Bioengineering I

Injectable devices as cell factory implants for therapeutic antibody production

Marwa Sallam, PhD

Senior Research Associate

Desai Lab/School of Engineering, Institute for Biology, Engineering and Medicine (I-BEAM), Brown University

CRS 2025 ANNUAL MEETING & EXPOSITION

PHILADELPHIA, PA JULY 13-18, 2025

BROWN

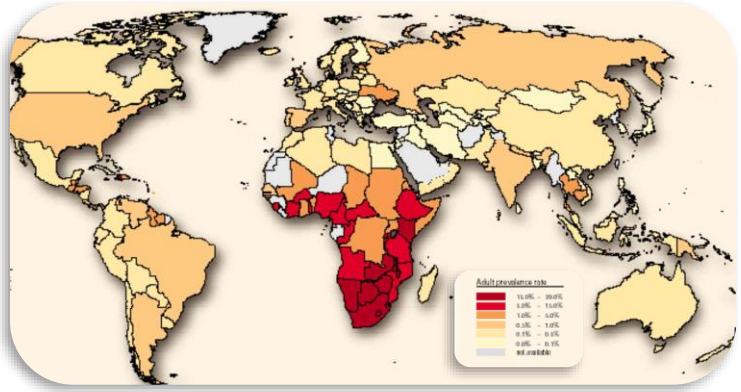
NEXT-GENERATION DELIVERY INNOVATIONS

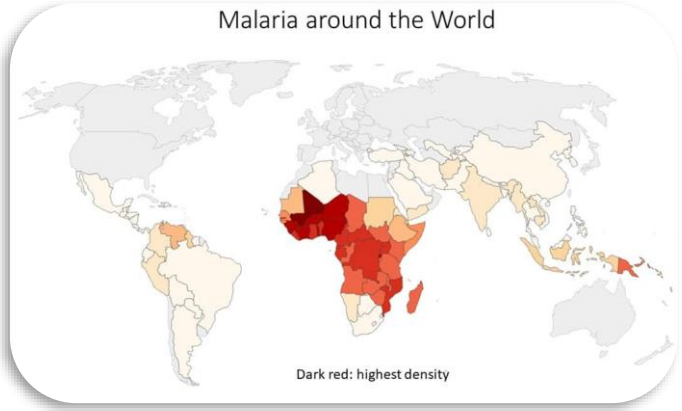
HIV & Malaria disease burdens are High in developing countries

65.6 % of global HIV (25.6 Million cases)

93.6% of global malaria (233 million Cases)

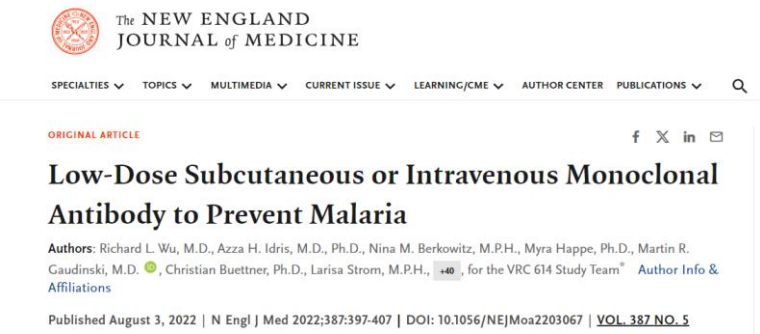
mAb improve prevention coverage in vulnerable populations.





HIV Suppression with mAbs 3BNC117

Malaria prevention with mAbs L9LS


The NEW ENGLAND JOURNAL of MEDICINE

SPECIALTIES TOPICS MULTIMEDIA CURRENT ISSUE LEARNING/CME AUTHOR CENTER PUBLICATIONS

ORIGINAL ARTICLE

Low-Dose Subcutaneous or Intravenous Monoclonal Antibody to Prevent Malaria

Authors: Richard L. Wu, M.D., Azza H. Idris, M.D., Ph.D., Nina M. Berkowitz, M.P.H., Myra Happe, Ph.D., Martin R. Gaudinski, M.D., Christian Buettner, Ph.D., Larisa Strom, M.P.H., +40, for the VRC 614 Study Team* Author Info & Affiliations

Published August 3, 2022 | N Engl J Med 2022;387:397-407 | DOI: 10.1056/NEJMoa2203067 | VOL. 387 NO. 5

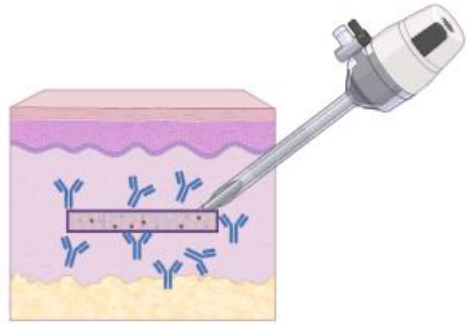
Effective prevention & treatment of chronic HIV & malaria require strict protocol adherence

- Long term daily dosing of HIV anti-retroviral therapy
- Chemoprophylactic malaria treatments: 4 monthly treatment courses /year

Cost and accessibility are major challenges limiting large scale use of mAbs

Gaebler, et al., Nature (2022), Kayentao et al., N Engl J Med (2024)

