## SHAPING THE FUTURE OF PEDIATRIC FORMULATION DEVELOPMENT

CERSI
University of Maryland

# Microneedle-Based Biologics:

## A Next-Generation Platform for Pediatric Delivery

### AFFILIATIONS


KOCH INSTITUTE
for Integrative Cancer Research at MIT

Massachusetts Institute of Technology

Prof. Robert Langer Group

Pioneering drug delivery technologies and biomaterials to improve human health.

Sonika Chibh, PhD
Visiting Scientist

# The Gap Between Innovation and Delivery

## INJECTIONS

- Painful and fear inducing
- Clinic/healthcare professional dependent
- High caregiver burden
- Cold chain challenges

## ORAL DRUGS

- Taste, odor, leading to poor acceptance
- Frequent dosing required
- Variable absorption and GI degradation

**A Potential Alternative for Pediatric Biologics**

## MICRONEEDLE PATCHES

- Minimally invasive, pain free
- Home/self-administration
- High acceptability
- Thermostable formulations

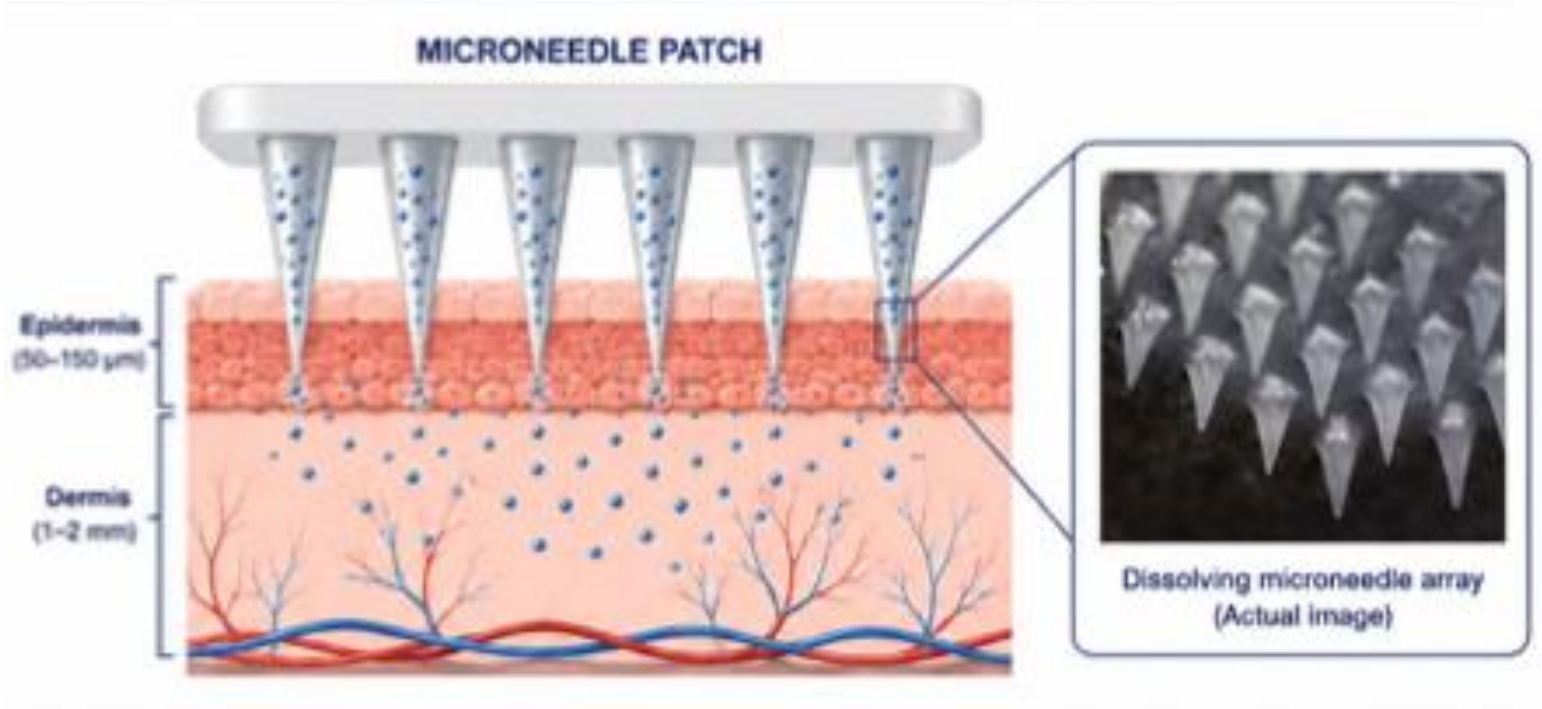
**The future of pediatric biologics delivery is not just about better drugs-It's about better delivery experiences.**

