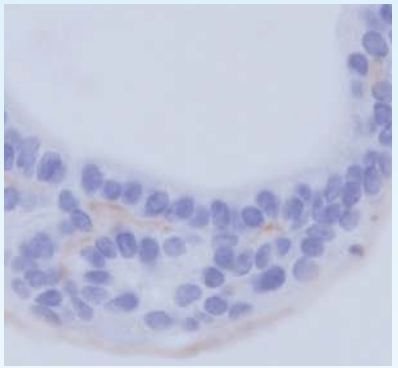
• miR-based technology makes them mature, functional and stable.

THE PRODUCT : MImoPancreas capable of producing insulin

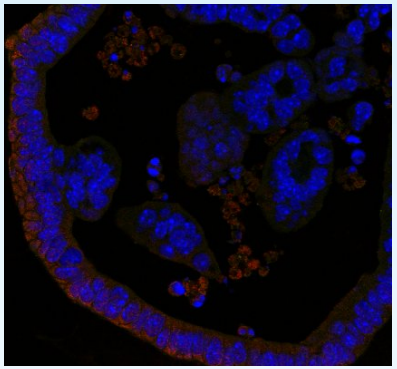
miRNA-exposed pancreatic organoids efficiently generate insulin-producing cells

Control pancreatic organoids

Insulin (IHC)

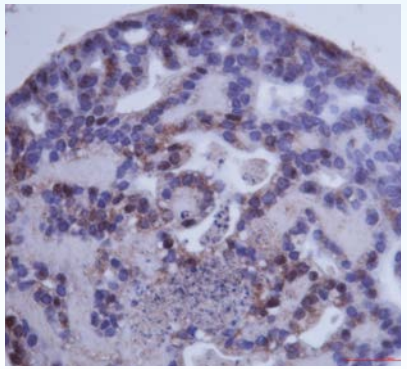


Insulin/ Mucin1/ Dapi (IF)

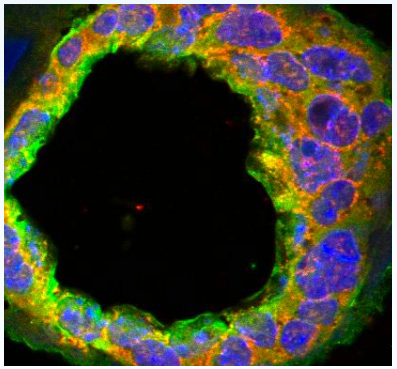


MImoPancreas

Insulin (IHC)



Insulin/ Mucin1/ Dapi (IF)



THE MECHANISM OF ACTION of our miR, deeply studied during the last 5 years on stem cells

