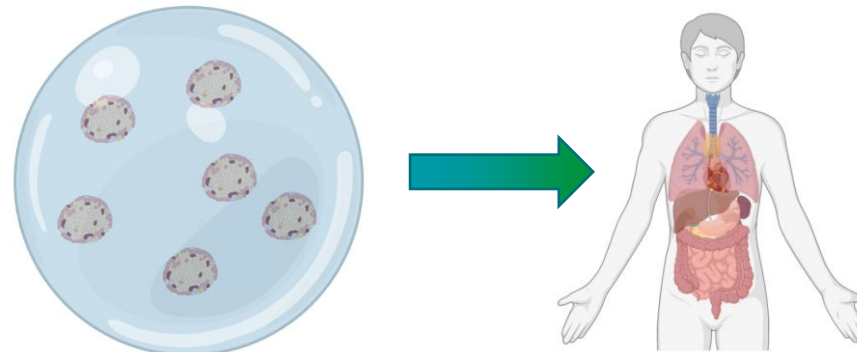


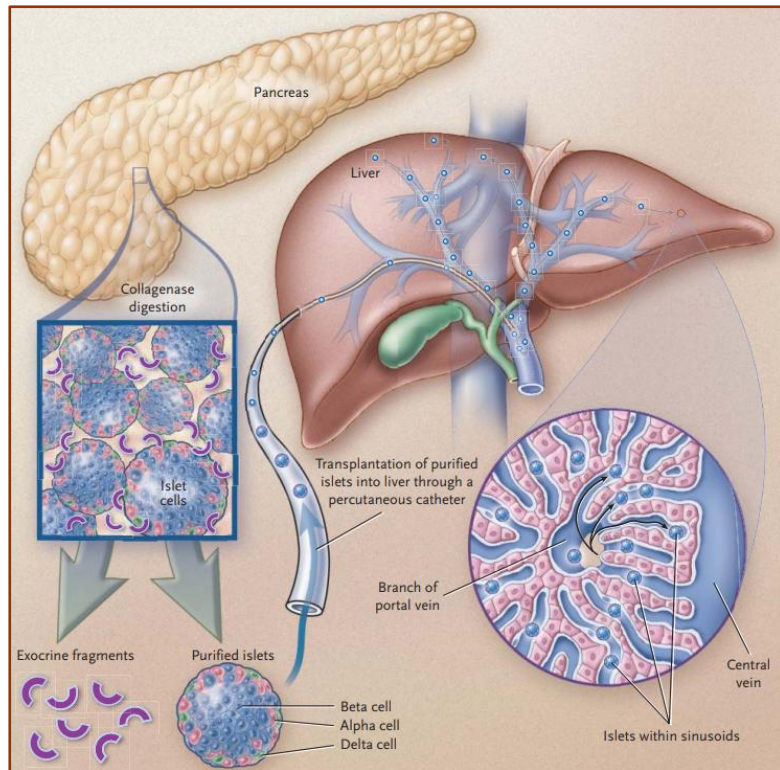
ADO12, a new allogenic islet encapsulation device for islet transplantation without immunosuppression

Anne-Lise Gaffuri, PhD

*A. Geissler, O. Jouannot, X. Gaume, C. Gautier, Y. Courbebaisse,
R. Eloy, K. Bouzakri, O. Soula*