# Microneedle-array Patches (MAPs)

Microneedle Patches are minimally invasive delivery systems designed to administer biologic therapeutics through micron scale projection into the skin.

Biologics that can be delivered:

- Vaccines
- Proteins
- Peptides
- Nucleic acids
- Virus like particles



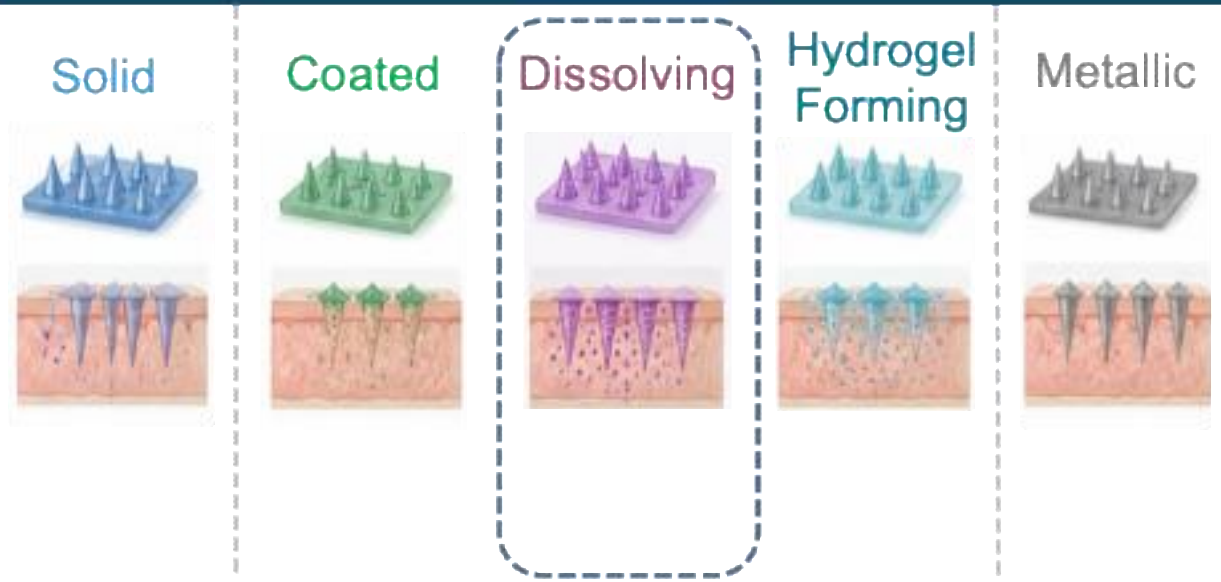

Precise delivery

Minimally invasive

Thermostable delivery

# Microneedle Patches (MAPs): Different Designs, One Goal

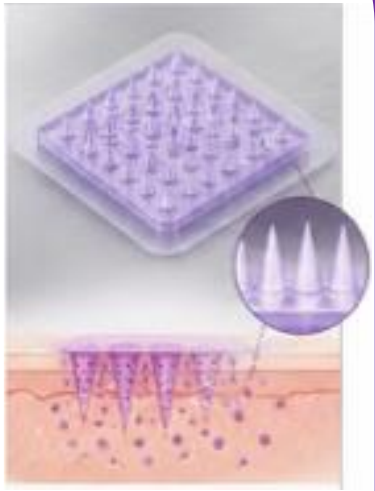
## TYPES OF MICRONEEDLES




Dissolving MNPs uniquely combine high performance with a child-friendly experience-
Making them the most promising platform for next-generation pediatric biologics delivery.

