

How to deliver a therapeutic dose of encapsulated human islets?

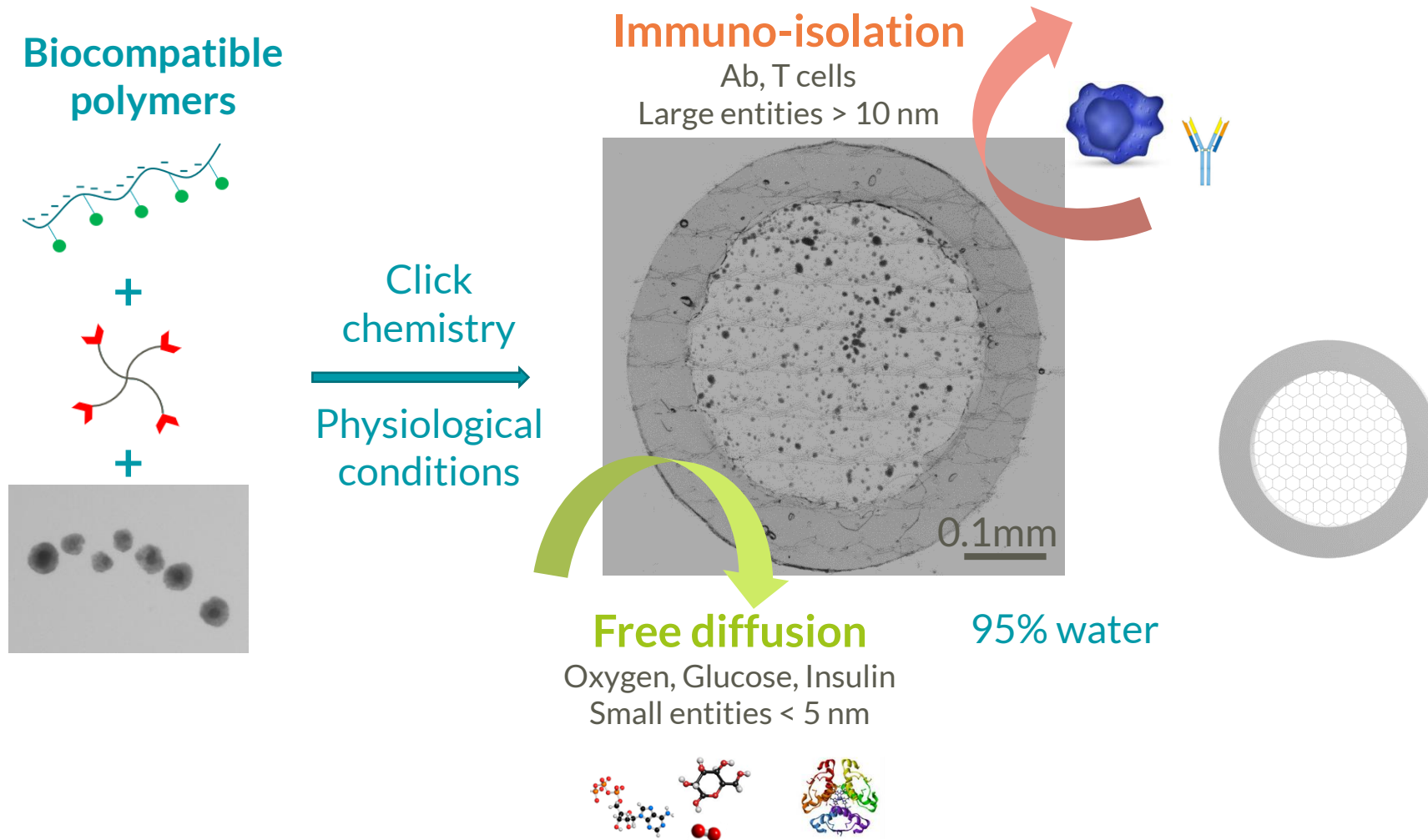
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Disclosure

- Employee and shareholder of ADOCIA

AdoShell[®] Islets: Immunoprotective Hydrogel for Pancreatic Islets



Objective & Plan

Demonstrate that AdoShell[®] Islets is a **scalable** biocompatible immuno-isolant biomaterial for islet transplantation without immunosuppression

