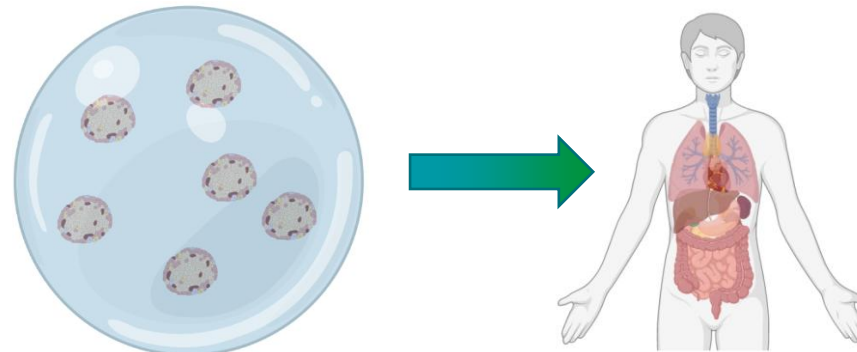


# AdoShell<sup>®</sup> Islets shows long-term *in vitro* and *in vivo* survival and functionality of encapsulated pancreatic islets

Ouardane Jouannot

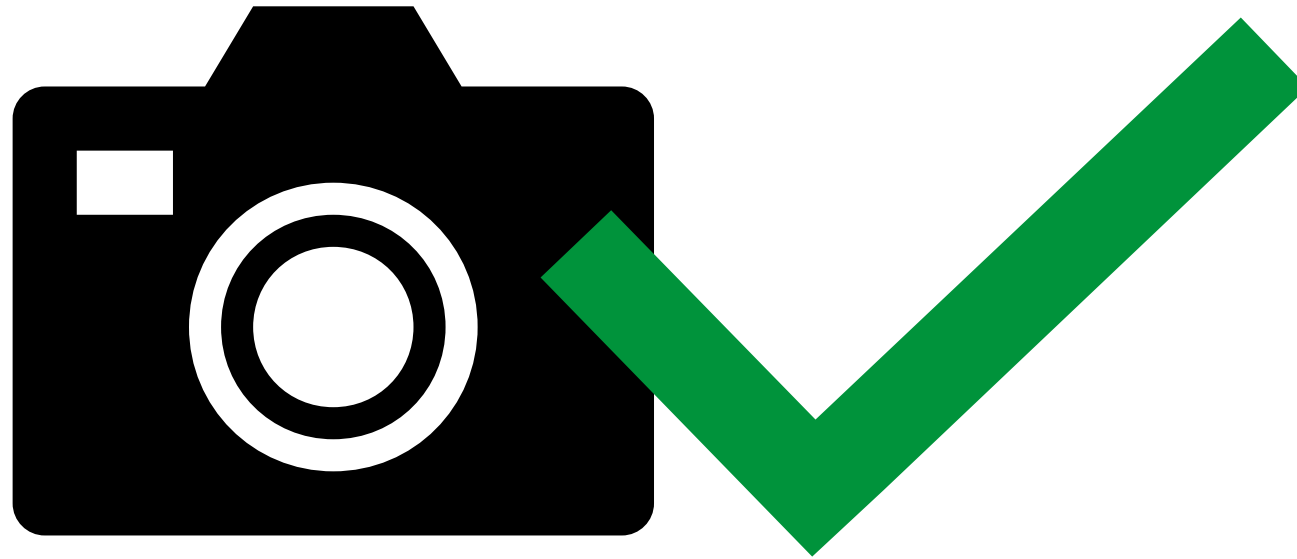
Alexandre Geissler, Anne-Lise Gaffuri, Xavier Gaume, Camille Gautier,  
Yann Courbebaisse, Rosy Eloy, Karim Bouzakri, Olivier Soula



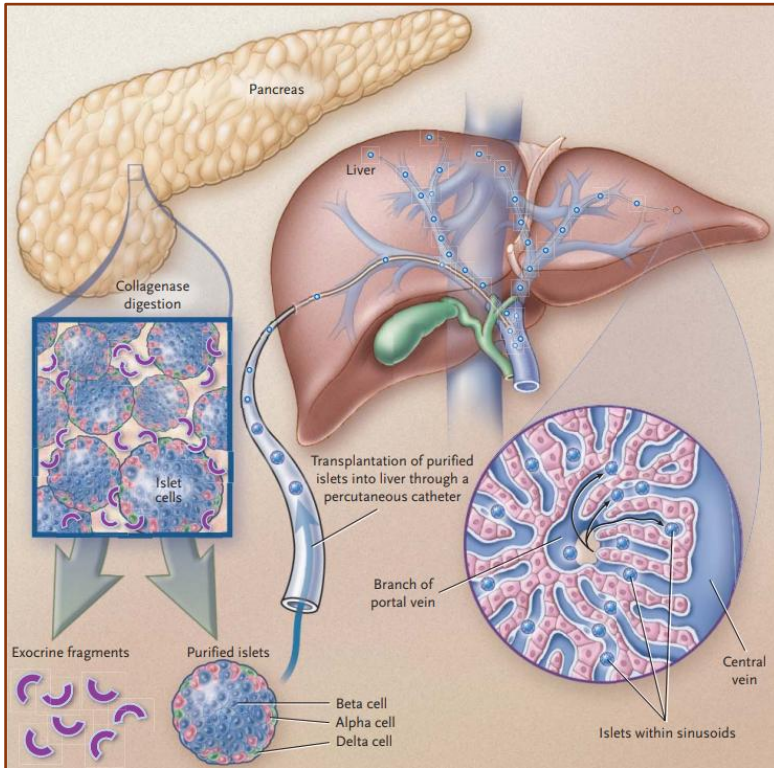
# Presenter disclosure

- Ouardane Jouannot
  - Employee : [ADOCIA](#)
  - Shareholder: [ADOCIA](#)
- Research was conducted by ADOCIA team