## WHY DISSOLVING MICRONEEDLES?

- High Biologic Compatibility
- High Drug Loading
- No Removal Needed
- Improved Safety Profile
- Better Patient Experience
- Ideal for Pediatric use

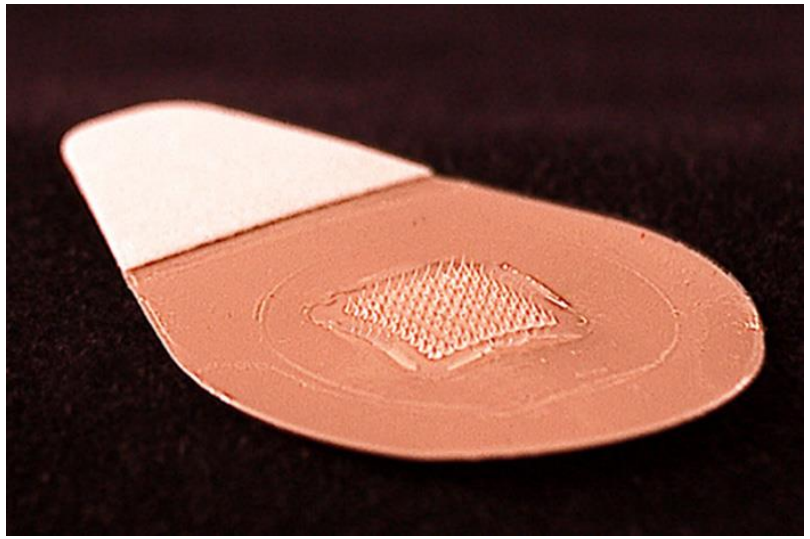


**DELIVER.
DISSOLVE.
DISAPPEAR.**

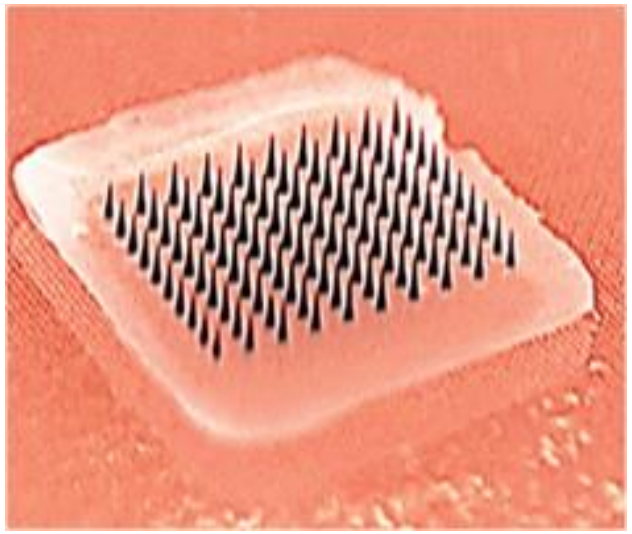
**“Dissolving microneedles combine biologic compatibility with patient-centric delivery”.**

# Clinical Translation of Microneedle Influenza Vaccination

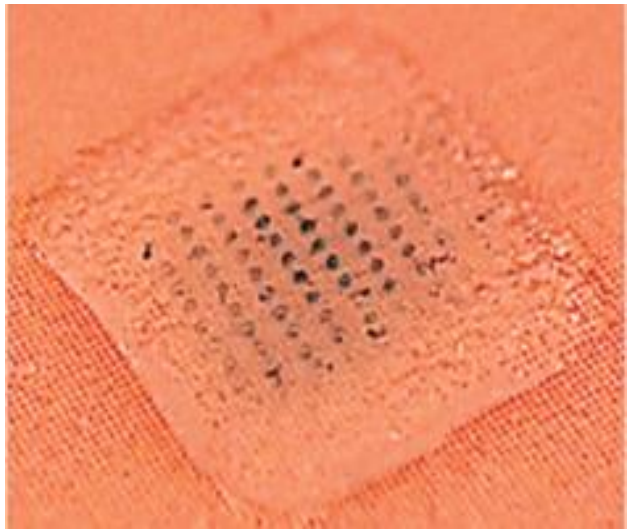
## Dissolving microneedle patch for influenza vaccine delivery