1

In vitro functionality

Long-term *in vitro*
functionality of
encapsulated islets

2

In vivo efficacy

Ability to control
hyperglycemia in
STZ rats

3

Biocompatibility

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

4

Scale-up

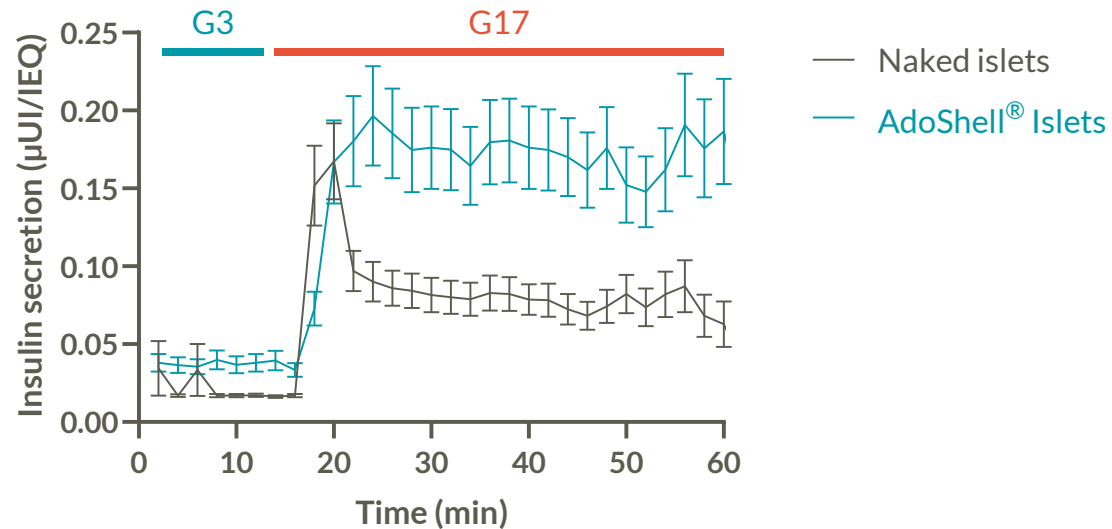
Geometry for human
application



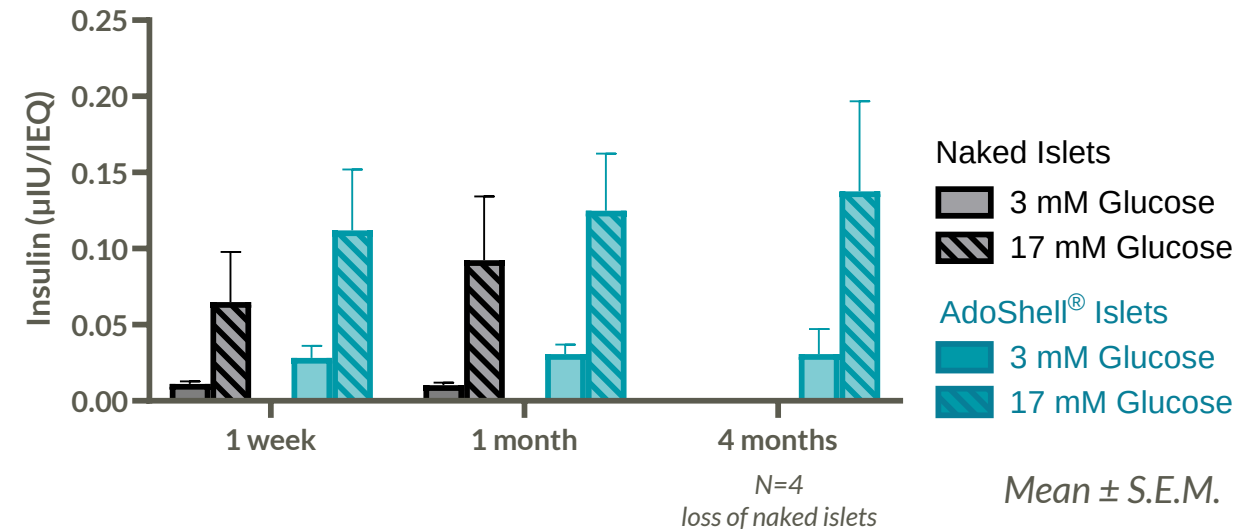
In vitro functionality of AdoShell® Islets

AdoShell® Islets from Human preparations (Dynamic GSIS)

Kinetic comparison (N=11, up to 15 days)



Long term stability (N=6, up to 4-months)