Photography is allowed

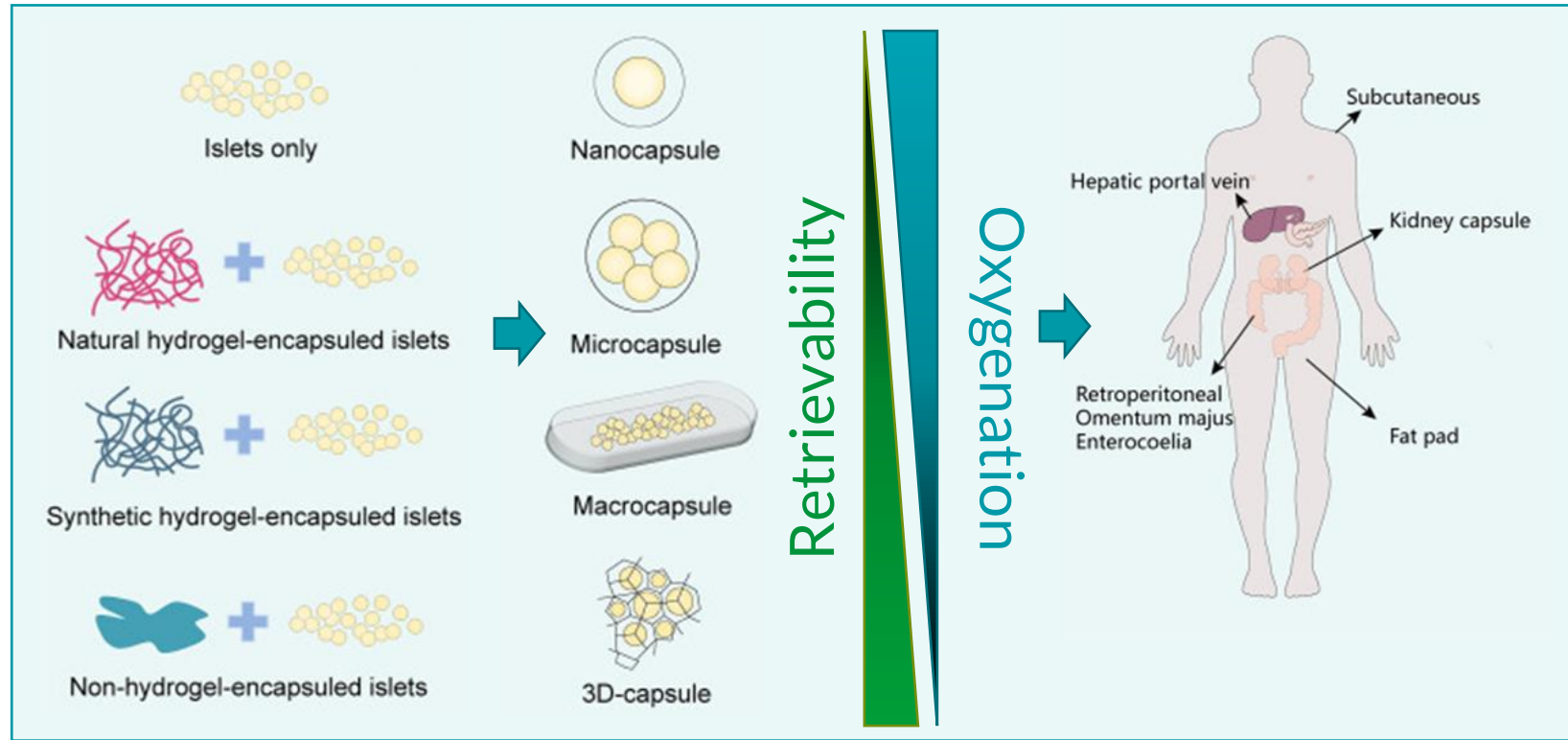


# Islet transplantation



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

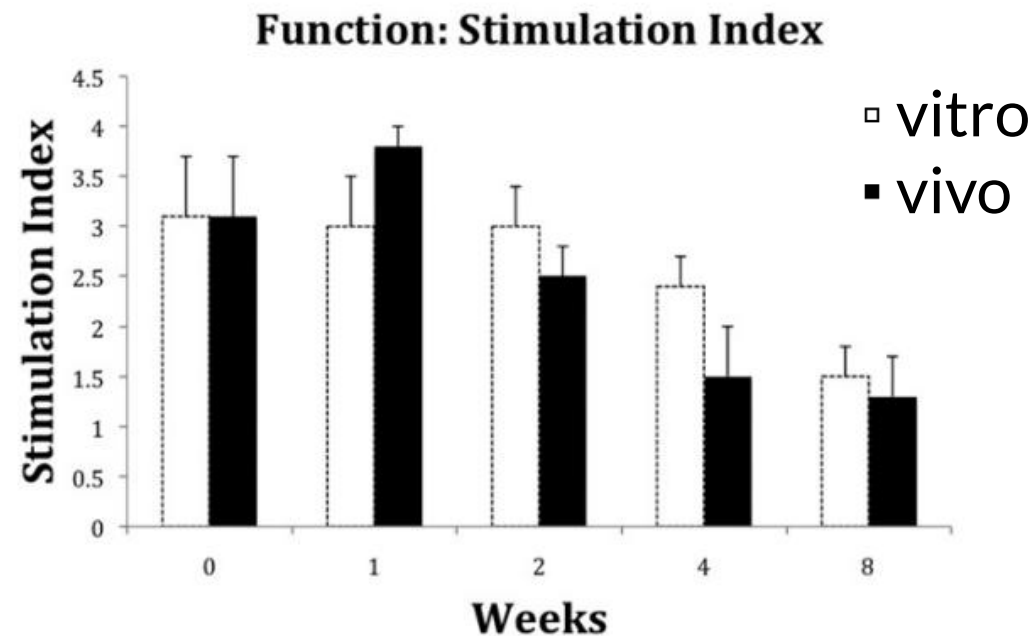
# Islet encapsulation for transplantation without immunosuppression