Islet transplantation



R. Paul Robertson. The New England Journal of Medicine, 2004

Life-long immunosuppression

Toxicity to grafted islets

Increased risk of developing malignancies

- Lymphomas, malignancies of the skin

Increased risk of developing infections

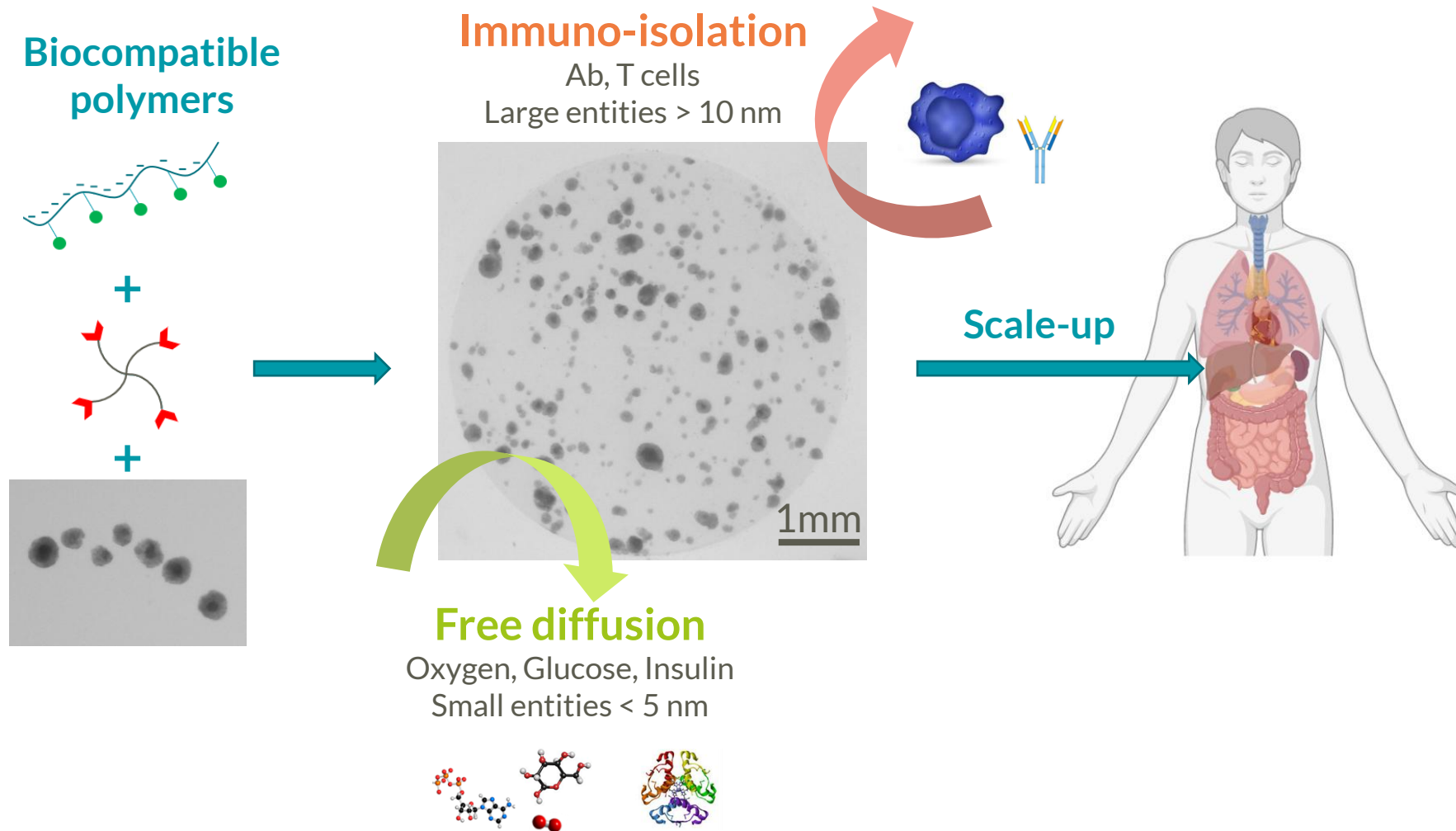
- Bacterial, viral, fungal, and parasitic infections, including parasitic infections