Microneedle Patch



Under microscope



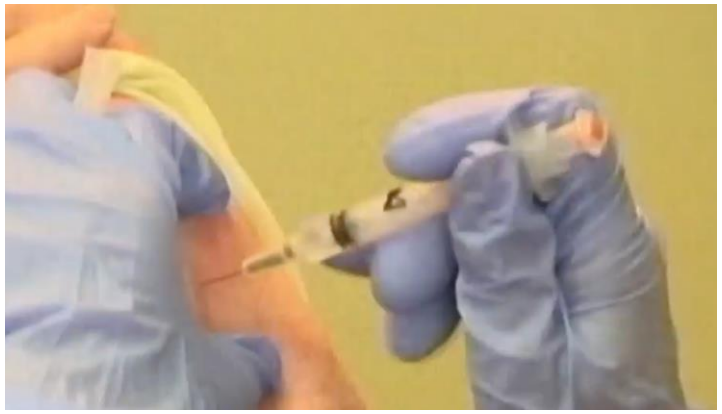
After dissolving

**Phase I clinical trial:** “Conducted by Emory University in collaboration with Georgia Institute of Technology”

**Safe and well tolerated:** “Dissolvable MNPs were safe and well tolerated by study participants”

**Published in “*The Lancet*”:** Results of this study were published June 27, 2017 in “The Lancet”

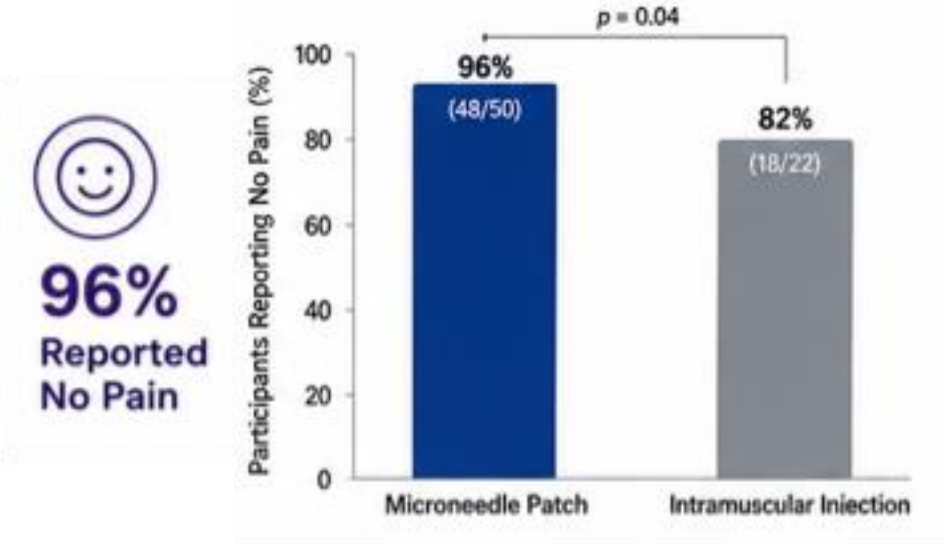
# Microneedle Patch for Flu Vaccination (against Influenza)