Adapted from Zhang Q, *et al.* Front Immunol. 2022

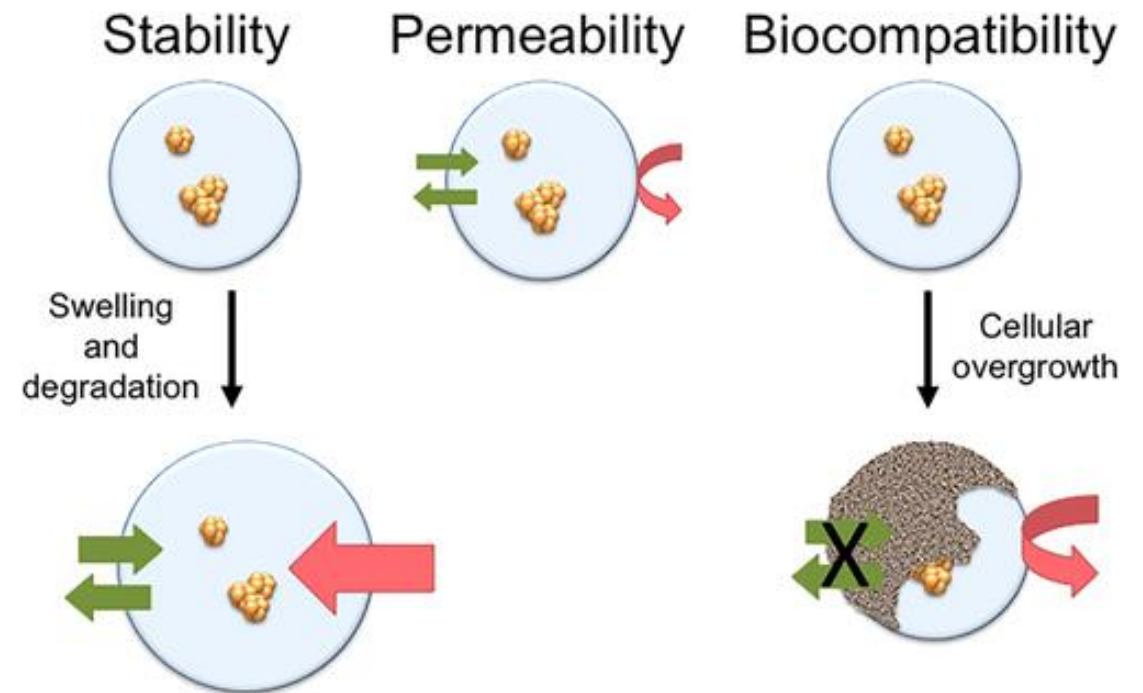
# Challenges for the field

## Loss of encapsulated islet functionality



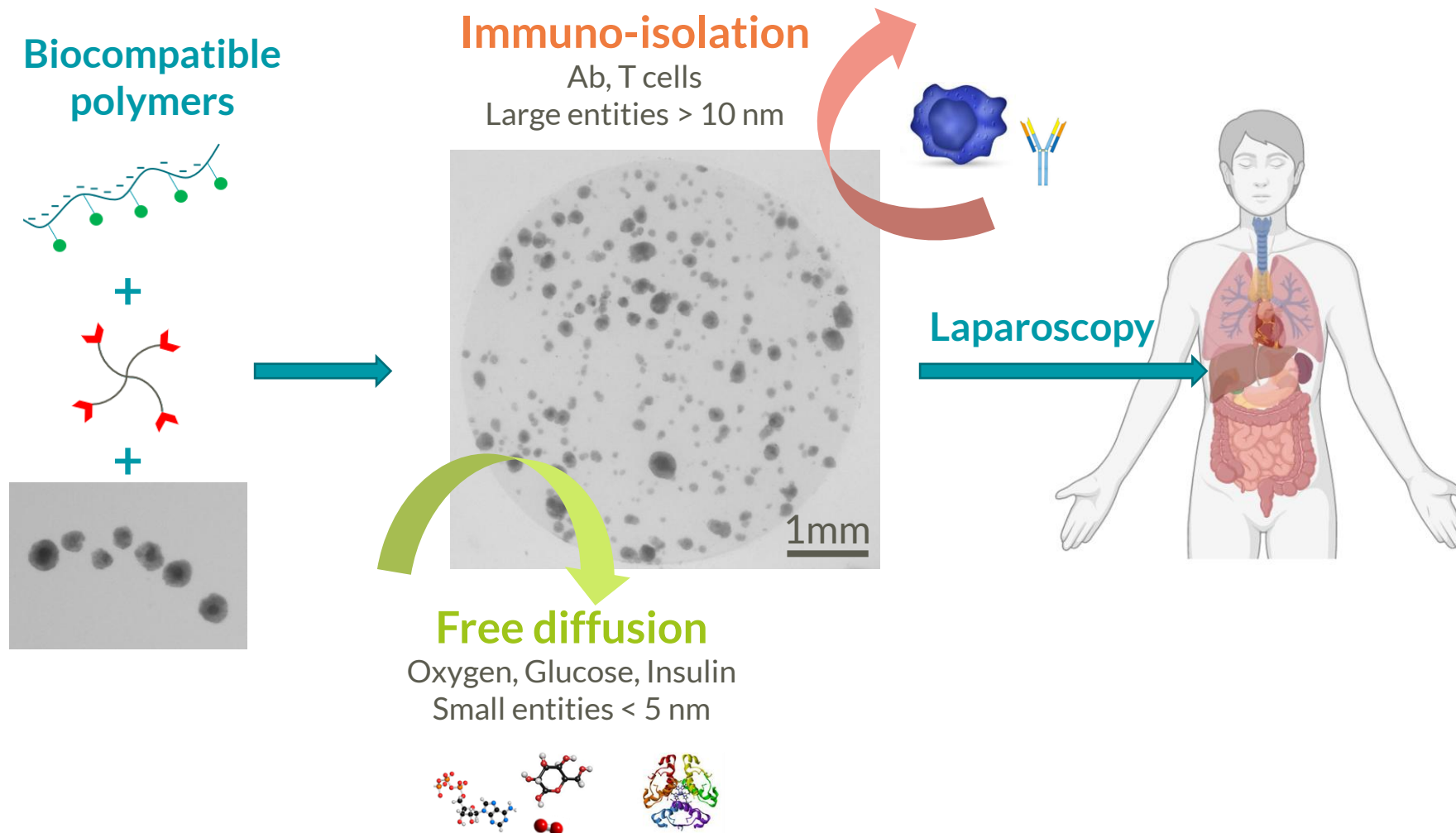
Lamb M, *et al.* Transplant Proc. 2011

## Fibrosis



Strand, *et al.* STEM CELLS Translational Medicine. 2017.

# AdoShell<sup>®</sup> Islets: Immunoprotective Hydrogel for Pancreatic Islets



Non biodegradable  
biocompatible hydrogel

Simple encapsulation

Long term in vitro  
functionality

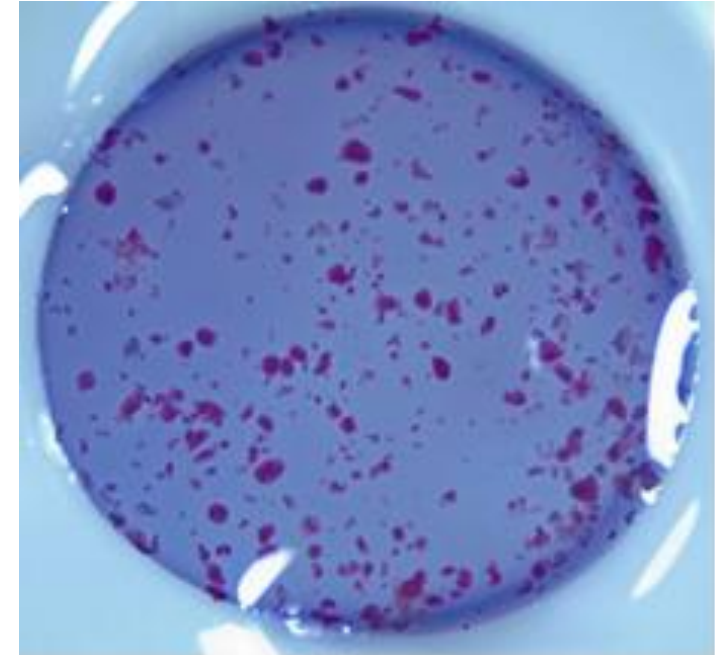
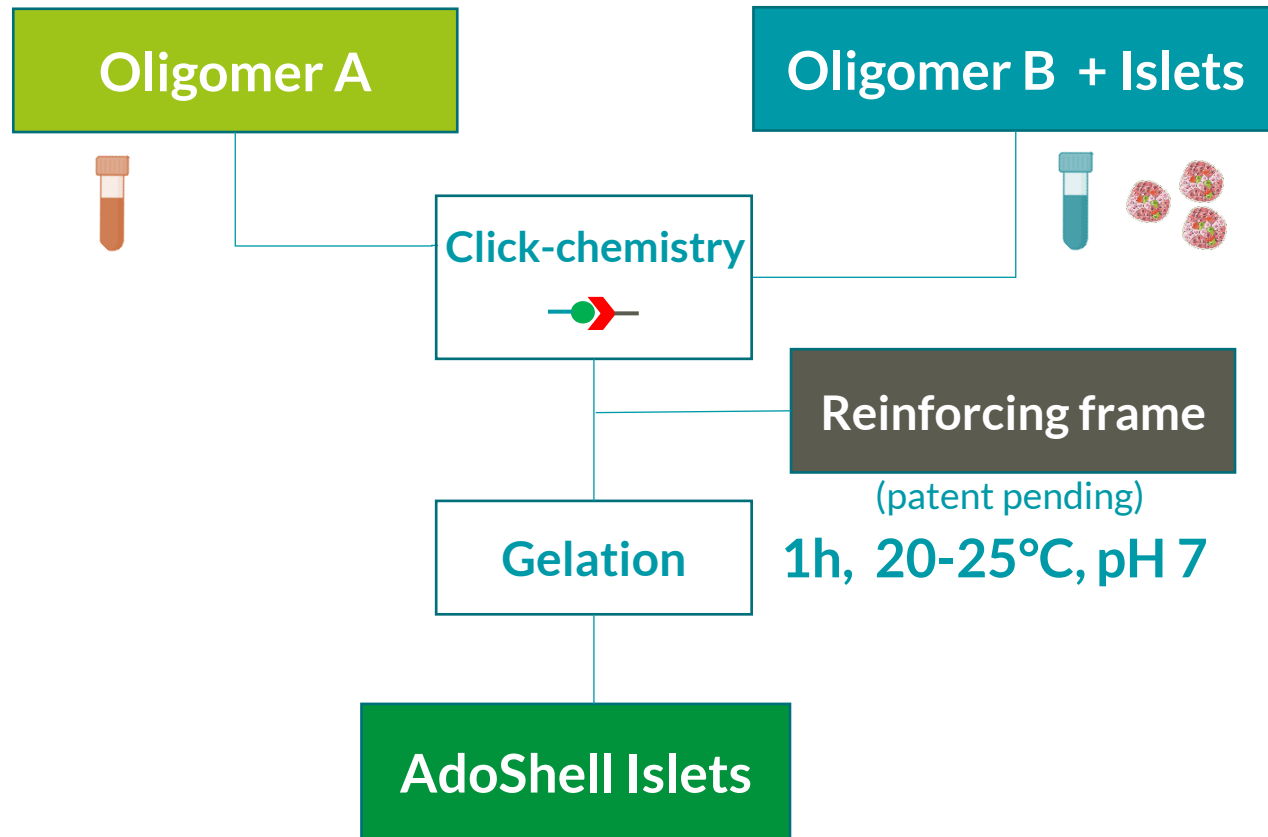
In vivo efficacy