Anemia

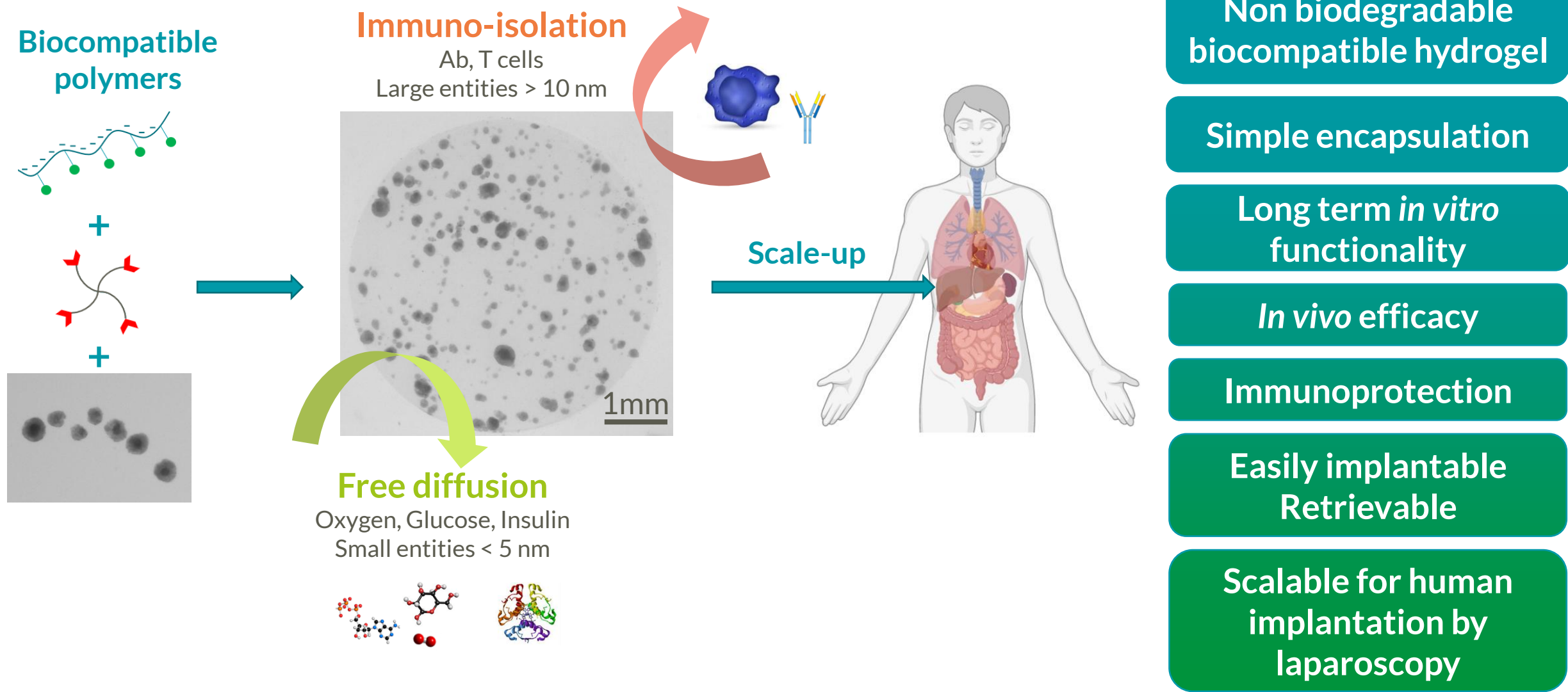
- Sometimes requiring transfusion

Donislecel-jujn, Lantidra, FDA

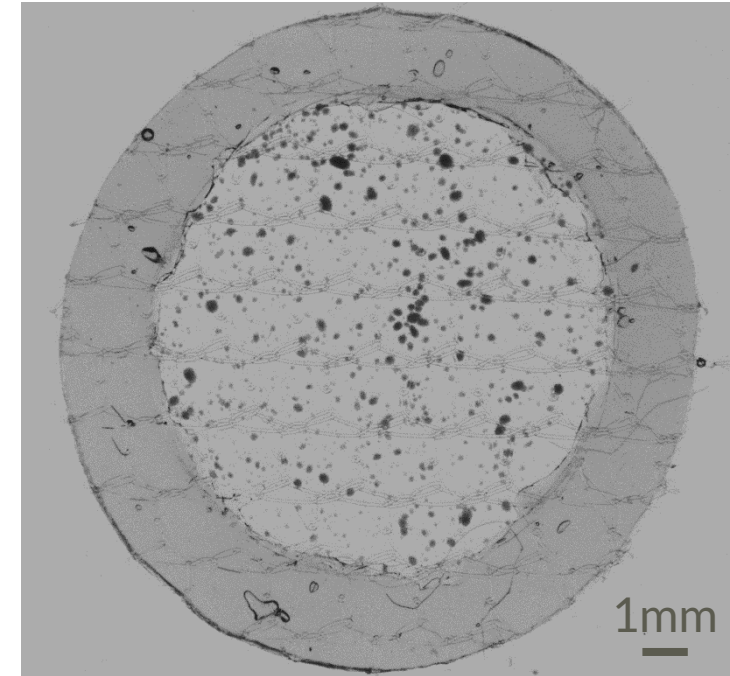
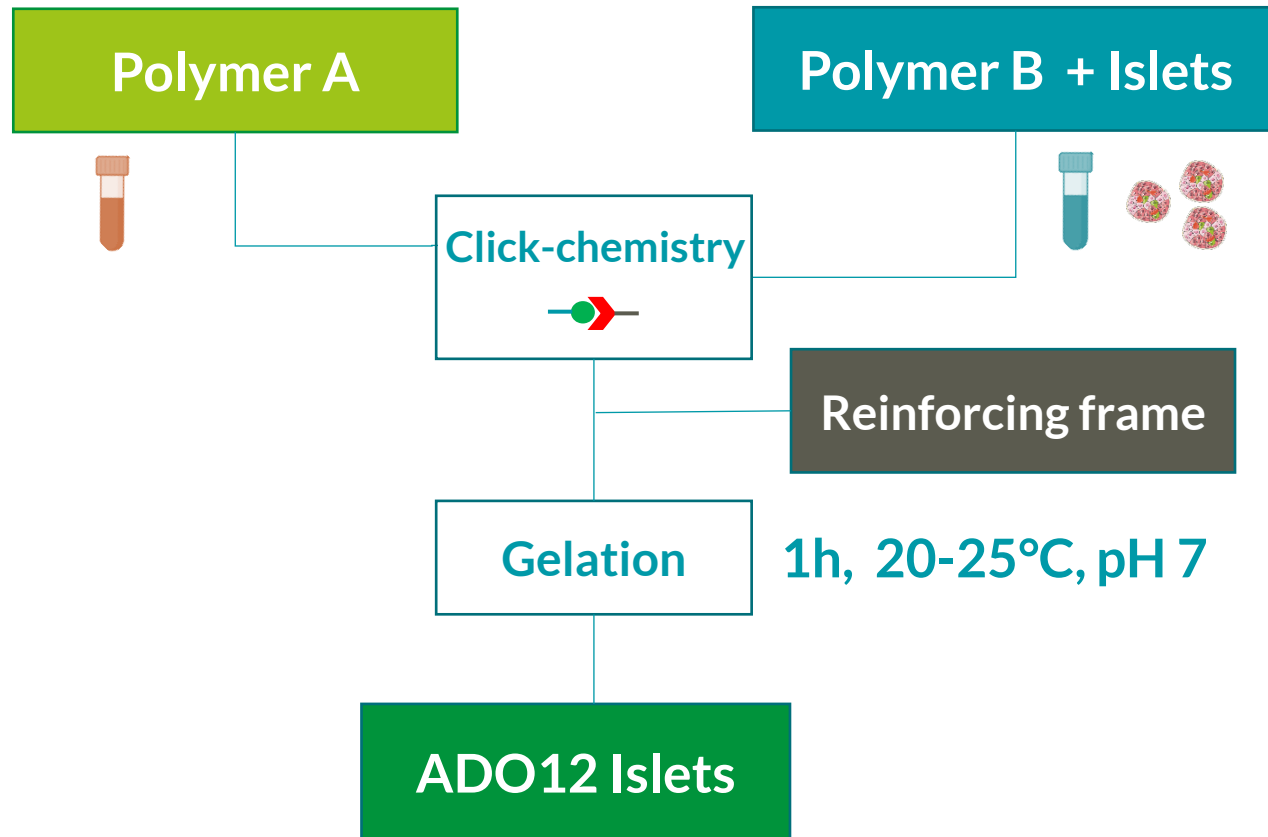
ADO12: Immunoprotective Hydrogel for Pancreatic Islets