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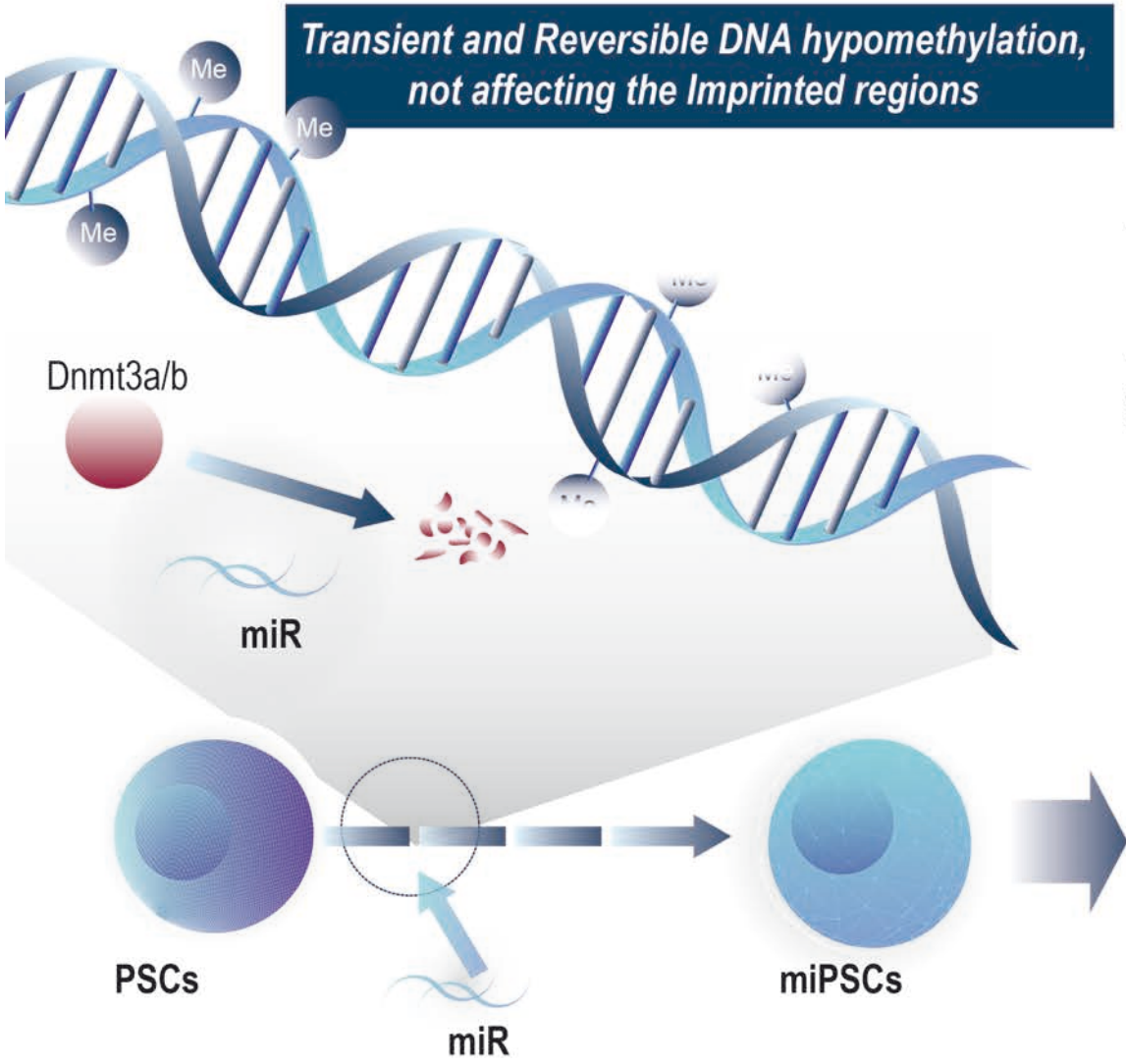