Immunoprotection

Easily implantable  
Retrievable

Scalable for human

# AdoShell® Islets: Aqueous Encapsulation Process



Simple and biocompatible process including reinforcement frame (*undisclosed*) for mechanical resistance, manipulability, and suturing

Patent #US2022220228A1 / Unpublished patents.

Application #EP22184569.6, #EP22184568.8 and #EP22184567.0

# Objective & Plan

Demonstrate that AdoShell® Islets 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

# AdoShell® Islets immunostaining

1

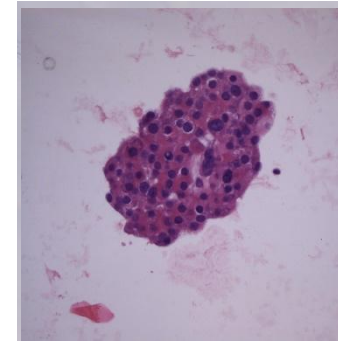
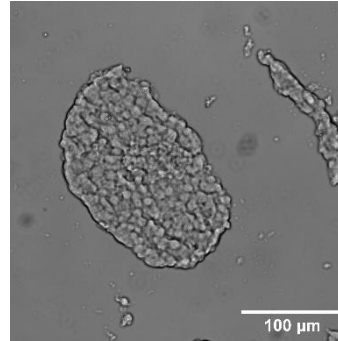
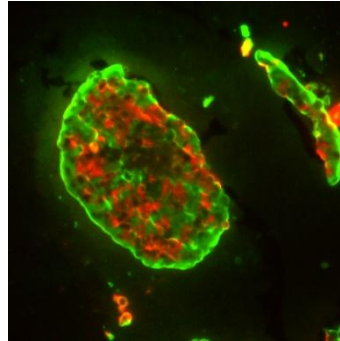
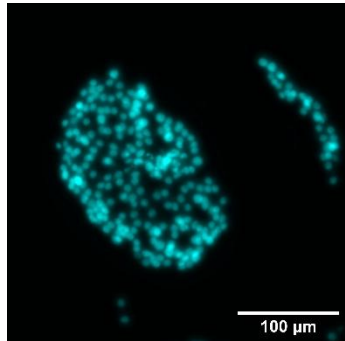
Nuclei

Insulin /  
Glucagon

Brightfield

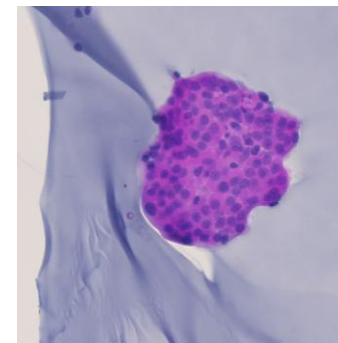
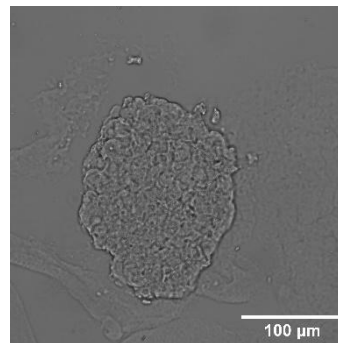
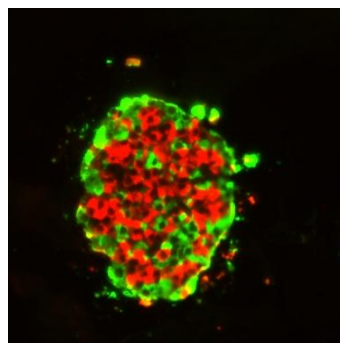
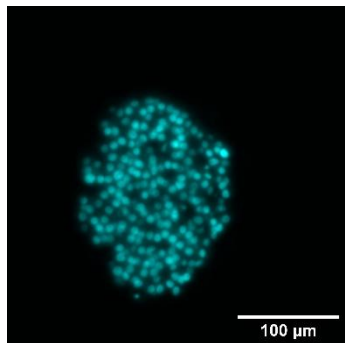
H&E