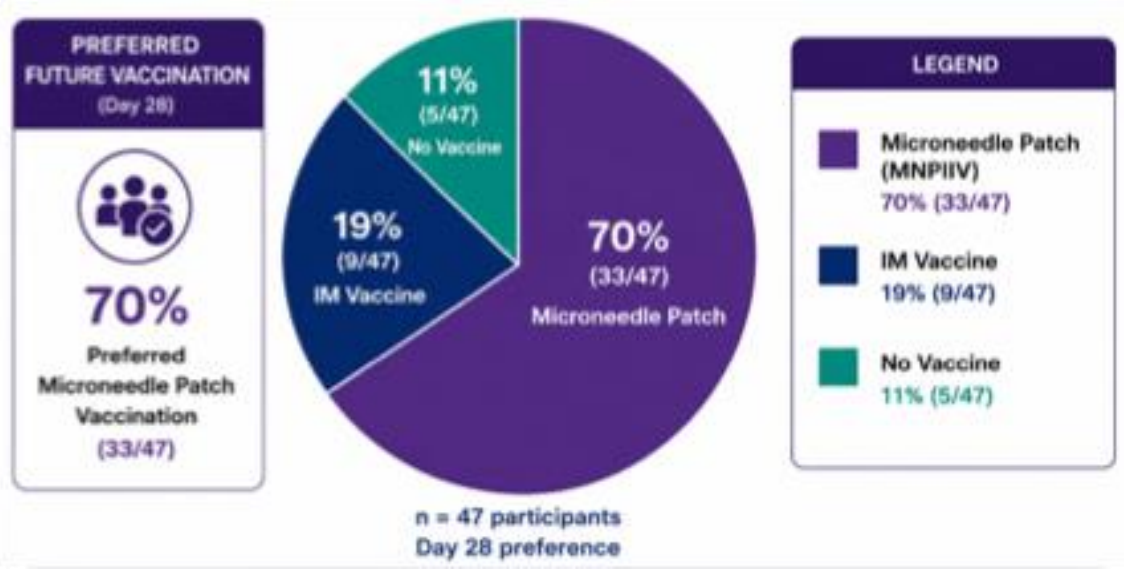


Intramuscular Injection

Administered MNP by healthcare-worker (applied for 20 min)

Self administered MNP (applied for 20 min)



# Pediatric Clinical Translation of MRV Microneedle Vaccination

First data in children | Well tolerated and safe | Comparable Immunogenicity | Consistent with Preclinical data

## STUDY DESIGN AND POPULATION

**Total enrolled & vaccinated (285)**

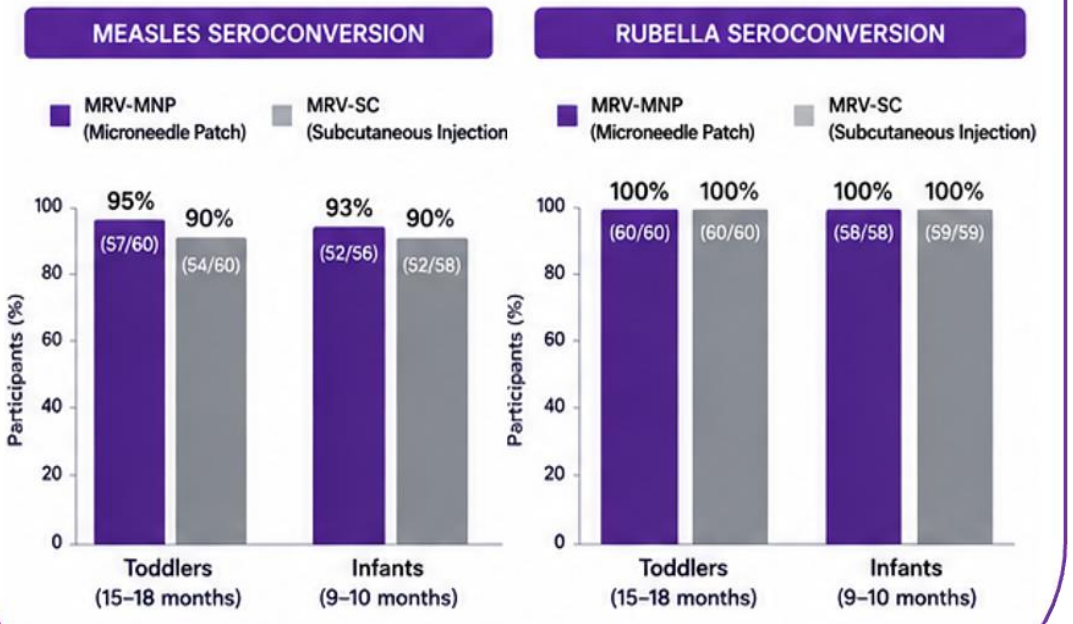
- **Adults** 18-40 years n=45
- **Toddlers** 15-18 months n=120
- **Infants** 9-10 months n=120

MRV-MNP → + Placebo SC injection

MRV-SC → + Placebo SC MNP

## IMMUNOGENECITY (AT DAY 42)

Seroconversion rates for MRV-MNP were similar to MRV given by SC injection




First clinical study of MAP vaccination in children.