ADO12: Immunoprotective Hydrogel for Pancreatic Islets



ADO12: Aqueous Encapsulation Process



Simple and biocompatible process including reinforcement frame for mechanical resistance, manipulability and suturing

Objective & Plan

Demonstrate that ADO12 is a biocompatible immuno-isolant biomaterial for islet transplantation without immunosuppression

1

In vitro functionality

Long-term *in vitro* functionality of encapsulated islets

2

Biocompatibility

Local tolerance of the biomaterial in rat, rabbit, and pig

3

In vivo functionality

Long term survival of encapsulated islets in STZ rats

4

In vivo efficacy

Ability to control hyperglycemia in STZ rats

1

2

3

4

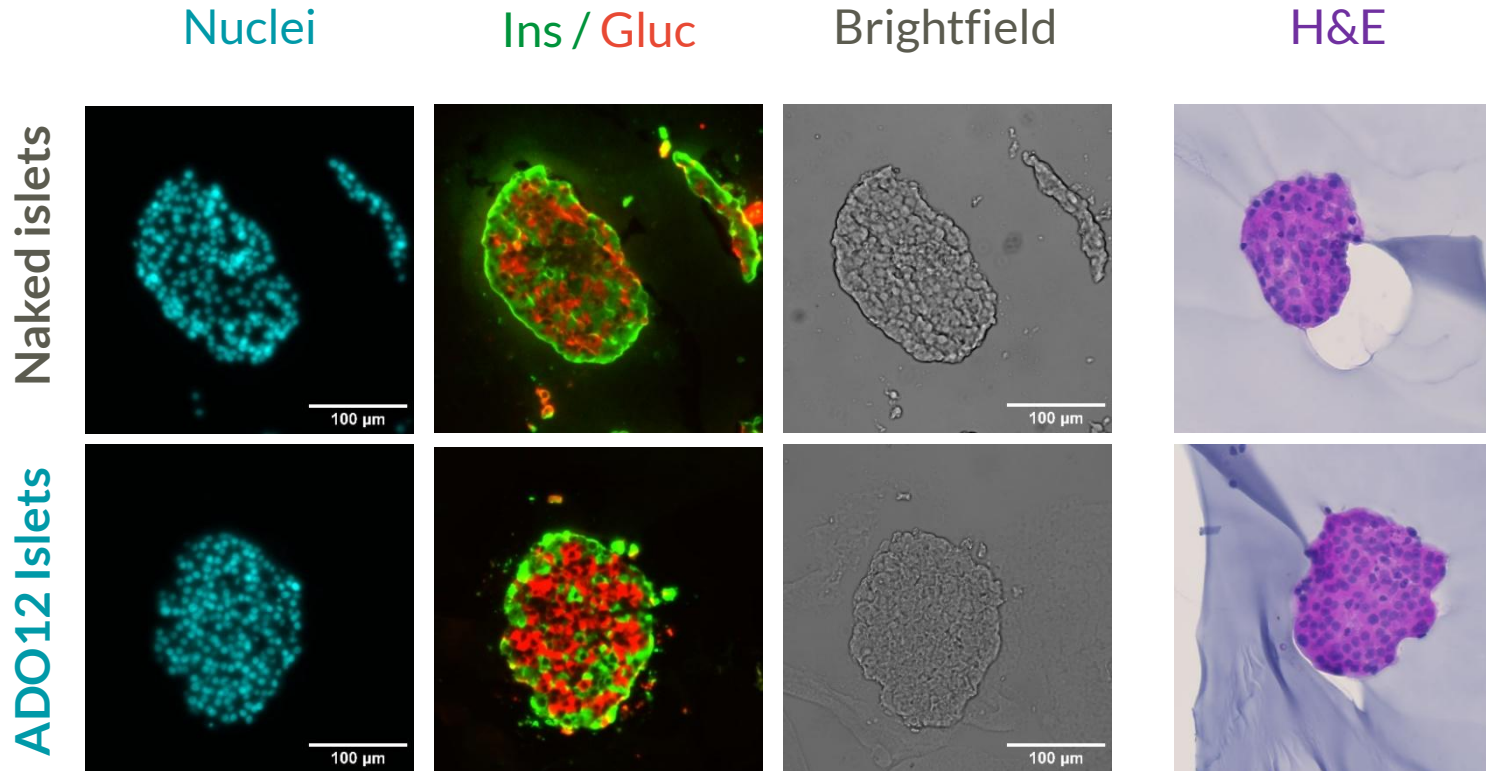
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In vitro characterization of ADO12 Islets