Naked islets



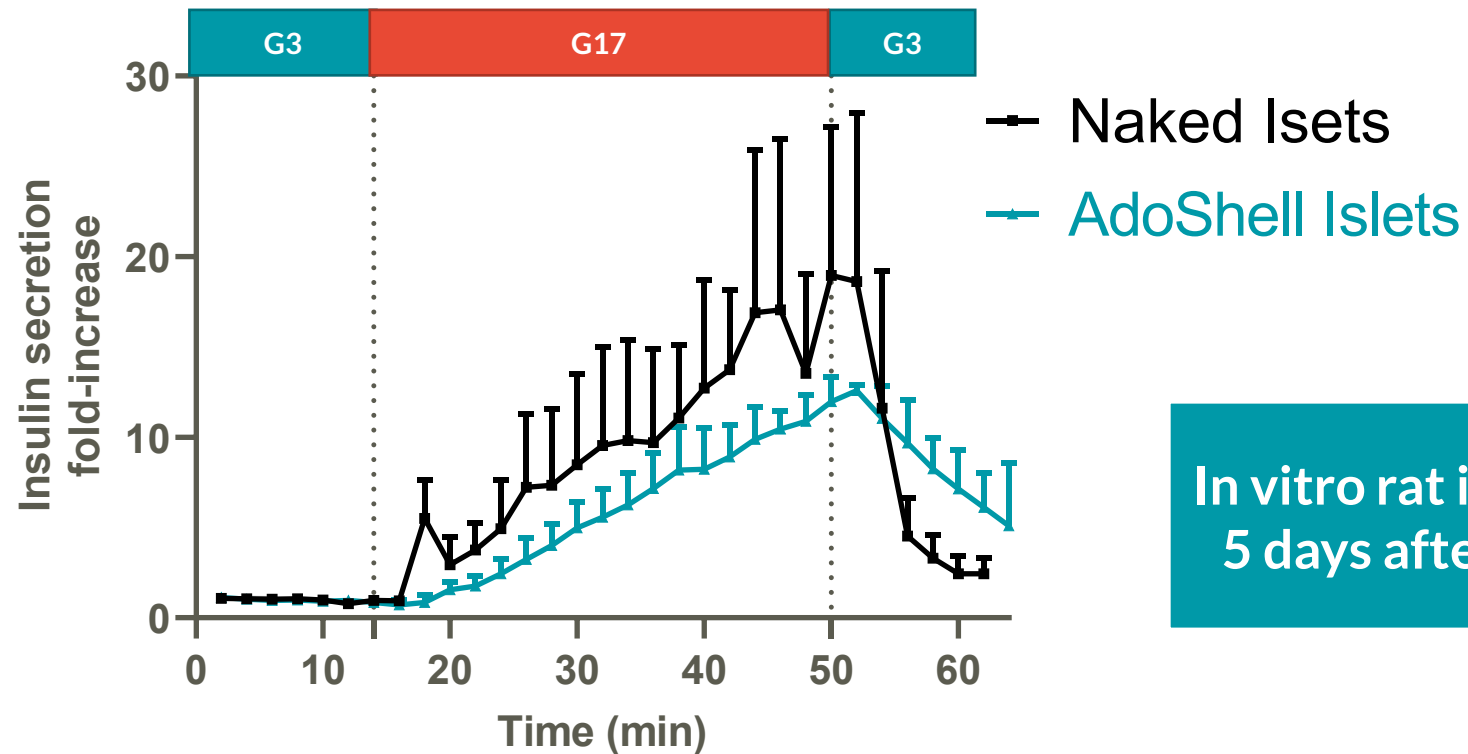
Human Islets  
tested within 1 week

AdoShell Islets



Encapsulation maintains human islet morphology

# Perifusion of AdoShell® Islets

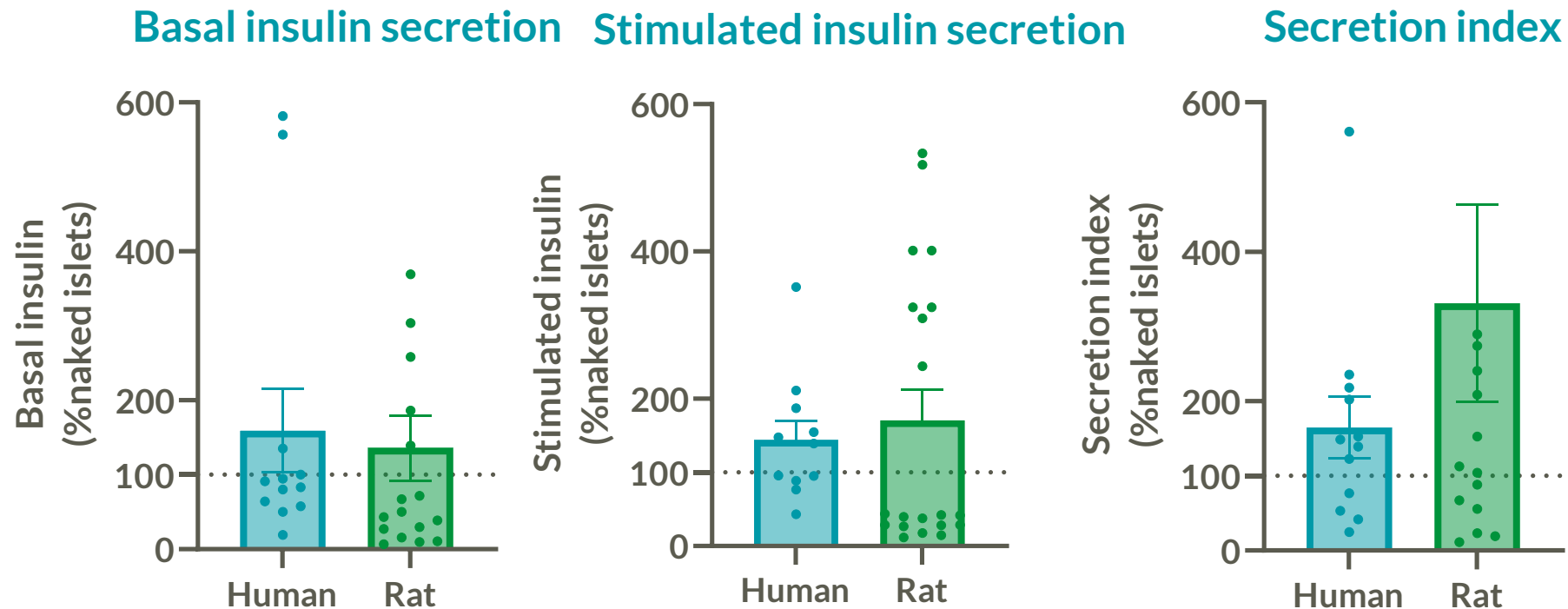


In vitro rat islet functionality  
5 days after encapsulation

AdoShell® maintains islet functionality.  
Insulin release kinetics is minimally delayed (~4min)

# Perifusion of AdoShell Islets: quantification and reproducibility

1



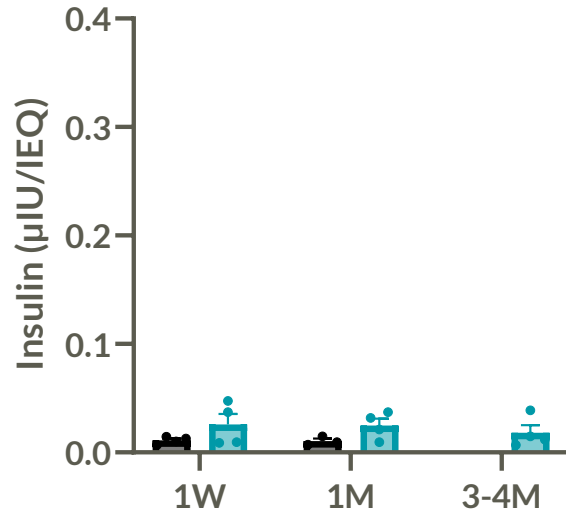
AdoShell Islets from  
N=12 human prep  
N=16 rat prep  
Tested within 1 week

mean ± s.e.m.

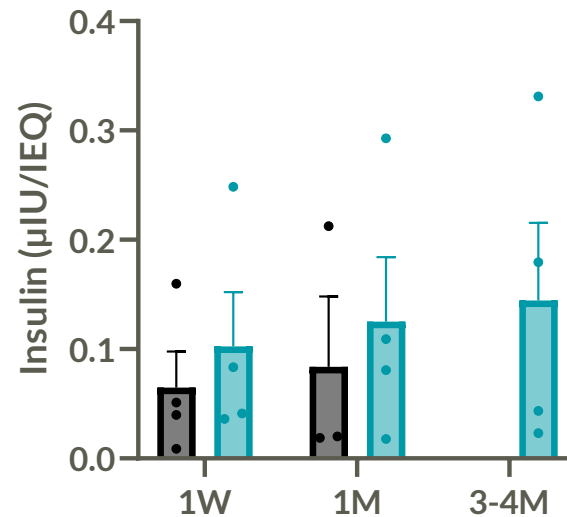
Encapsulation demonstrates high biocompatibility with good reproducibility