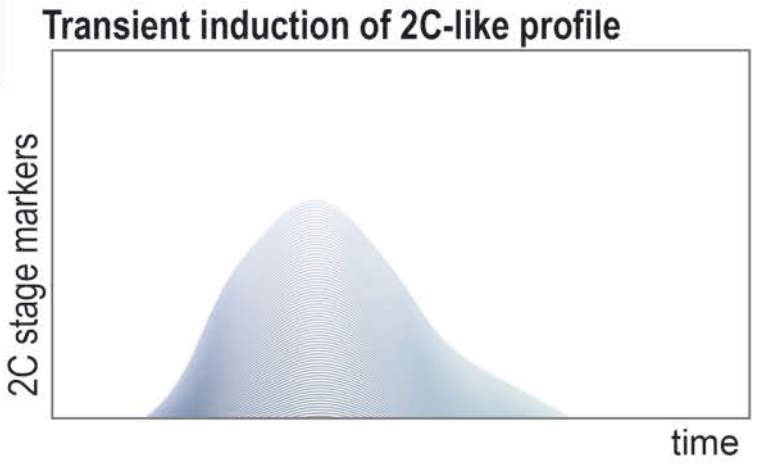
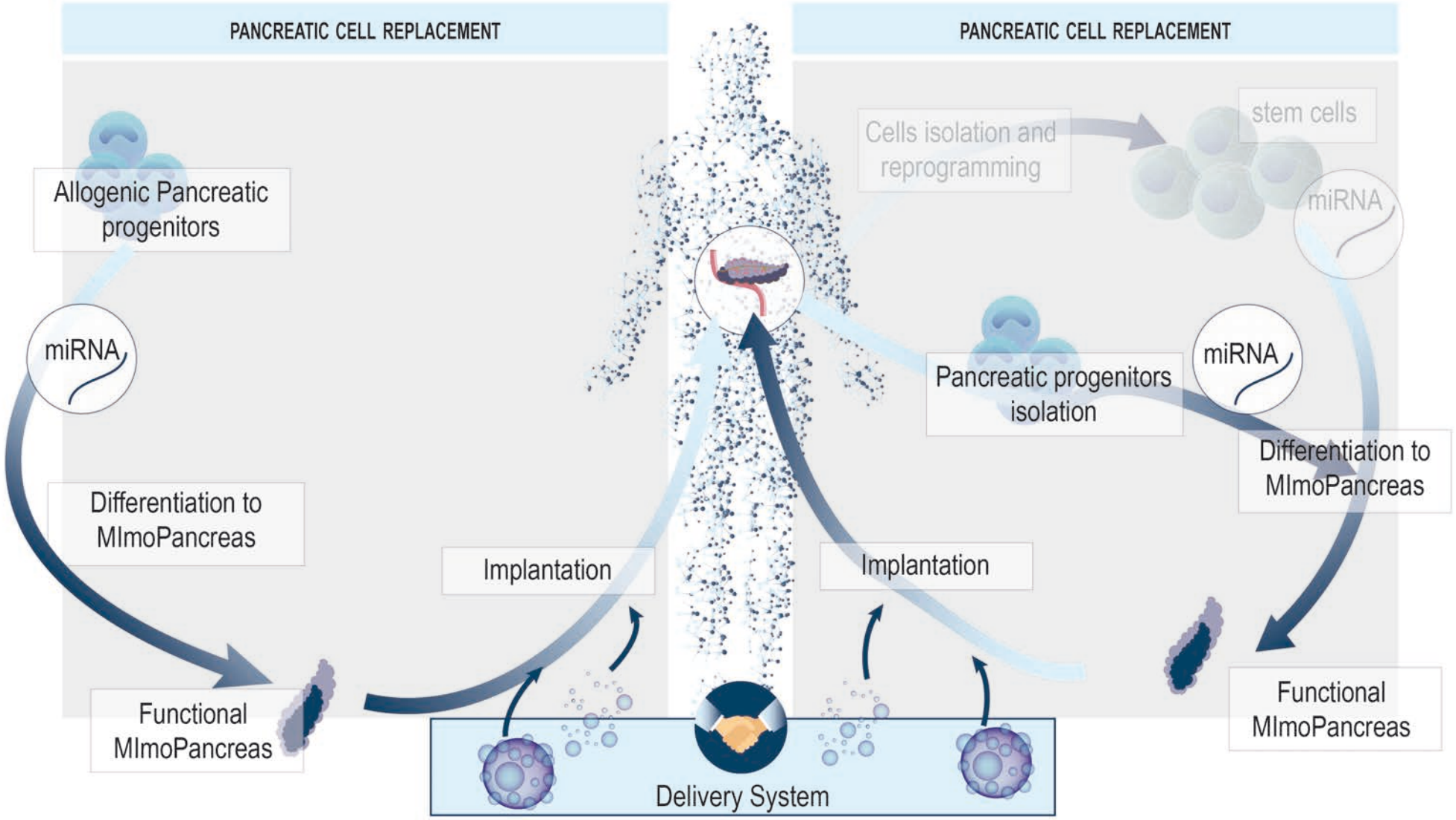