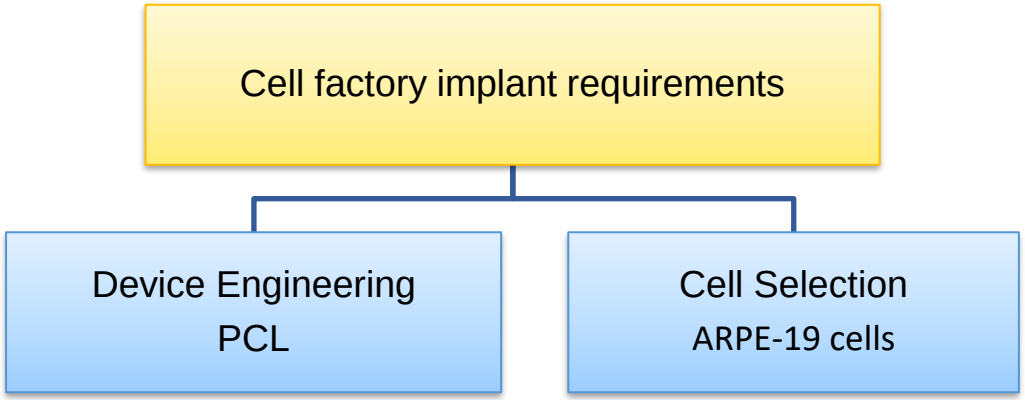
Injectable cell factory Implants

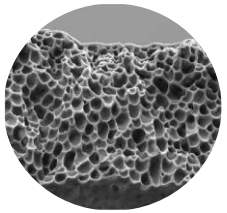


Challenge : IV or SC Administration of Abs is limited by the rate of systemic clearance, necessitating frequent dosing.

Requirement **:** long-term sustained delivery with reduced costs & improve patient compliance in low resource settings

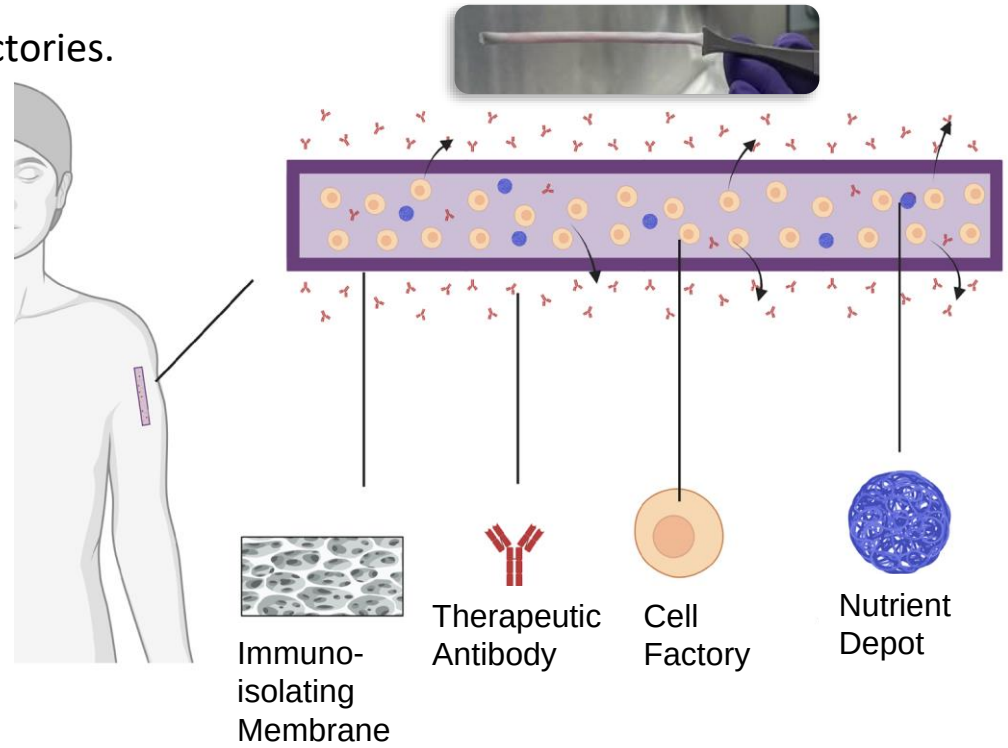
Approach: minimally invasive implantation to deliver antibody-producing cell factories.