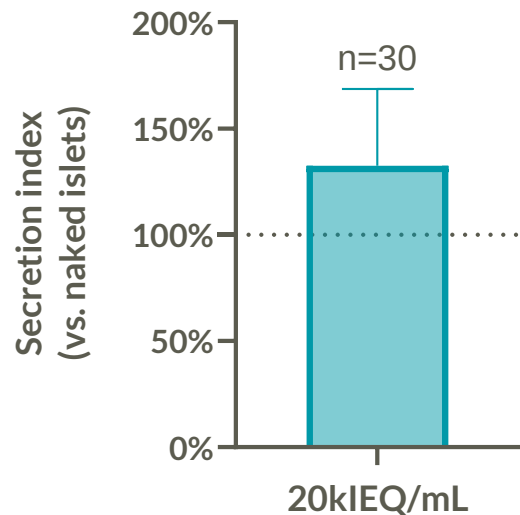
Encapsulation maintains rapid insulin release kinetics (2min delay)

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

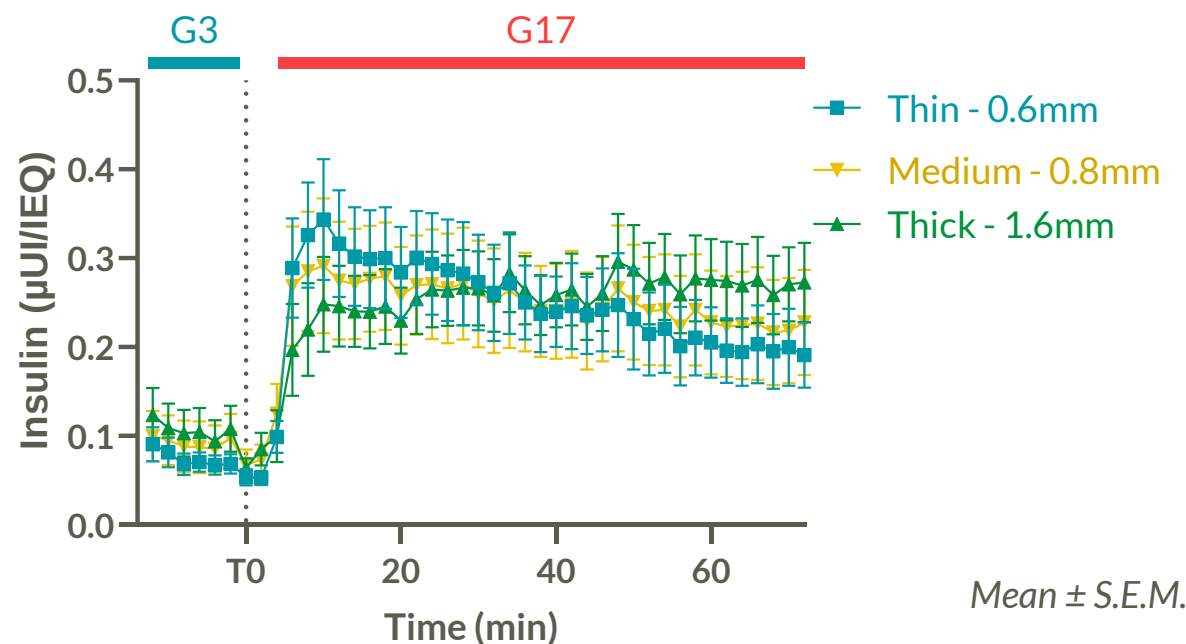
In vitro functionality of AdoShell® Islets

AdoShell® Islets from Human preparations, tested after up to 12 days (Dynamic GSIS)