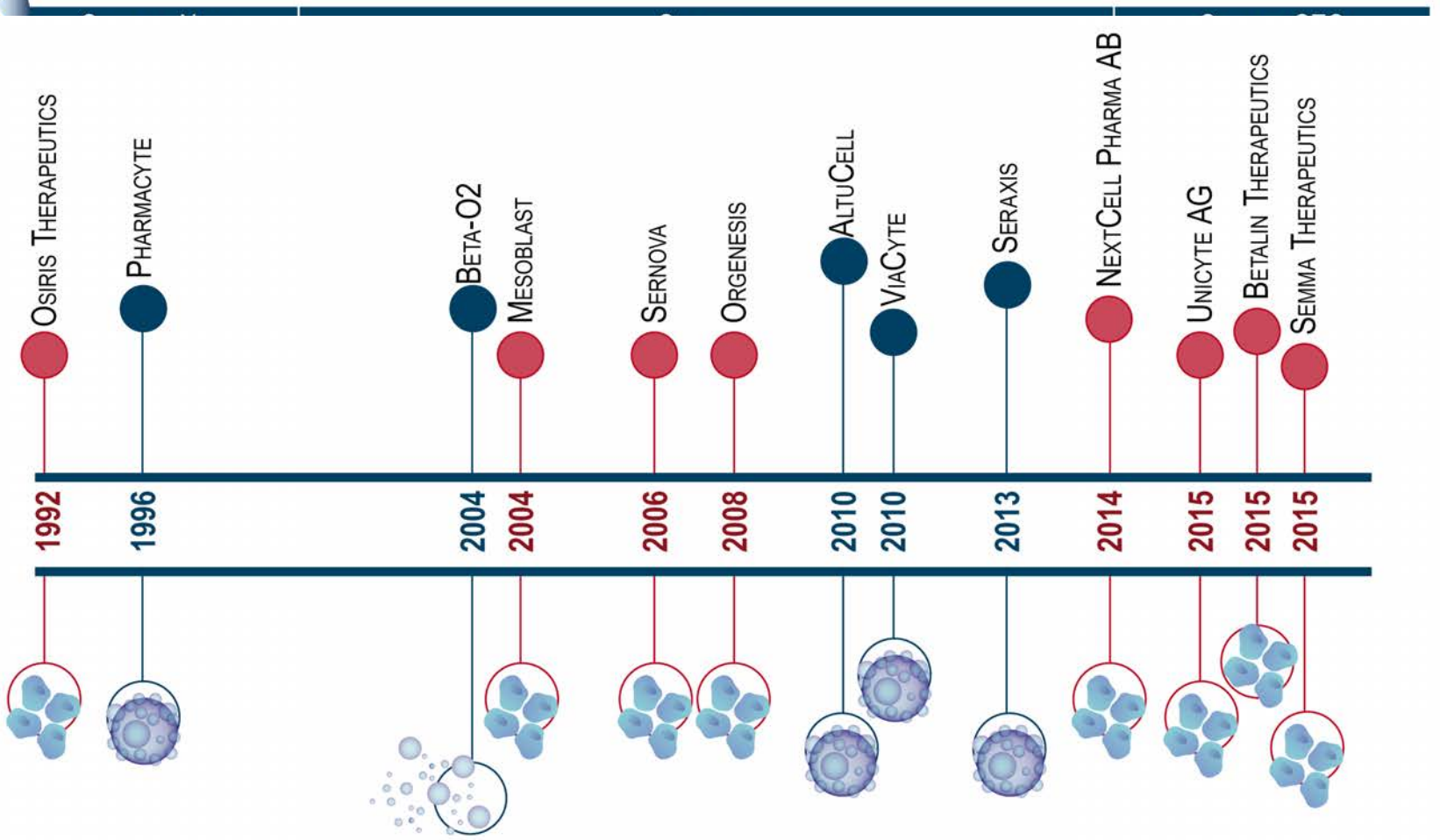
increased differentiation potencial

- embryoid bodies
- teratomas
- embryo-like structures
- 2n mouse chimeras
- 4n mouse complementation
- human-mouse interspecies chimeras
- tissue-specific development (i.e. cardiomyocytes...)