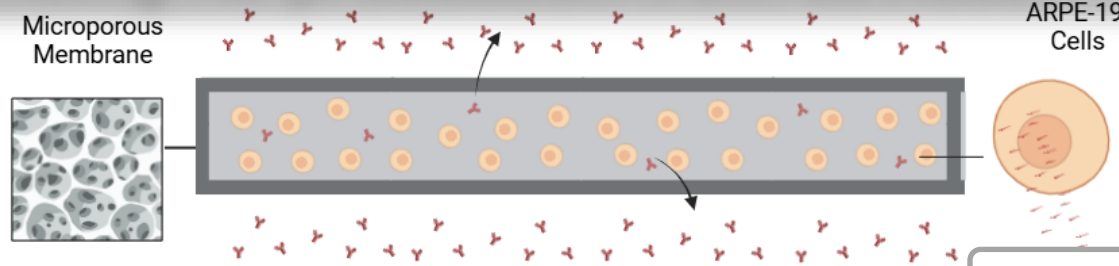


- ✔ Biocompatible
- ✔ Retrievable
- ✔ Microporous
- ✔ Immune-isolating

- ✔ Genetically Modifiable
- ✔ Clinically translatable
- ✔ Non -tumorigenic



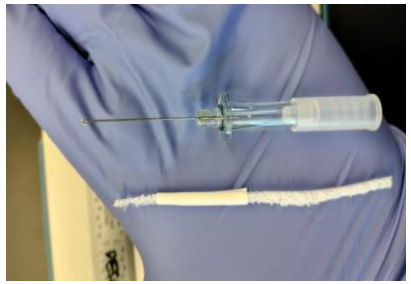
Optimizing Ab production from devices



Device Engineering

- Device membrane thickness
  - Porosity/ tortuosity
  - Surface properties

Internal scaffolding higher surface area for cell attachment



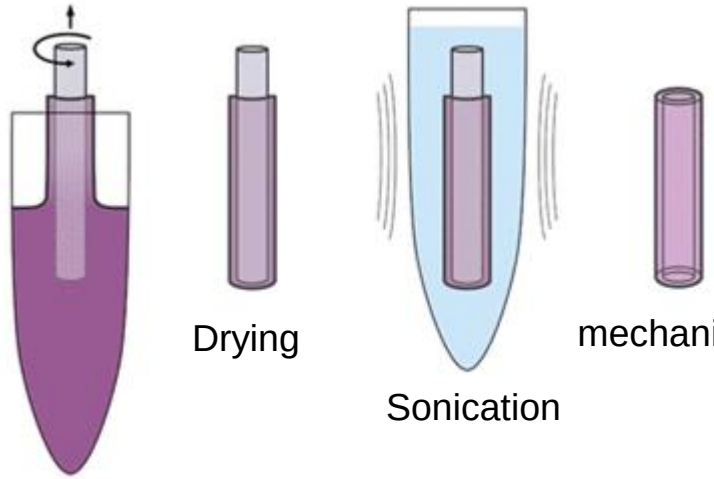
Cell Engineering

Daily antibody production per cell

Omid Veiseh/ Rice University

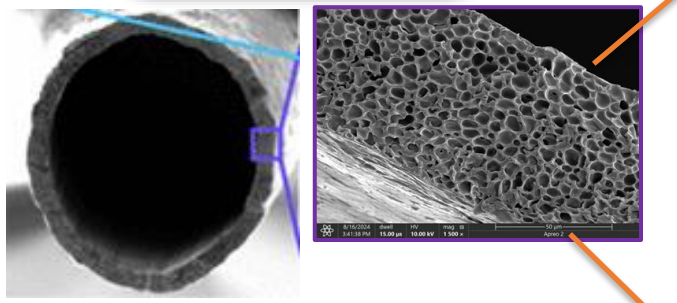
- L9LS Ab (1 pg/cell/day)
- 3 BNC117 Ab (16 pg/cell/day)

Fabrication of Injectable Tubular PCL Device



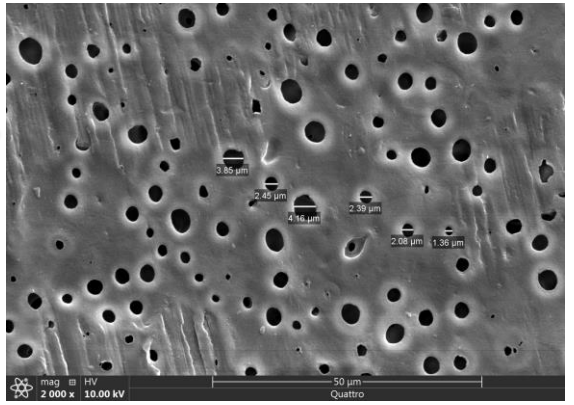
dip-cast from PCL-PEG solution

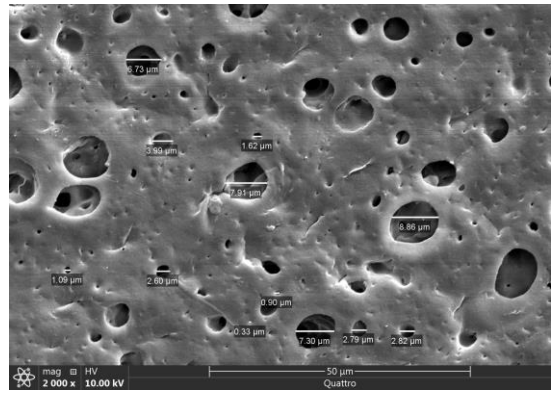
Dip casting



Device cross section

Inner surface





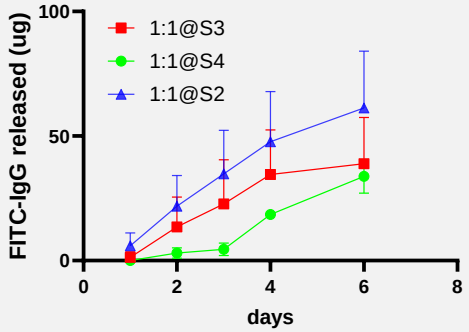
Outer surface

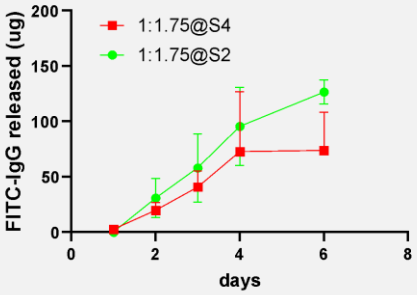
Bernards D, et al *ACS Materials Au* (**2023**)

Draw speed affects device wall thickness/tortuosity and Ab release

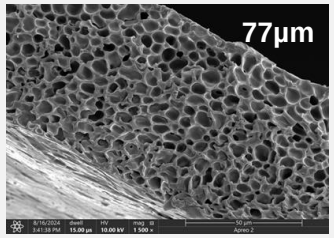
Optimization of device composition by varying porogen amount (PEG) and dip casting parameters (draw speed mm/s)

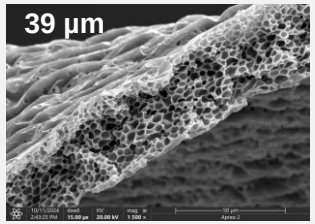
PEG:PCL (mg/ml) ratio Speed	150:150 1:1	150:180 1:1.2	130:190 1:1.5	120:210 1:1.75	110:220 1:2
2 mm/sec	1:1@S2	1:1.2@S2	1:1.5@S2	1:1.75@S2	1:2@S2
3 mm/sec	1:1@S3	1:1.2@S3	1:1.5@S3	1:1.75@S3	1:2@S3
4 mm/sec	1:1@S4	1:1.2@S4	1:1.5@S2	1:1.75@S4	1:2@S4