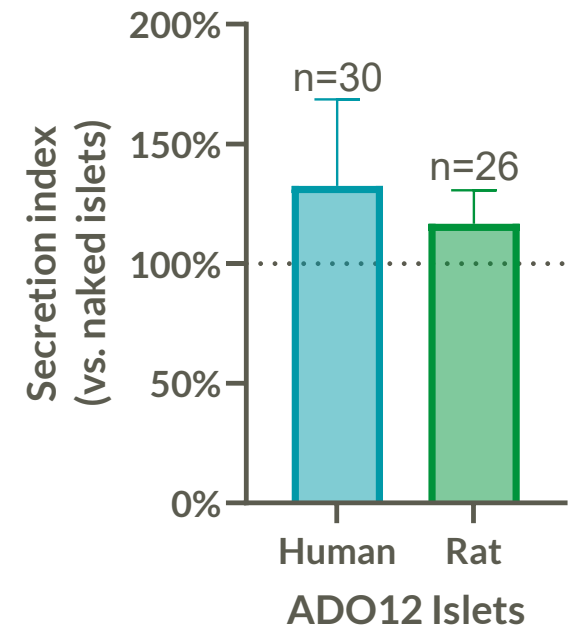
Human Islets, tested within 1 week

Dynamic GSIS, up to 2 weeks

N=7 Human preparations
N=6 rat preparations



Secretion index



Encapsulation in ADO12 maintains human islet morphology
ADO12 demonstrates a reproducible compatibility with islets

1

2

3

4

5

In vitro long-term functionality of ADO12 Islets

ADO12 Islets from N=6 human preparations, tested after up to 4 months (Dynamic GSIS)



Robust *in vitro* functionality of encapsulated human islets

No loss of functionality over at least 4 months, while naked islets are lost after 1 month

1

2

3

4

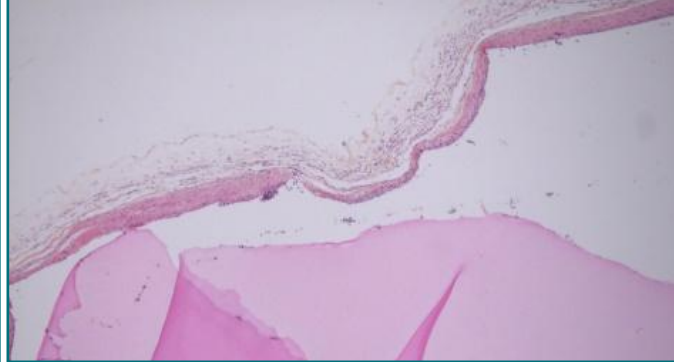
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ADO12 Islets Tolerance in Animal

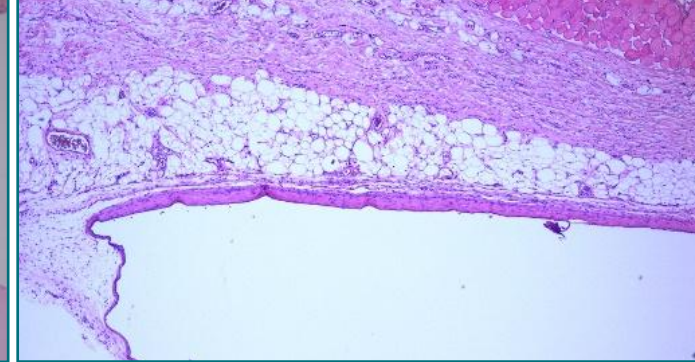


ADO12

3 Months Rat SC



1 Month Rabbit SC



ADO12 Islets

7 Months Rat peritoneum / Allo



- ✓ No cell infiltration
- ✓ No fibrosis
- ✓ No inflammation
- ✓ No degradability

Well tolerated in different tissues of different species
No cell infiltration in the hydrogel as required for immunoprotection