Density impact



Thickness impact



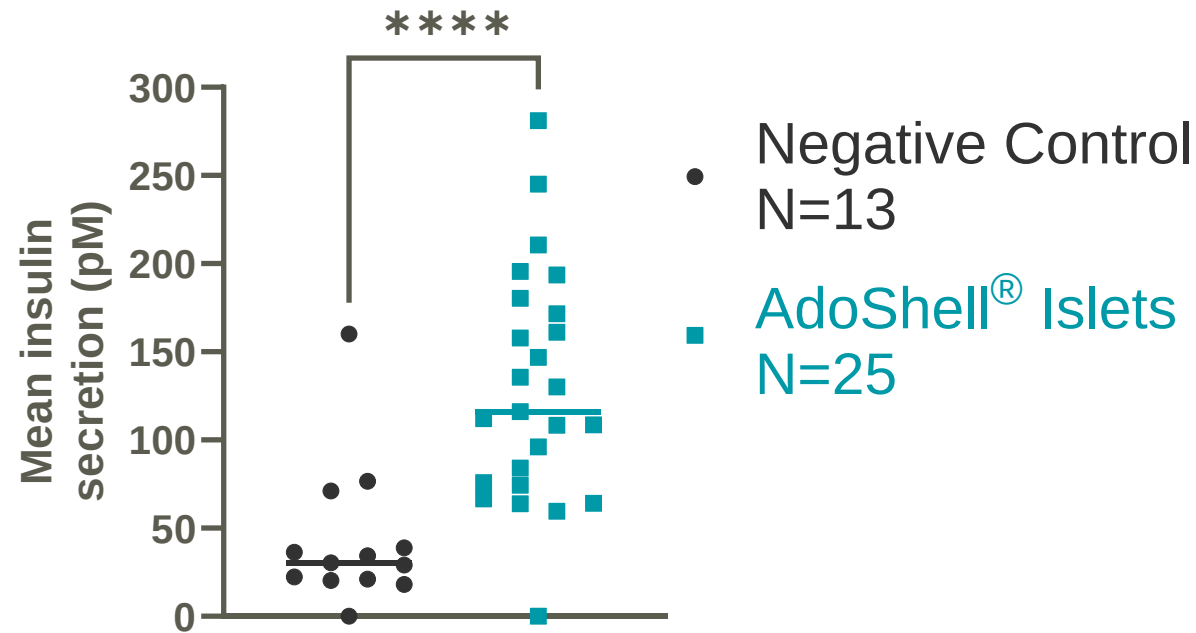
Mean ± S.E.M.

20kIEQ/mL allows high functionality of encapsulated islets
~1mm thickness does not impact the kinetics of insulin release



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

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

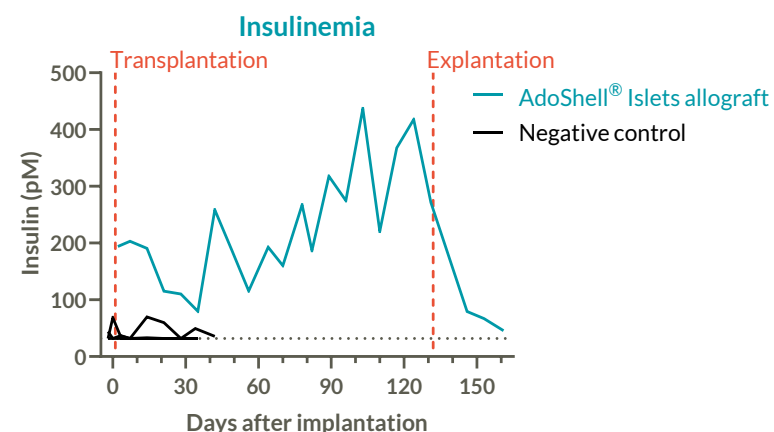
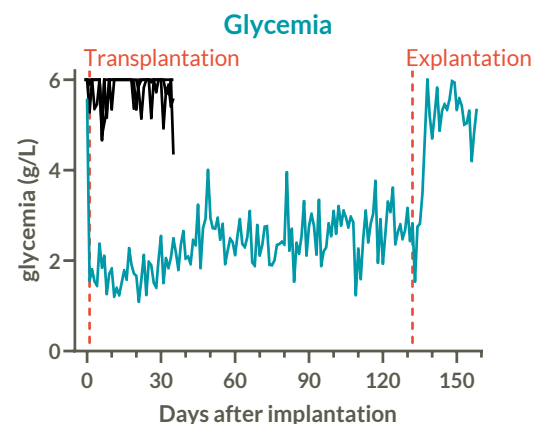