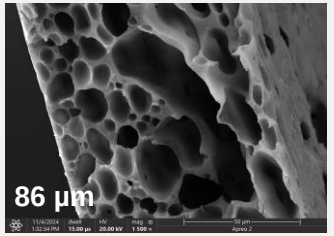


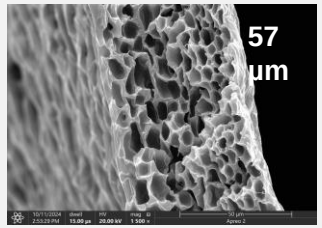
2 mm/Sec





4 mm/Sec

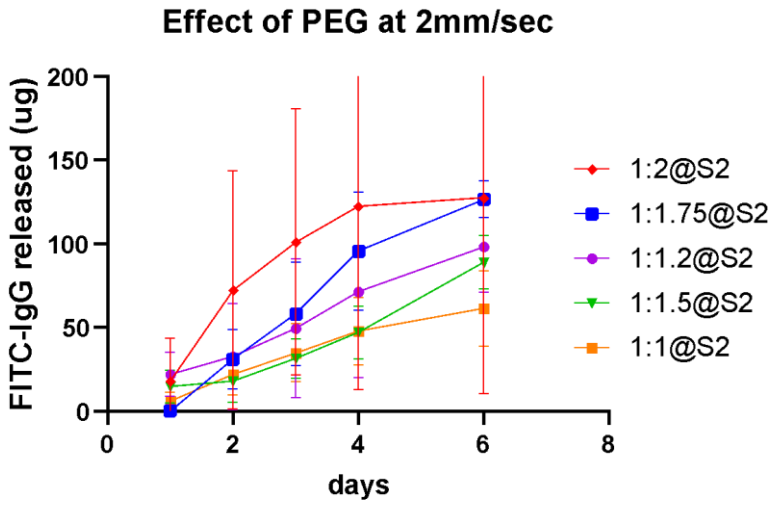


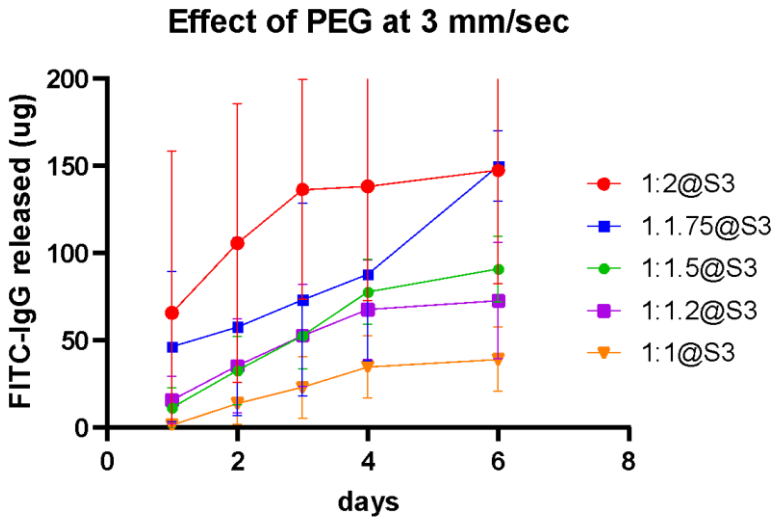


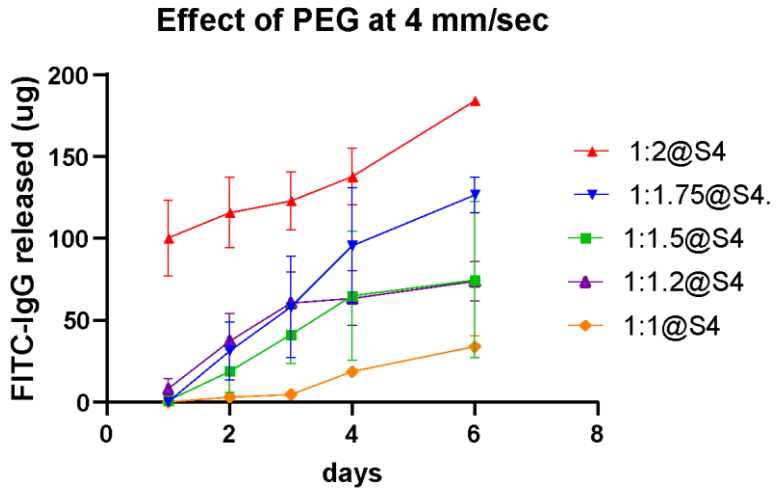
1:1 PCL:PEG

1:1.75 PCL:PEG

Ab release increases with increasing porogen content at different draw speeds

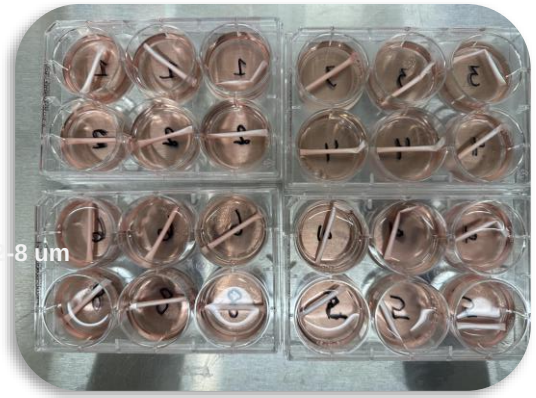