THE TECHNOLOGY : MImoPancreas for cell replacement

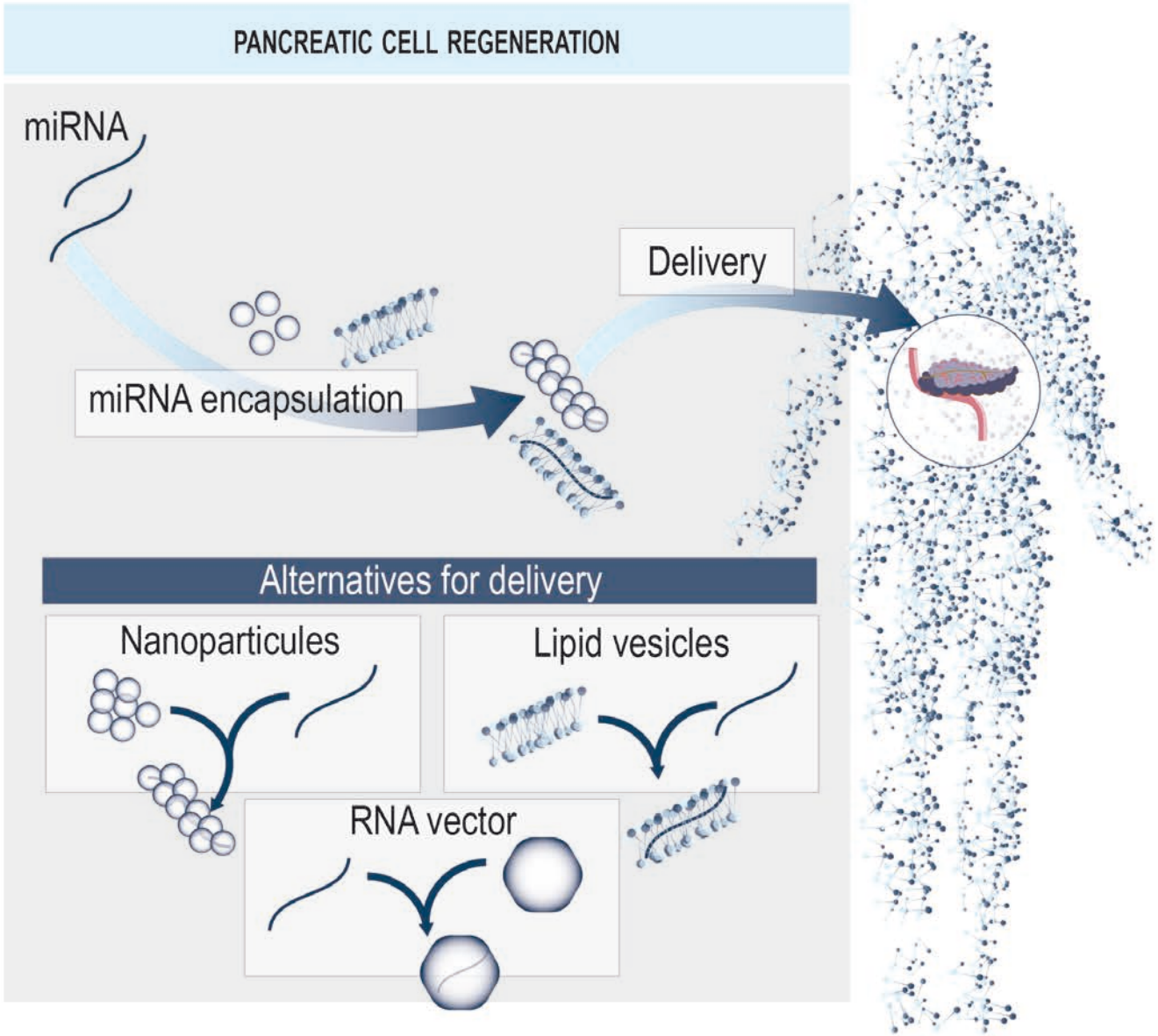


Top companies trying to develop Cell Therapy for T1D : our STRATEGIC ALLIANCES



Unicyte AG	Pancreatic islets derived from Human liver stem cells	CEO: Florian Jehle Web: http://www.unicyte.ch/
Osiris Therap.	Prochymal is an adult human mesenchymal stem cells (MSCs) product	CEO: Samson Tom, PhD Web: http://www.osiris.com/

We have a MITIGATION ALTERNATIVE… miR-based strategy in pancreatic cell regeneration



THE TEAM – stem cell biology frontier research

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MARÍA SALAZAR ROA, PHD
PROJECT MANAGER (CNIO)

MARCOS MALUMBRES, PHD
SCIENTIFIC ADVISOR (CNIO)

CAROLINA POLA, PHD
DIRECTOR OF INNOVATION & INTERNATIONAL AFFAIRS AT CNIO

ADVISORS

Petra Krauledat
(CEO at PNPResearch)
Peter Bryant
(professor at IE Business School)
José Luis Cabero
(CEO at AELIX)
Sotirios Karathanasis
(VP at NeoProgen)

BASIC AND TRANSLATIONAL RESEARCH IN CELL CYCLE AND STEM CELL BIOLOGY

GEMMs models, drug discovery projects with small molecules, advanced therapy approaches for cell therapy and organoid development.

More than 10 years of experience in technology transfer, scientific communications and innovation

OTHER TEAM MEMBERS

- Carolina Villarroya, PhD *Junior Postdoc*
- Nuria García, *PhD student*
- Aicha El Bakkali, *Technician*

SCIENTIFIC APPROACH AND CAPABILITIES

Mouse models to study the cell cycle machinery

Mechanisms regulating the cell division cycle and its effects on cell fate, disease and therapy

Function of microRNAs in stem cell biology, regenerative medicine and tumor development

How progenitor cells and cancer stem cells control their self-renewal and proliferative properties