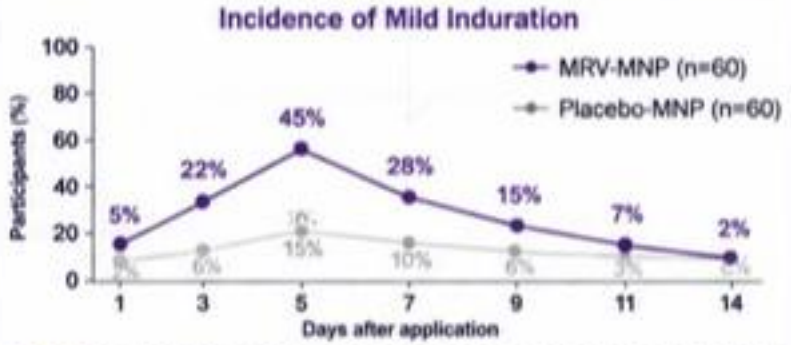
*The Lancet, 2024*

# Safety and Tolerability of MRV-MNPs in Toddlers

## LOCAL SKIN REACTIONS

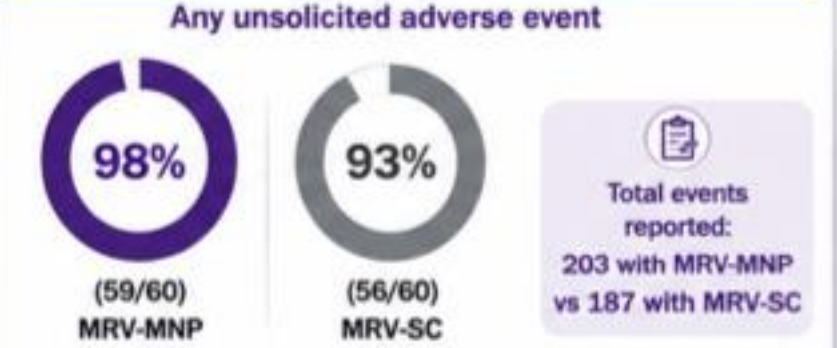
**83%**
(50/60)
Mild local reactions with MRV-MNP