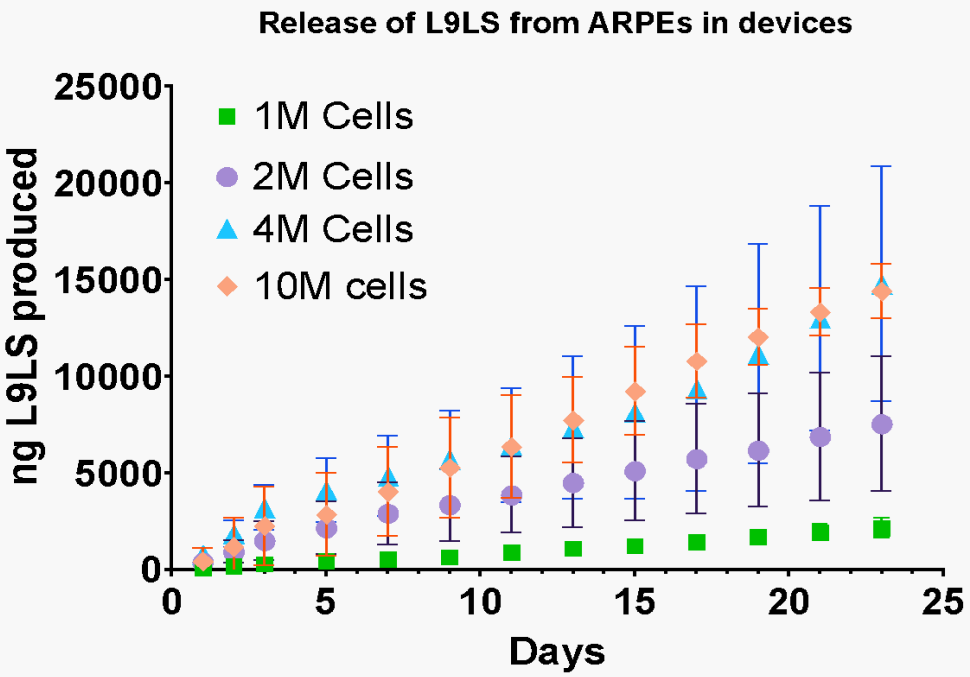


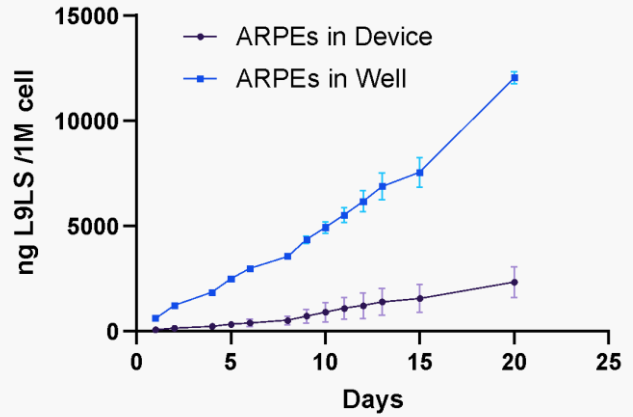


HOWEVER, compromise between porosity and integrity of devices

Cumulative release of L9LS from ARPEs in devices

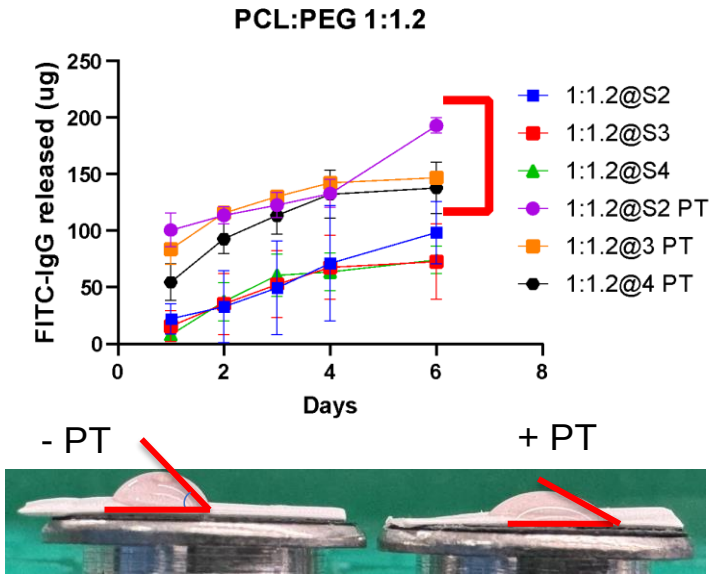


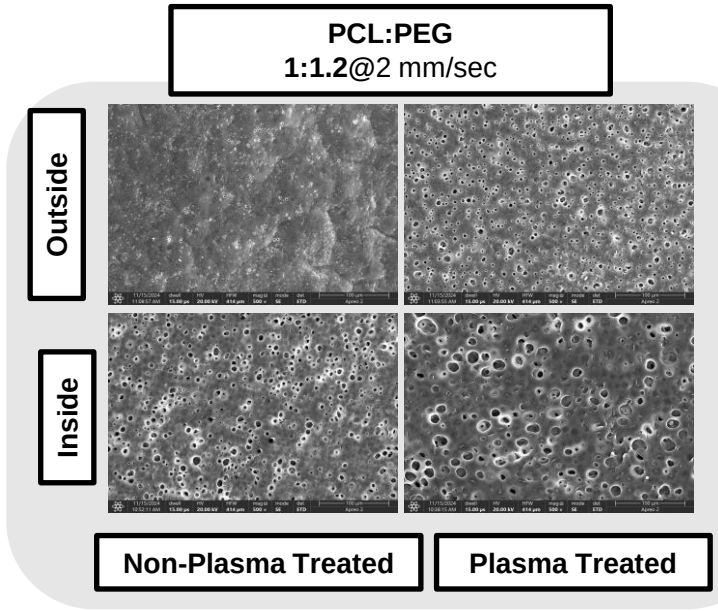


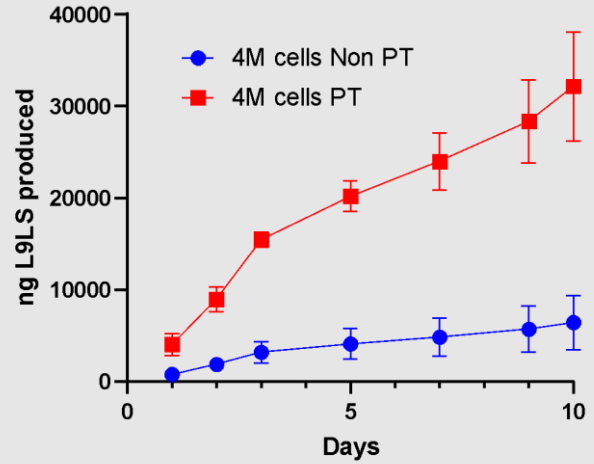


15-20% release from devices

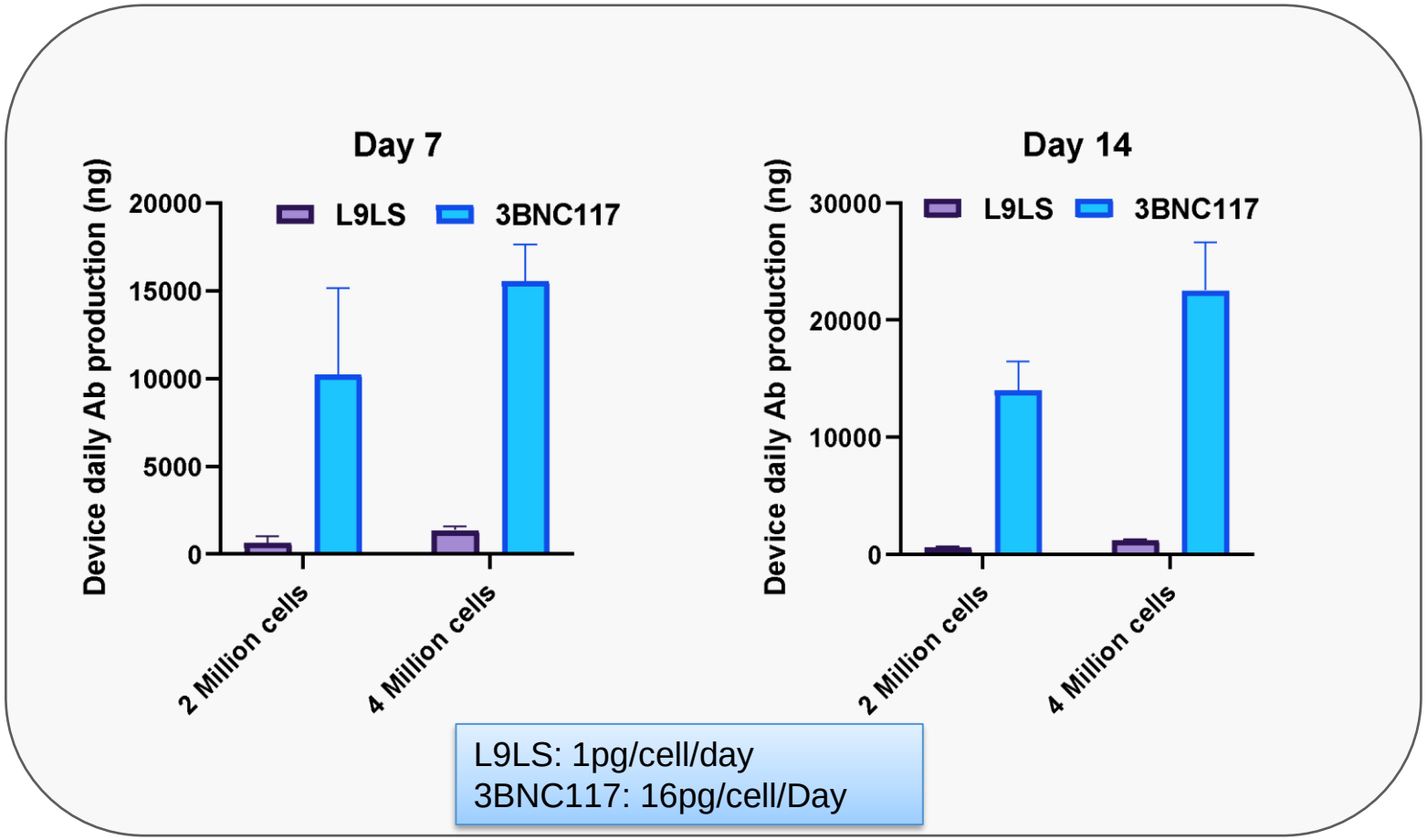