Robust insulin secretion from encapsulated **allogenic** islets over 1 month

In vivo efficacy in a diabetic immunocompetent rat model

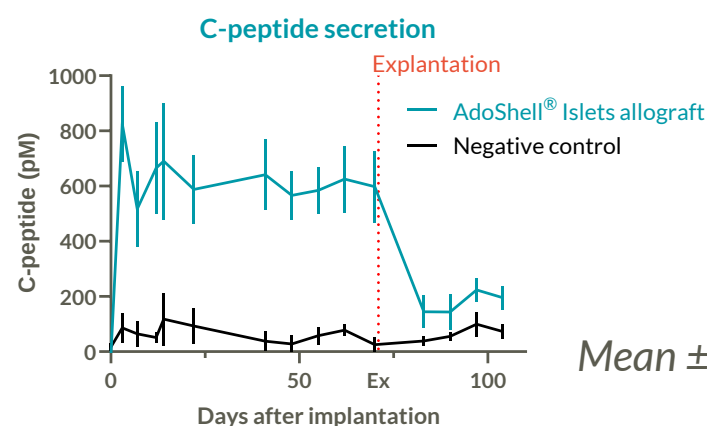
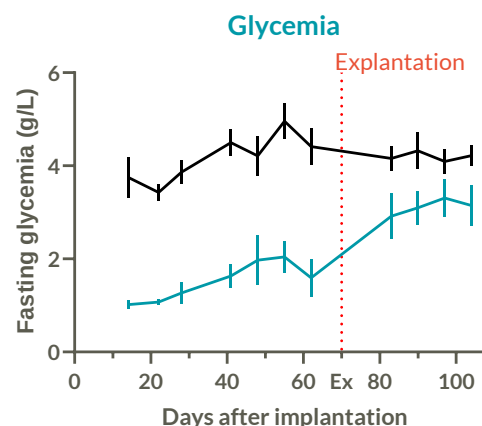
Study 1

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



Study 2

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



Mean $\pm$ S.E.M.

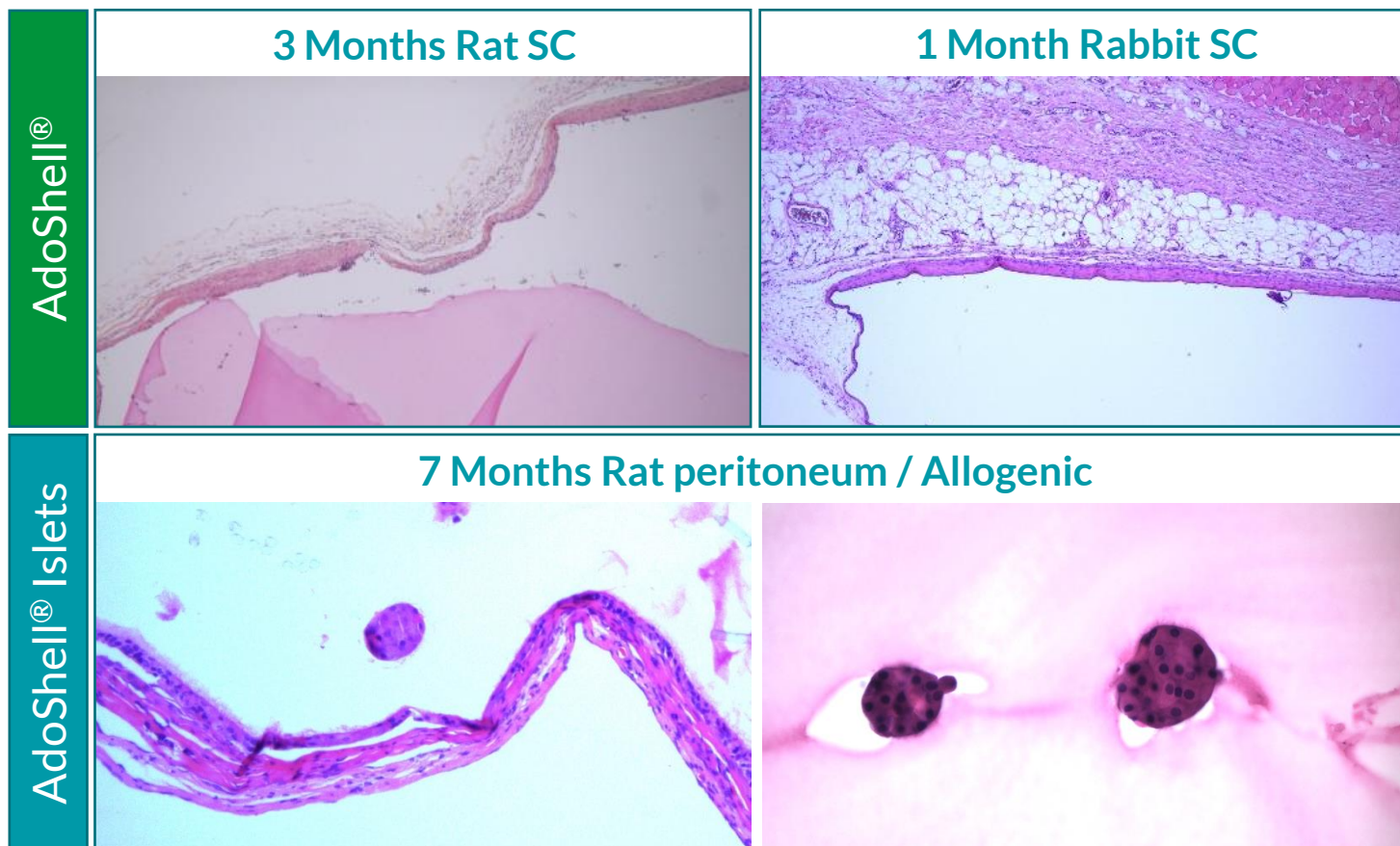
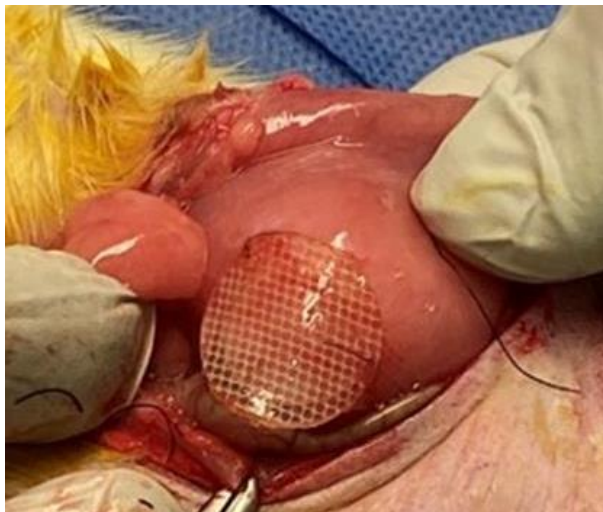
AdoShell® Islets lead to reduction of glycemia paired with steady secretion of insulin