# Long-term functionality of AdoShell® Islets

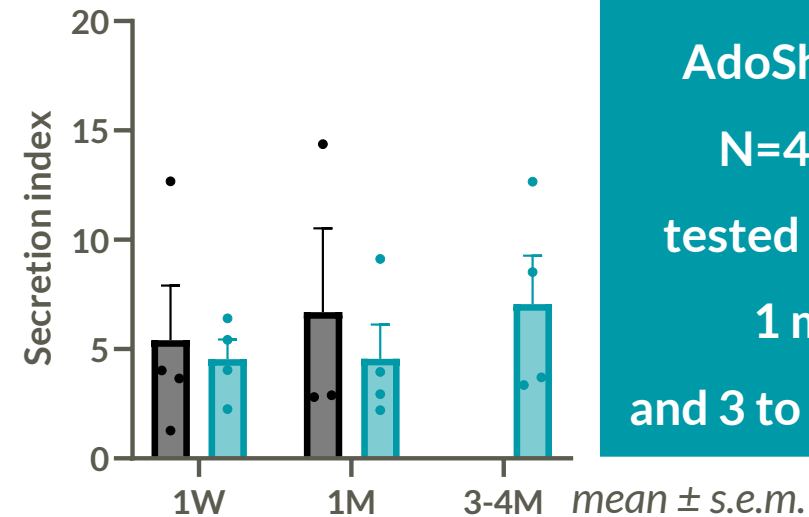
Basal insulin secretion  
3mM Glucose



Stimulated insulin secretion  
17mM Glucose



Secretion index



- Naked islets
- AdoShell Islets

AdoShell Islets from  
N=4 human prep  
tested at 1 week (1W)  
1 month (1M)  
and 3 to 4 months (3-4M)

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

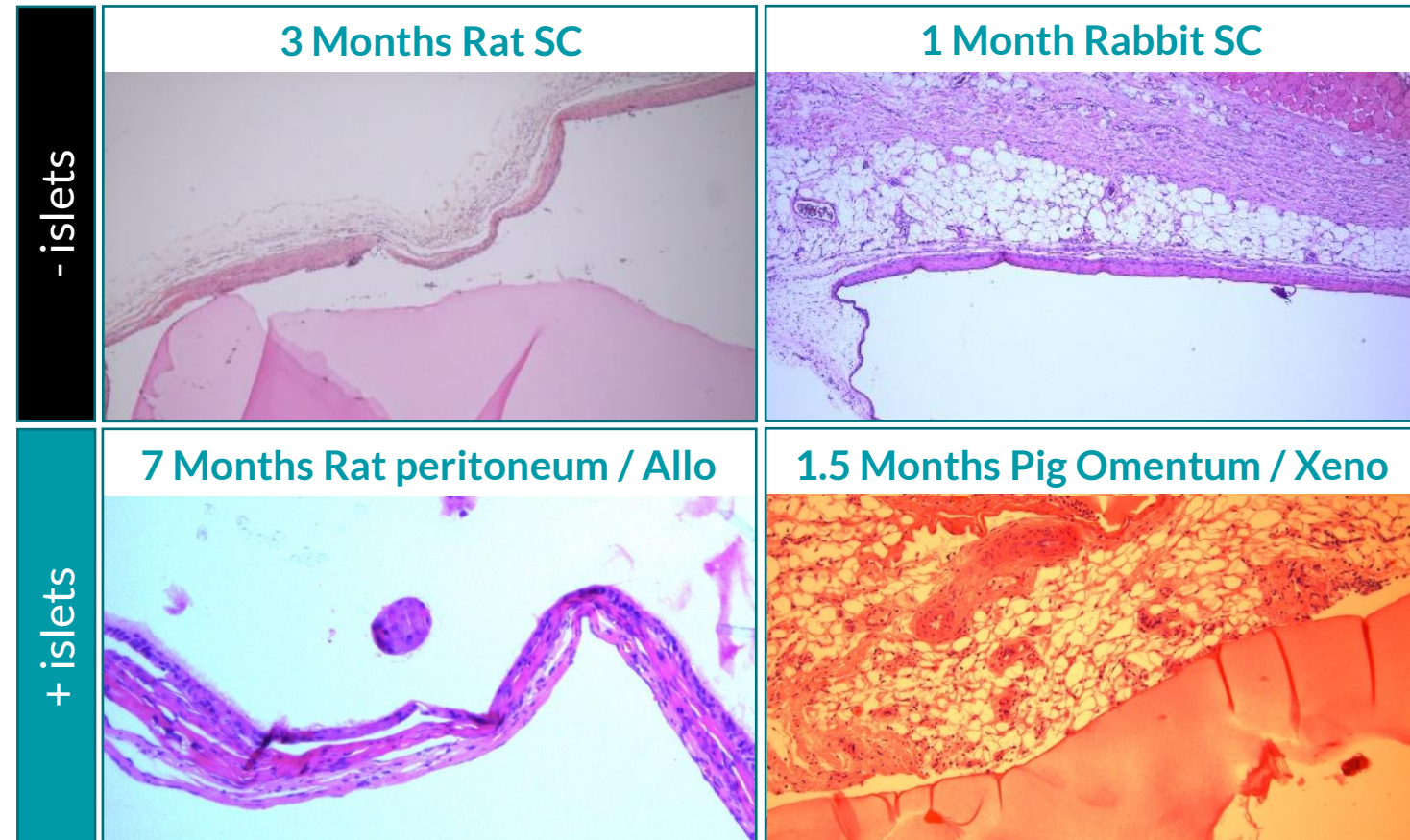
# AdoShell® Tolerance in Animal

2

AdoShell biocompatibility equivalent to inert compound (HDPE) after 4 weeks of SC implantation in **rabbit** and 13 weeks in **rat**.

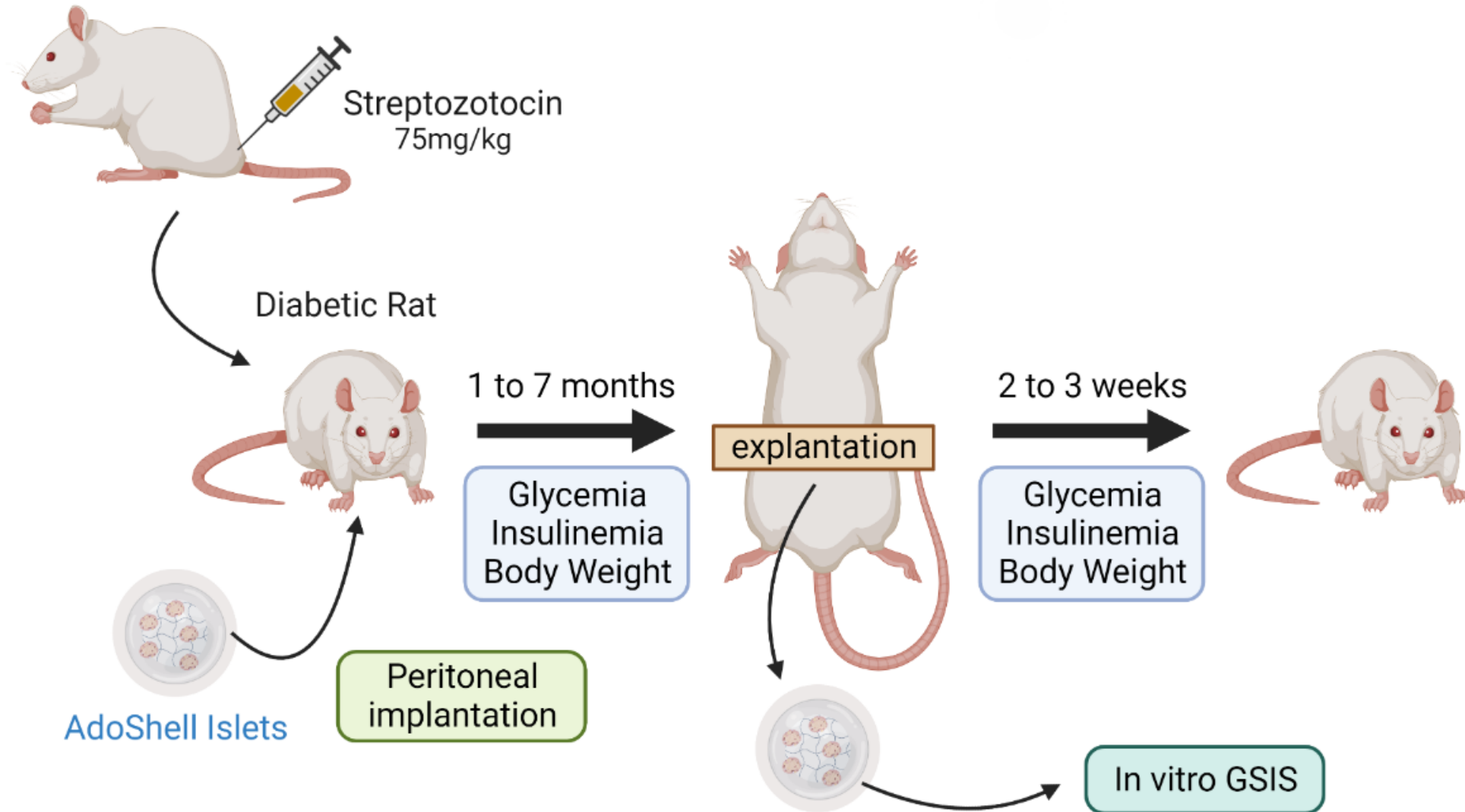
(ISO 10993 evaluation)