Plasma treatment enhanced Ab release





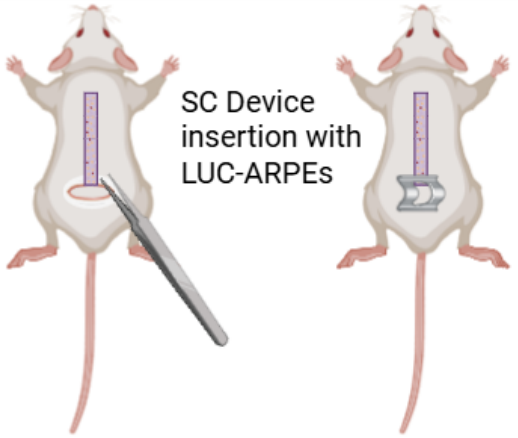


Higher productive cells Increase Device Ab output

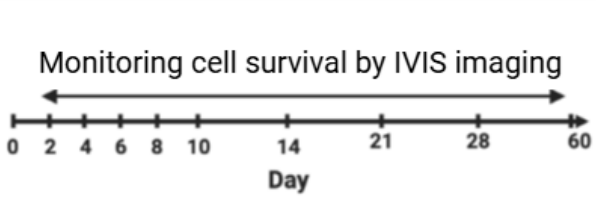


L9LS: 1pg/cell/day
3BNC117: 16pg/cell/Day

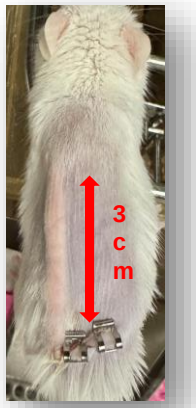
ARPEs survive in SC implanted devices

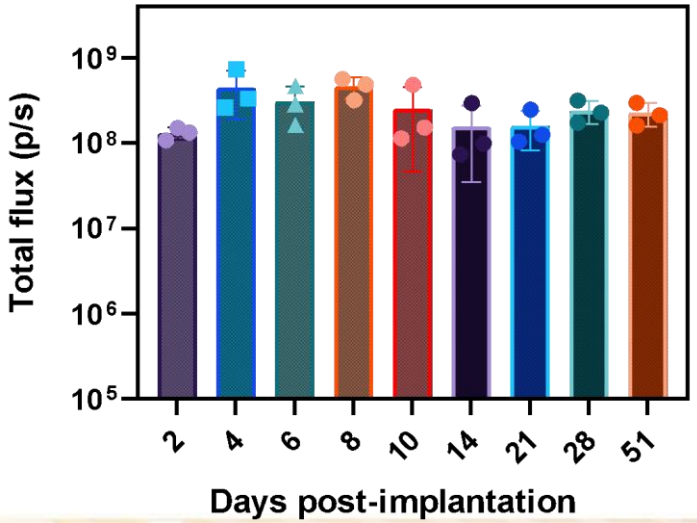


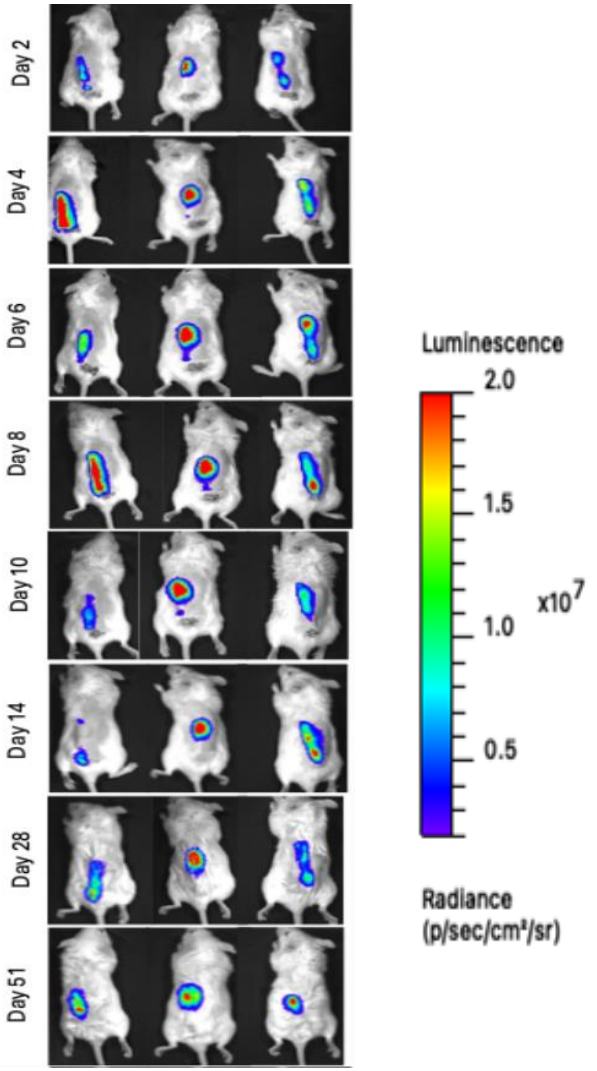