AdoShell® Islets demonstrates immune protection

Explants were easily and safely retrieved



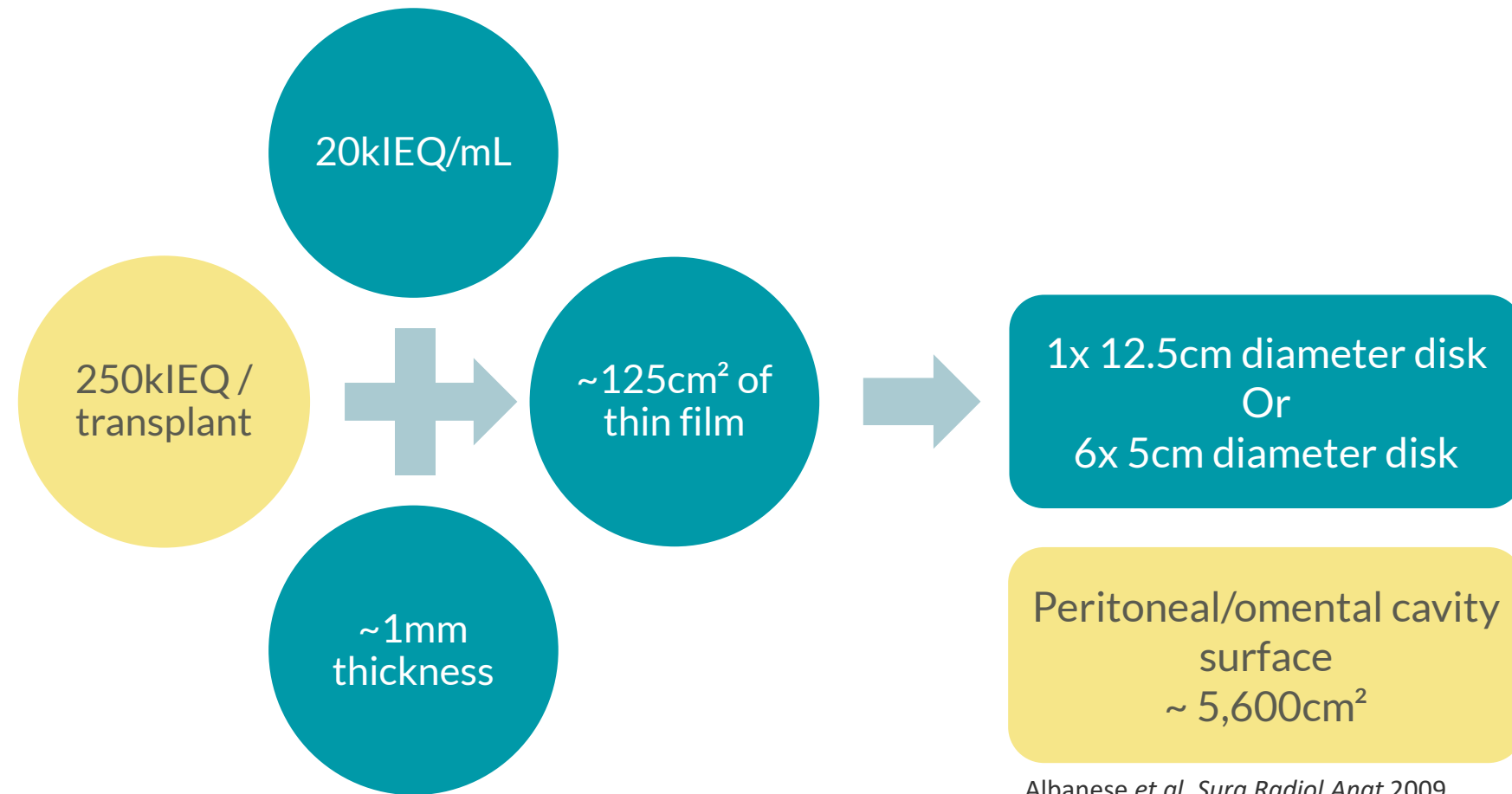
AdoShell® Islets tolerance & survival



Well tolerated in different tissues of different species