- ✓ No Cellularity
- ✓ No Fibrosis
- ✓ No inflammation



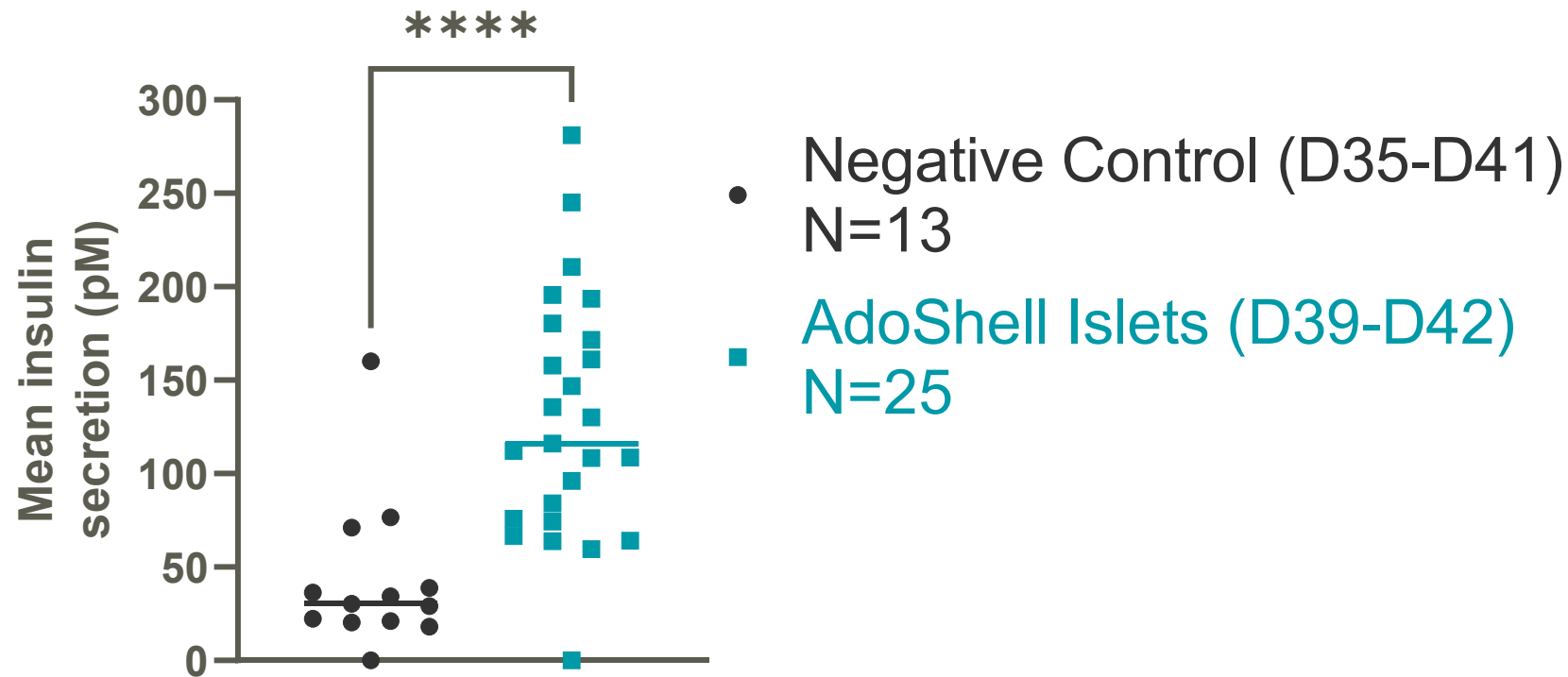
Well tolerated in different tissues of different species  
No inflammation, no fibrosis, and no biodegradability  
No cell infiltration as required for immunoprotection

# Islets Transplantation in Diabetic Rats: Study Protocol



## AdoShell® Islets: *in vivo* insulin secretion in diabetic rats

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

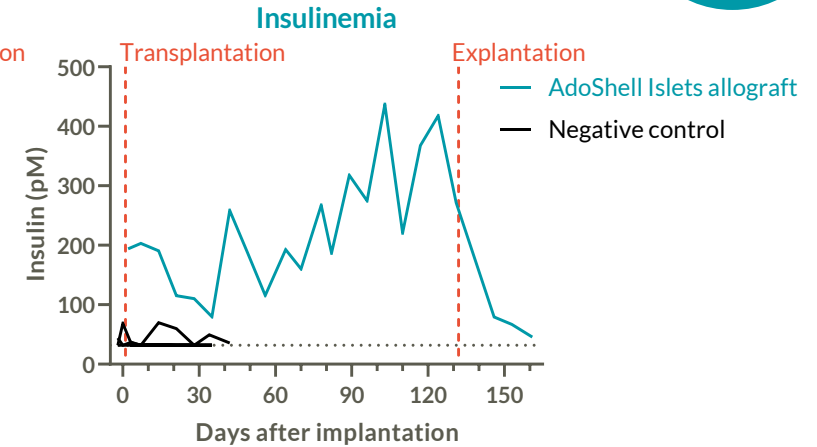
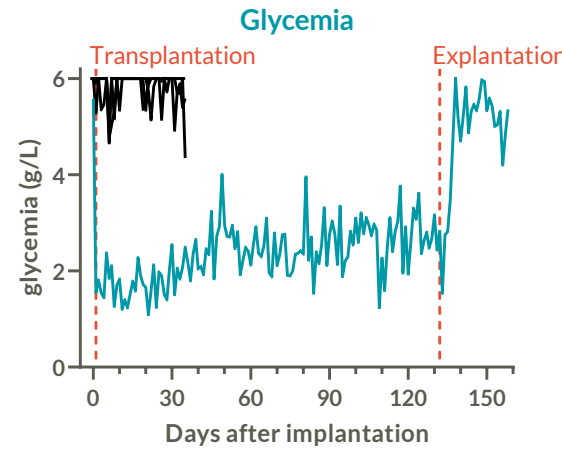