1

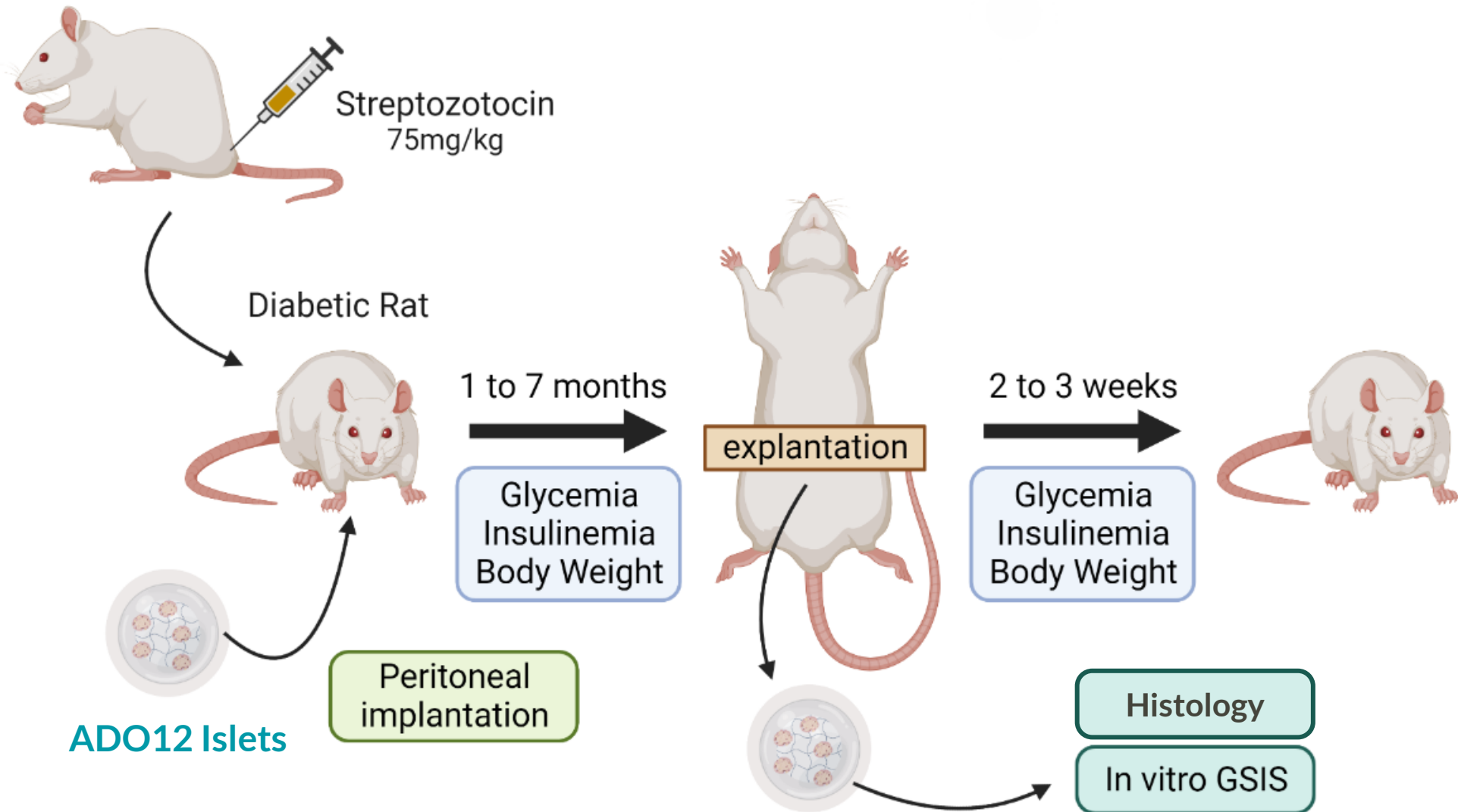
2

3

4

5

Islets Transplantation in Diabetic Rats: Study Protocol



1

ADO12 Islets:

2

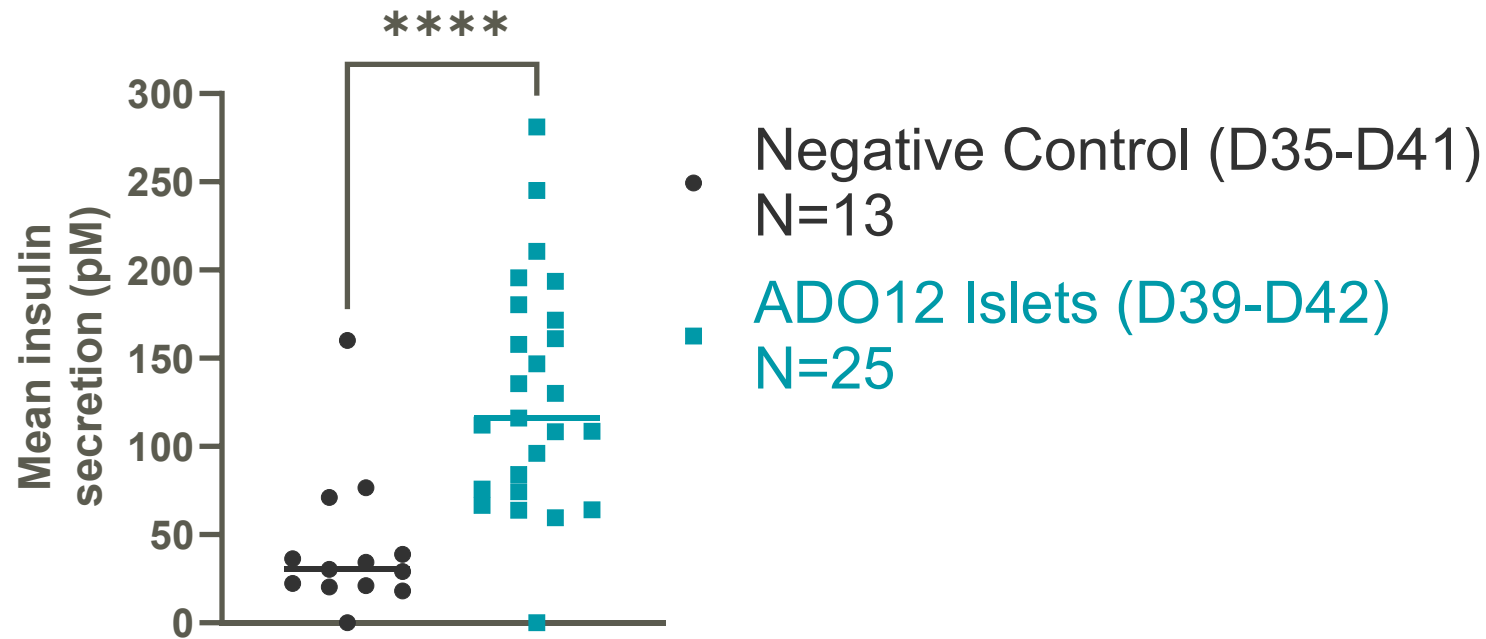
in vivo insulin secretion in immunocompetent diabetic rats