No cell infiltration in the hydrogel demonstrates immunoprotection
Survival of islets after 7 months in rat



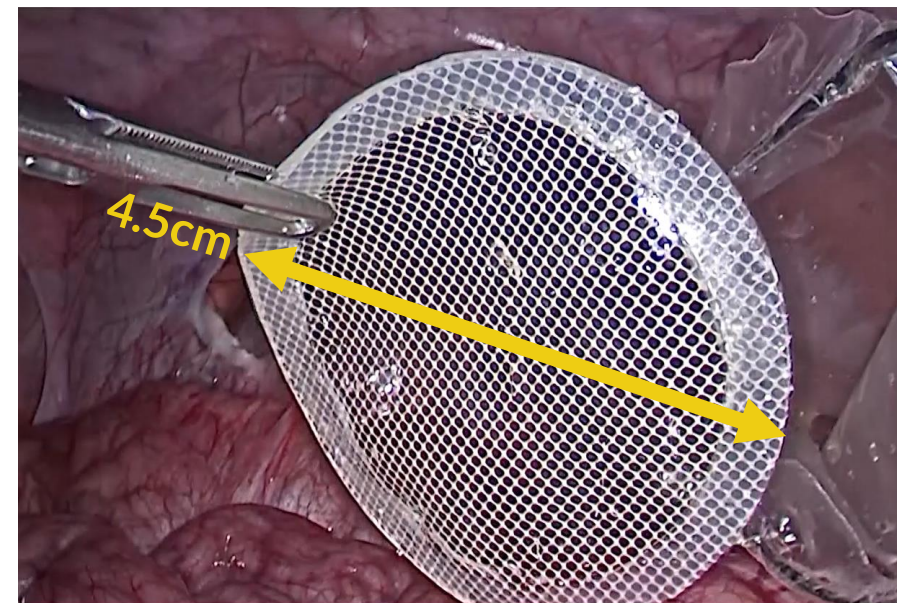
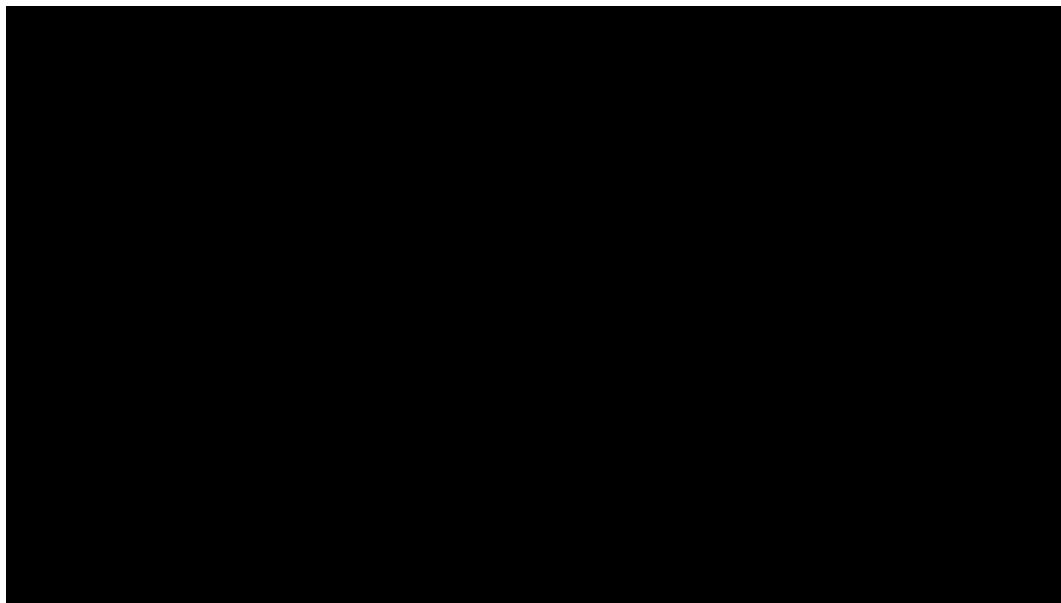
4 Scale-up to implant 250kIEQ