**77%**
(46/60)
Mild induration (most common event)



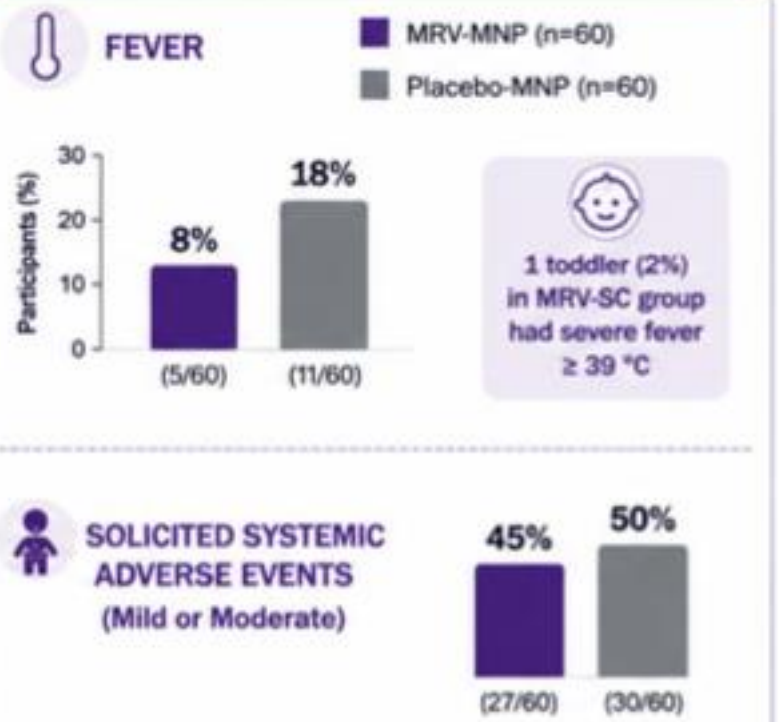

All local reactions were mild and transient

## UNSOLICITED ADVERSE EVENTS




No major safety concerns identified

## SYSTEMIC SAFETY




Systemic events were comparable to control

# Translational MAPs Success Toward Next Generation Polio Vaccines

***Building on the first pediatric microneedle vaccine success toward VLP-based polio vaccines.***

## CLINICAL VALIDATION

THE LANCET

MNPs for measles-rubella, vaccination in children, phase-1 trial

First pediatric trial of MRV vaccine delivered by MNPs in The Gambia

Well tolerated

Comparable immunogenicity

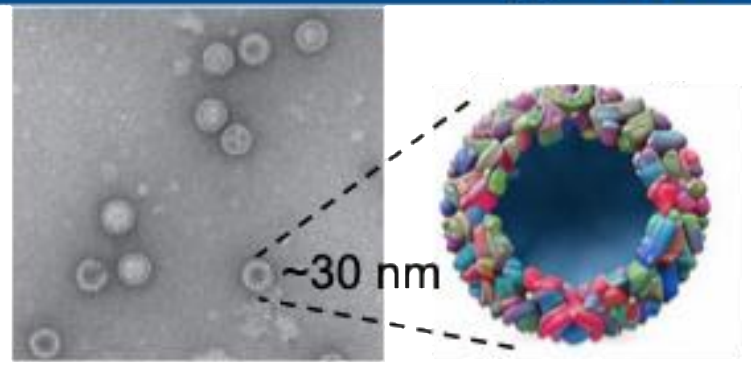
Enables next-generation biologic delivery

## POLIO VLP OPPORTUNITY WITH MAPs

| | |
|---|---|
| **Non-infectious VLPs** | Eliminates risk of vaccine derived poliovirus |
| **Thermostable** | Reduces cold-chain dependence |
| **Needle-free delivery** | Painless, easy to administer, no sharps waste |
| **Strong immunity** | Induce strong immunity |
| **Improved accessibility** | Wider coverage, better compliance, fewer visits |

# Overall Objectives

## (I) Polio VLPs delivering using microneedle patches (MAPs)

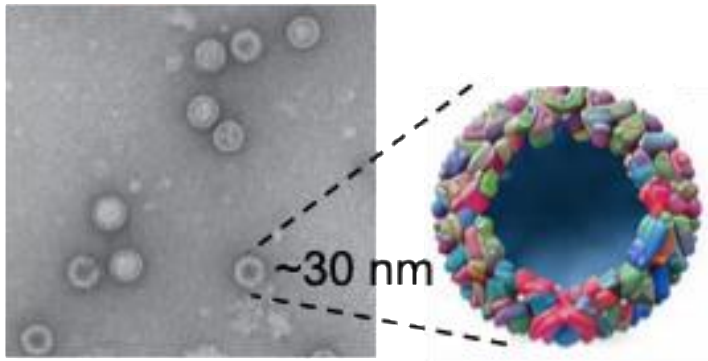



Polio virus like particles (VLPs)

Microneedle patch

Animal studies

## (II) Co-formulation of Polio-VLP with the pentavalent vaccines (Hib, HepB, WcP, Diphtheria, and Tetanus)




Polio virus like particles (VLPs)

Pentavalent

Microneedle patch

Animal studies

# Excipients screening using a vacuum-drying approach in 96-well plates to mimic the fabrication conditions of MAP formation

## THE CHALLENGE

- Drying stresses can destabilize VLPs and reduce antigen integrity
- MAP fabrication requires dehydration (vacuum drying/desiccation)
- Antigen preservation is critical for immunogenicity and vaccine efficacy

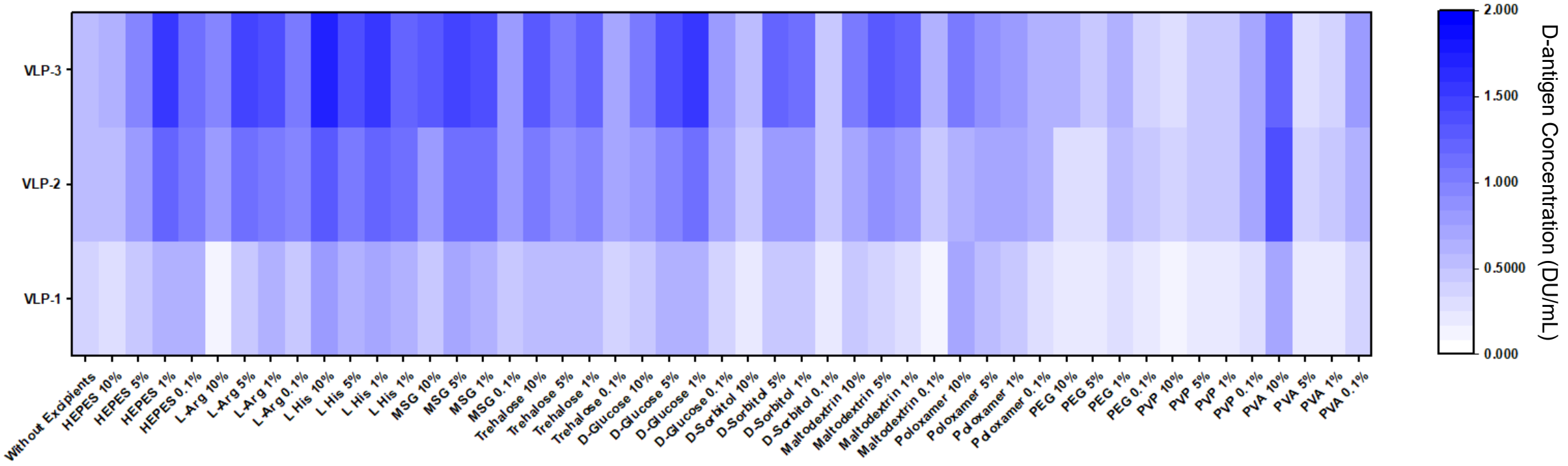
**Maintaining D-antigen integrity is essential for vaccine performance**