3

- Allogenic transplantation of ADO12 Islets in STZ diabetic rats at ~5kIEQ/rat
- Circulating insulin 35-42 days after implantation (5 independent studies)

4

5



Robust secretion of insulin of implanted encapsulated islets over 1 month

1

2

3

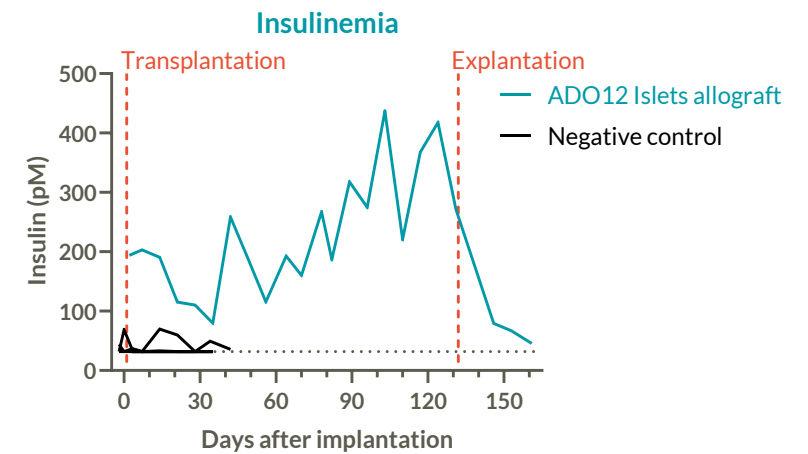
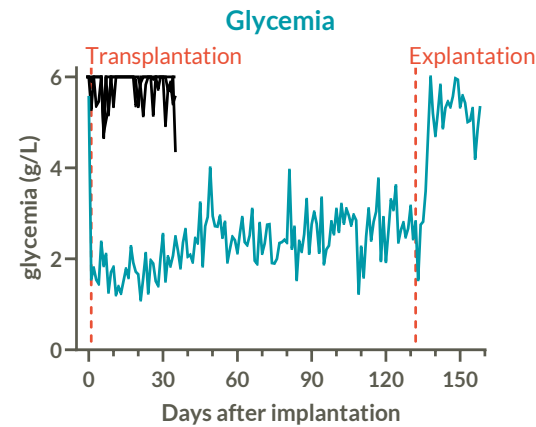
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In vivo efficacy in a diabetic immunocompetent rat model

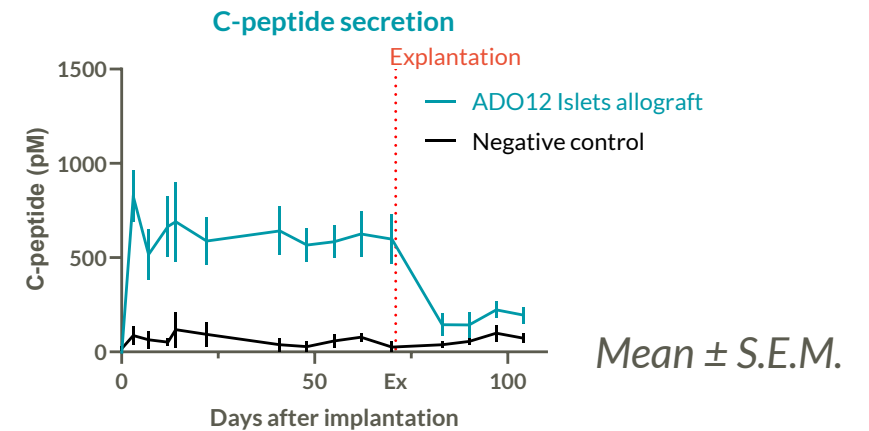
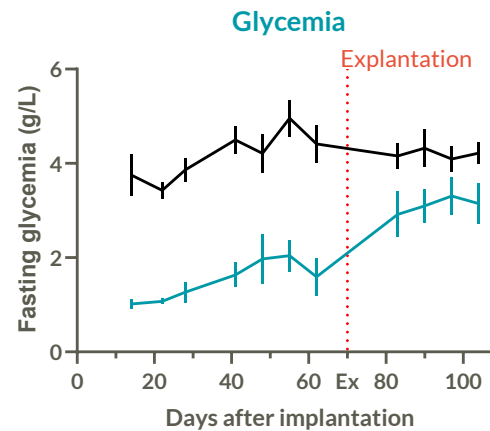
Study 1

Allogenic Tx into
immunocompetent STZ rats
(4kIEQ/rat)



Study 2

Allogenic Tx into
5 immunocompetent STZ rats
(21kIEQ/rat)



ADO12 Islets leads to reduction of glycemia paired with steady secretion of insulin
ADO12 Islets demonstrates immunoprotection
Explants were easily and safely retrieved