Albanese et al. Surg Radiol Anat 2009



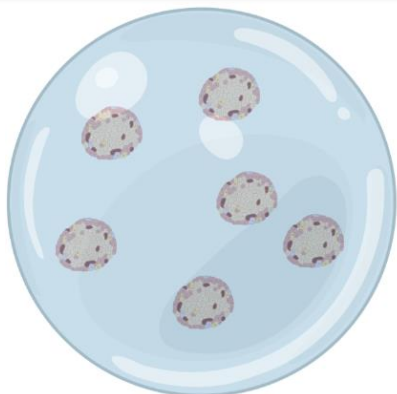
Laparoscopy Implantation in domestic pig



Easy and quick implantation/explantation by laparoscopy
Implant may be sutured on different sites: omentum, IP cavity, muscles ...



AdoShell® Islets



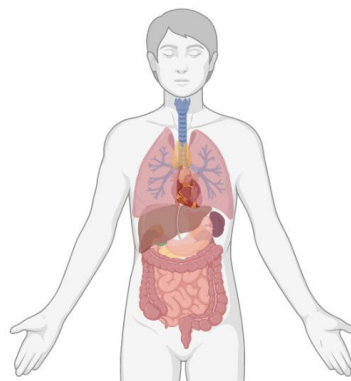
In vitro
functionality

Biocompatibility &
efficacy

Immunoprotection

Scale up and
surgical procedure

Ongoing

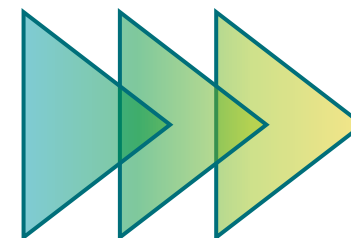


In vivo Human
Islets efficacy

Regulatory studies

First in Human
preparation

Perspectives



Partnership

Stem cells derived
islets

Other cell therapy
applications



Acknowledgements

- ADOCIA (Lyon, France)
 - Alexandre Geissler
 - Anne-Lise Gaffuri
 - Baptiste Plancq
 - Camille Gautier
 - Julie Brun
 - Maud Fumex
 - Nathalie Leclerc
 - Nicolas Laurent
 - Olivier Soula
 - Ouardane Jouannot
 - Romain Besnard
 - Xavier Gaume
 - Yann Courbebaisse



ADOCIA

innovative medicine
for everyone, everywhere



- CEED (Strasbourg, France)
 - Karim Bouzakri
 - William Bietiger
 - Allan Langlois
- Institut Cochin (Paris, France)
 - Raphael Scharfmann
- IRCAD (Strasbourg, France)
 - Jacques Marescaux
- CHU Lille (Lille, France)
 - François Pattou
 - Valéry Gmyr
- CHU Lyon (Lyon, France)
 - Olivier Thaunat