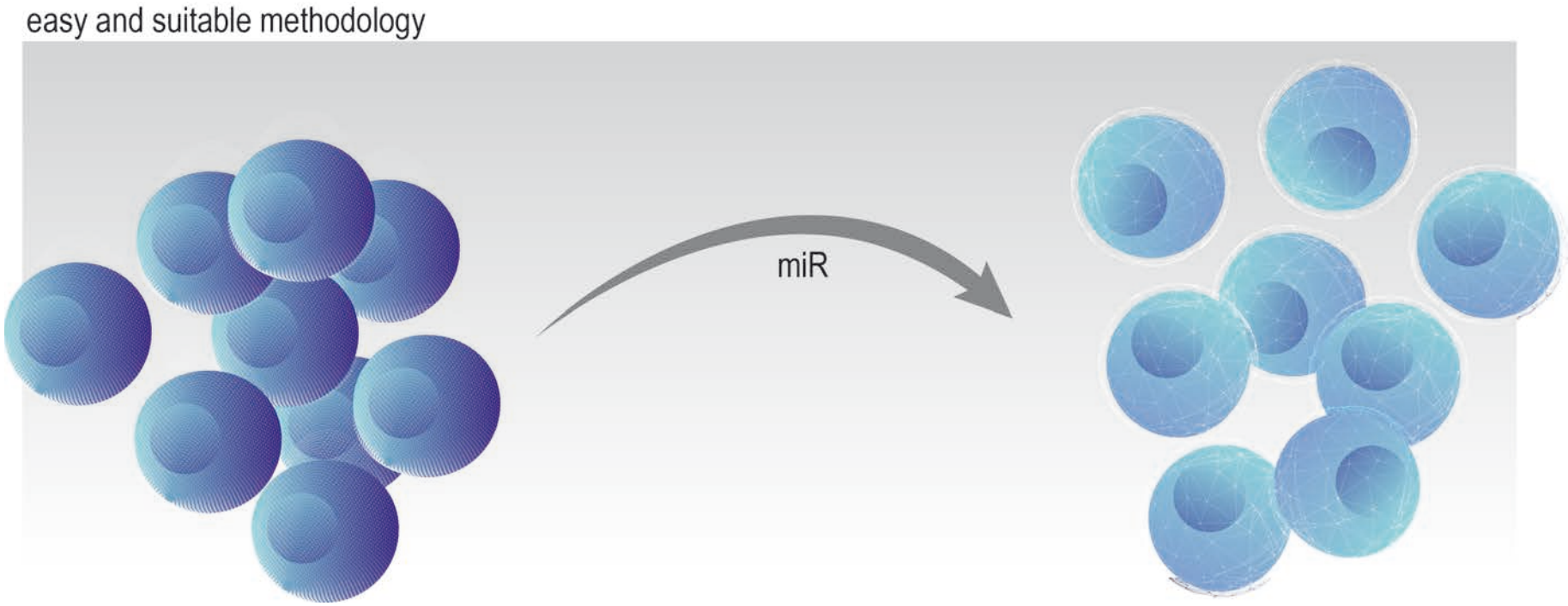
DISCOVERIES AND INNOVATIONS

Role of CKD4/CDK6 in cancer and disease mouse models

Cell cycle-dependent kinase Plk1 as regulator of vascular homeostasis

PP2-inhibitory kinase MASTL as a potential target for cancer – PoC *in vitro* and *in vivo* and drug discovery campaign ongoing.

Mouse models for miRNAs, with relevant properties in self-renewal and differentiation of stem cells.



…REVOLUTIONIZING REGENERATIVE THERAPY for **Type 1 Diabetes**

UPDATE for IDEA^2: key accomplishments

- We have **refined the sales pitch.**
- We are working on our **valorisation plan**. Our deadline to finish the document is November 8th.
- We are developing **new sets of experiments** on the lab to reinforce the original data. Getting ready to build a solid proof of concept.
- We are starting to set up the *in vivo* experiments, using Diabetes mouse models.
- We are applying to different competitive calls for getting funding and a PhD student to accomplish our PoC.

We are **mentored by three experts** on business, technology transfer, finance and commercialization tools: **Petra Krauledat** (Principal owner and Chief Executive Officer at PNPResearch Corporation; IDEA^2)**, Peter Bryant** (professor of entrepreneurship at IE Business School) **and José Luis Cabero** (life science manager, mentor and advisor- Chief Executive Officer at AELIX Therapeutics). They monitor our work and we have frequent meetings to follow up. We are also mentored by an expert on the field, **Sotirios Karathanasis** (Vice President R&D at NeoProgen).

We are **in conversations with Christopher Mann** (Scientific Regulatory Associate Director in *Asphalion*).
Chris and his team are experts on advanced therapies in endocrine diseases, and they are of great value to define the easiest and accessible strategy, in terms of Regulatory.

We are **in conversations with Gustavo Fuster** (European patent Attorney in Hoffmann Eitle).
He will help us to reinforce our patent and define the new IP protection, based on this project.

A miRNA-based strategy to impulse regenerative medicine in Diabetes

A new therapeutic approach for regeneration

María Salazar-Roa, PhD
Staff Scientist at CNIO
msalazar@cnio.es
linkedin/maria-salazar-roa

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