Robust secretion of insulin of implanted encapsulated islets over 1 month

# In vivo Efficacy in a diabetic rat model

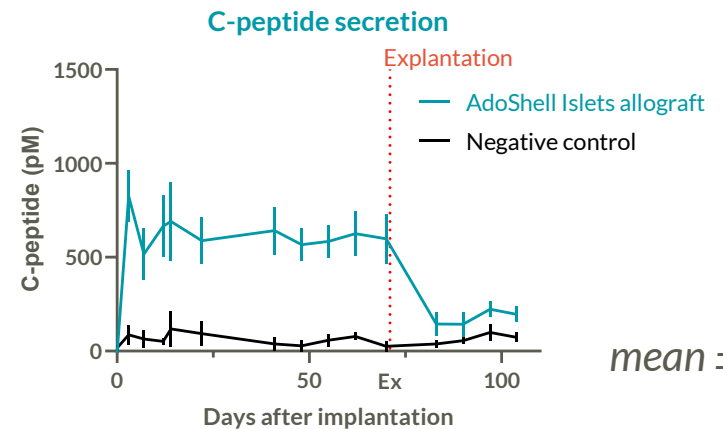
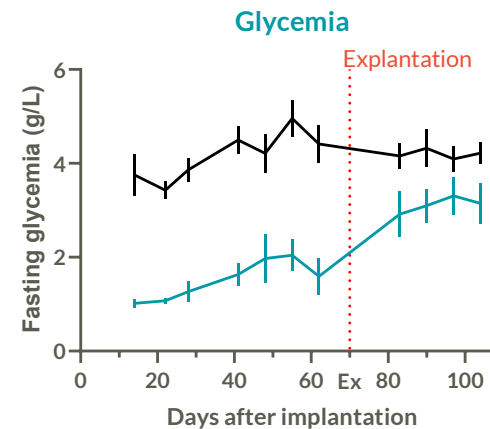
## Study 1

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



## Study 2

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

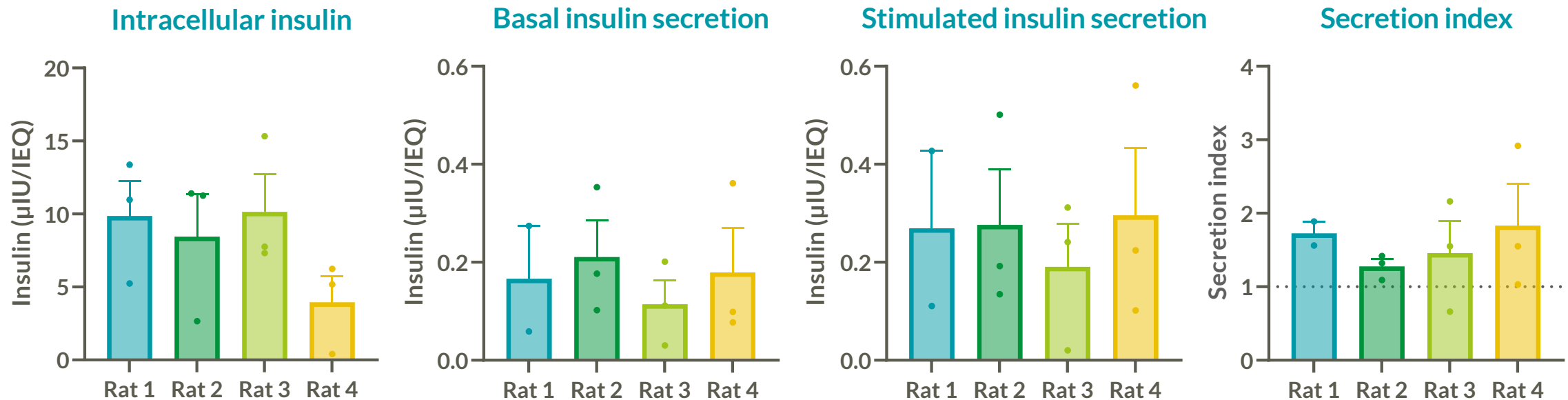


mean  $\pm$  s.e.m.

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

# AdoShell® Islets: *in vitro* explant functionality

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



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

## AdoShell®

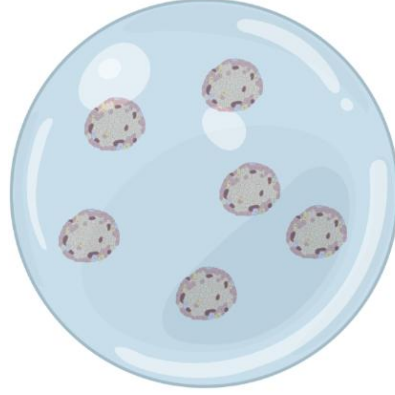


Non  
biodegradable  
biocompatible  
hydrogel

Suturable  
composite thin  
film

Easily implantable  
and retrievable

## AdoShell® Islets



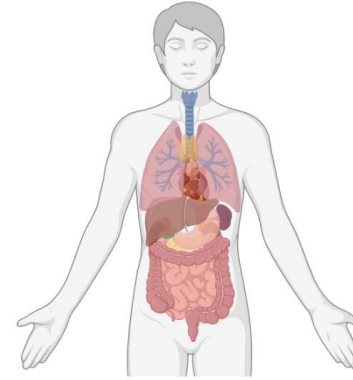
Simple  
encapsulation

Long term in vitro  
functionality

In vivo efficacy

Immunoprotection

## Ongoing

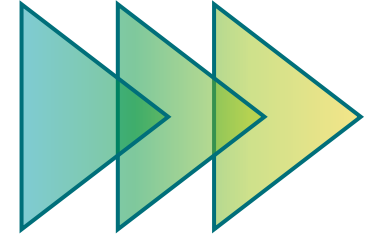


Scale up and  
surgical procedure

Regulatory studies

First in Human

## Perspectives



Partnership

Stem cells derived  
islets

Other cell therapy  
applications

## AdoShell®

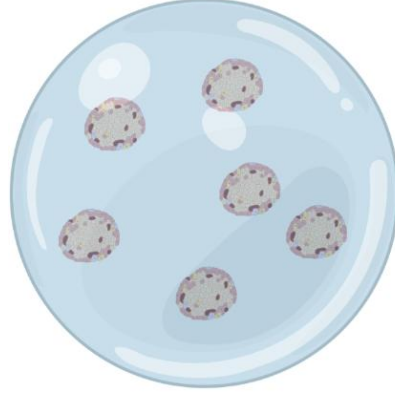


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## AdoShell® Islets



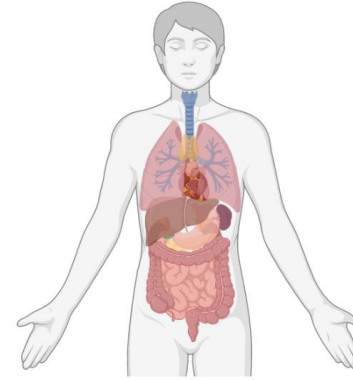
Simple  
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## Ongoing

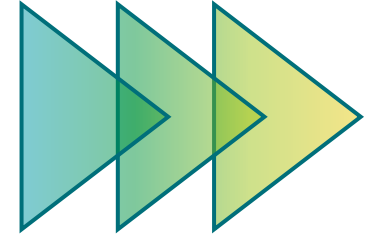


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surgical procedure

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## Perspectives



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Other cell therapy  
applications

# Acknowledgement

- ADOCIA (Lyon, France)
  - Alexandre Geissler
  - Ouardane Jouannot
  - Anne-Lise Gaffuri
  - Camille Gautier
  - Yann Courbebaisse
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