SC Device insertion with LUC-ARPEs



Retrieve the device for histopathology

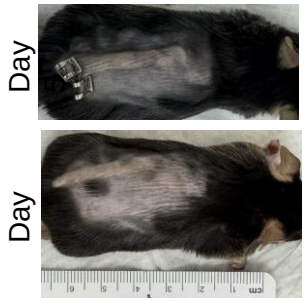


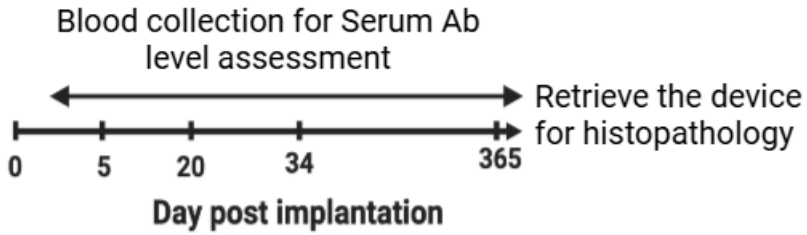




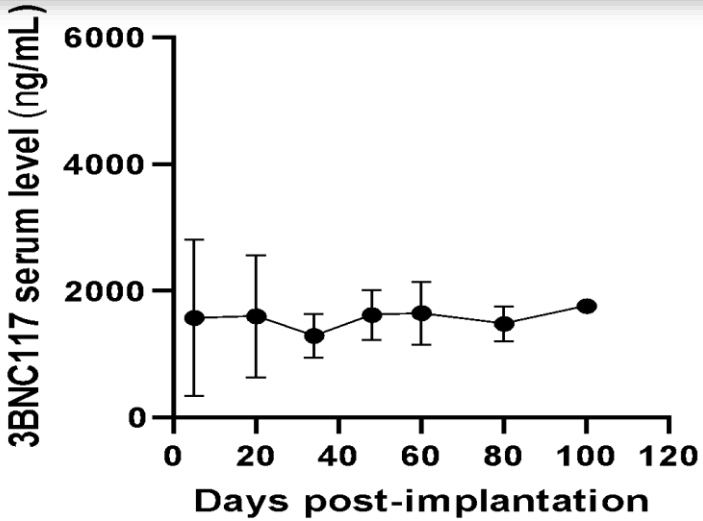
Akram Abbasi, PhD

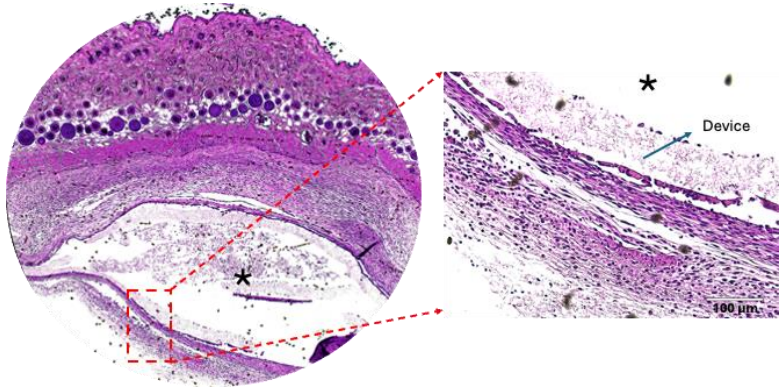
Long-term in vivo delivery of Abs from a single administration of cell encapsulation devices