1

2

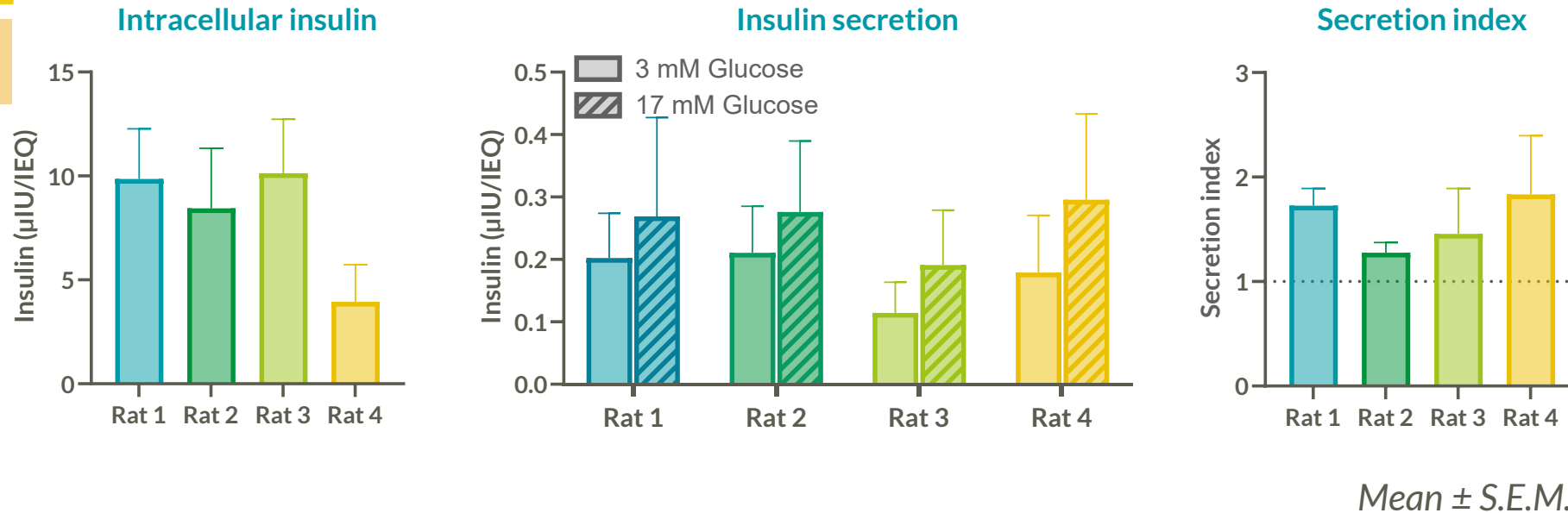
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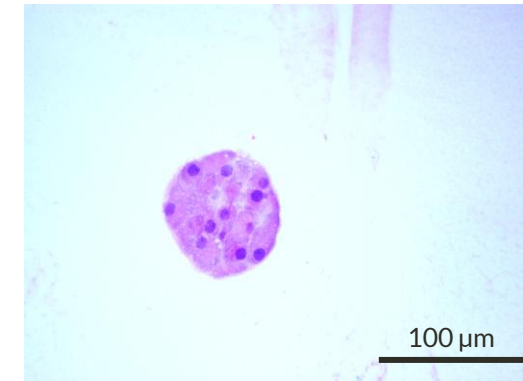
5

ADO12 Islets: *in vitro* explant functionality

- **Allografts** of encapsulated rat islets in STZ immunocompetent rats explanted after 7 months
- Evaluation in static GSIS and histology



H&E



Encapsulated islets explanted at 7 months showed insulin secretion in response to glucose, and intracellular insulin content

ADO12

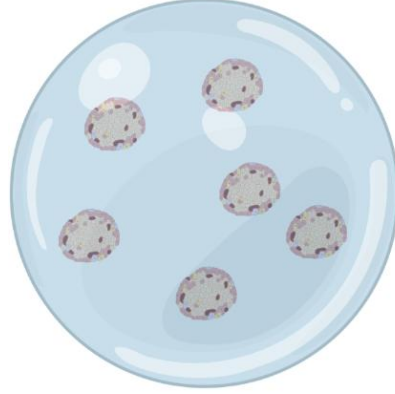


Non biodegradable
biocompatible
hydrogel

Suturable
composite thin film

Easily implantable
and retrievable

ADO12 Islets



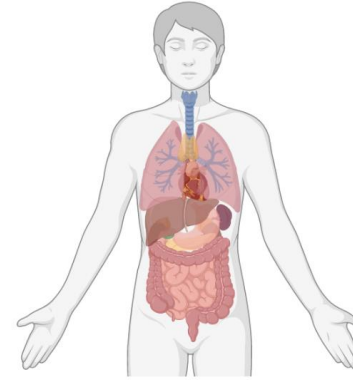
Simple
encapsulation

Long term *in vitro*
functionality

In vivo efficacy

Immunoprotection

Ongoing



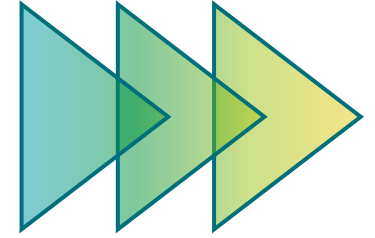
Optimization of *in vivo* Human Islets
function and efficacy

Scale up and
surgical procedure

Regulatory studies

First in Human

Perspectives



Partnership

Stem cells derived
islets

Other cell therapy
applications

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ADOCIA

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for everyone, everywhere



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for your kind interest

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