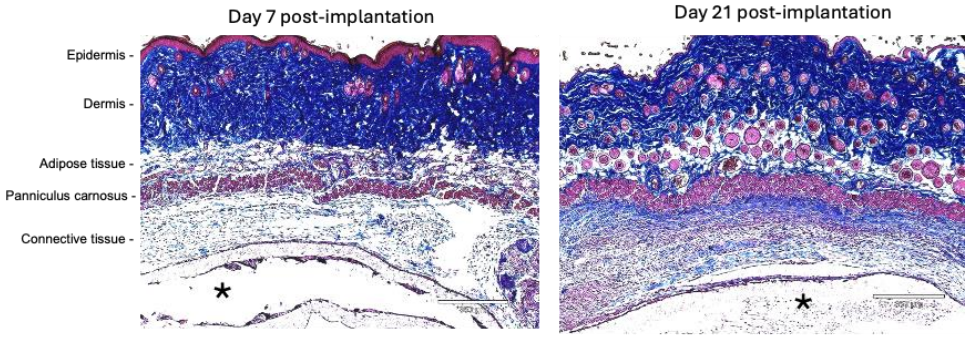


N=5





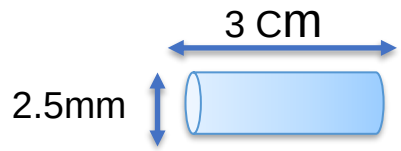
H&E staining showing that devices are tolerated without histopathological alterations



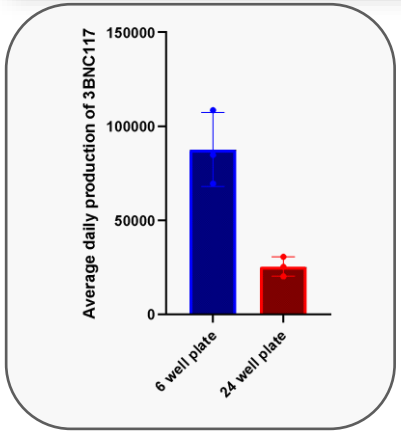
Maison trichrome staining showing minimal fibrosis

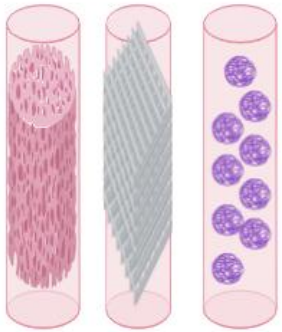
Conclusion & Future direction

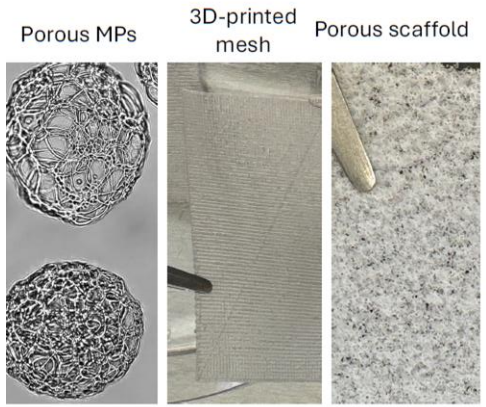
1. Porous PCL tubular devices offers highly modular simple scalable antibody factory design that functions irrespective of host stimulus
2. The implanted cell device can be placed with a single minimally invasive procedure
3. Encapsulated therapeutic cells produce sustained Ab serum levels for in-vivo



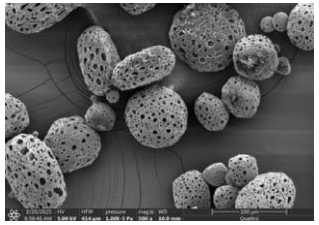
Microporous internal scaffolding for enhanced Ab production

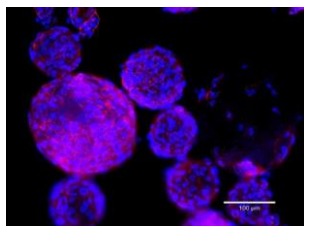


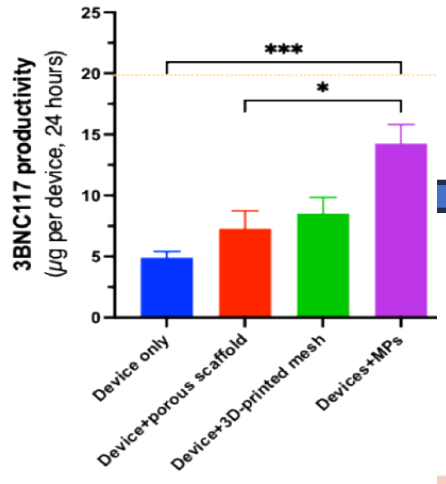


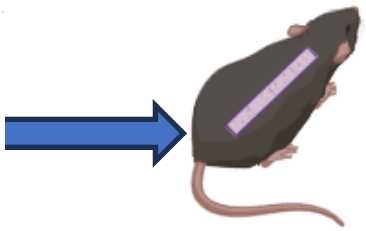


More Surface area, more Ab









Ongoing in vivo assessment

Acknowledgement

Desai Lab (Brown University | UCSF)

Tejal Desai
Akram Abbasi
Kareem Ebeid
Deblin Jana
Jingge Chen
Brendan Knittle
Audrey McCarthy
Stephen Arthur
Jean Jerome
Daria Smuk
Daniel Bernards
Bhushan Kharbikar
Nafisa Elghazali
Mollie Eva Hansen
Cynthia Perez
Preethi Raghavan
Justin Zhong

Omid Veiseh

Anthony Davis

(INV-063468)