## 96-well plate assay

VLPs + Excipients → Addition of mixture in 96-well plate → Vacuum drying for 24 h → D-antigen measured using ELISA

Excipients screening using a vacuum-drying approach in 96-well plates to mimic the fabrication conditions of microneedle patch formation.

# ELISA results of excipients screening using 96-well plate assay to simulate the microneedle patch formation

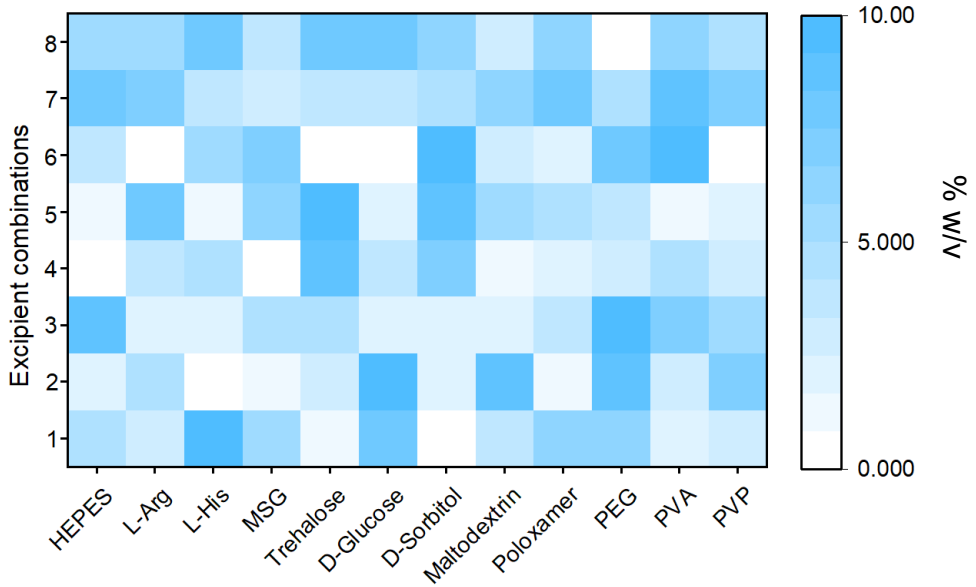



- VLP-1, VLP-2 and VLP-3 were mixed together in 5:1:4 ratio with different percentage of excipients and dried under desiccator for overnight. ELISA was performed to evaluate the stability of VLPs (I, II and III) in the presence and absence of different percentage of excipients ranging from (10% to 0.1%).

- The results demonstrated enhanced stabilization of VLPs when formulated with excipients.

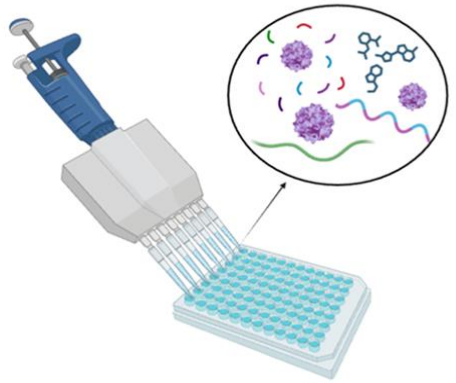
# AI assisted excipient screening to stabilize VLPs in 96-well plate assay

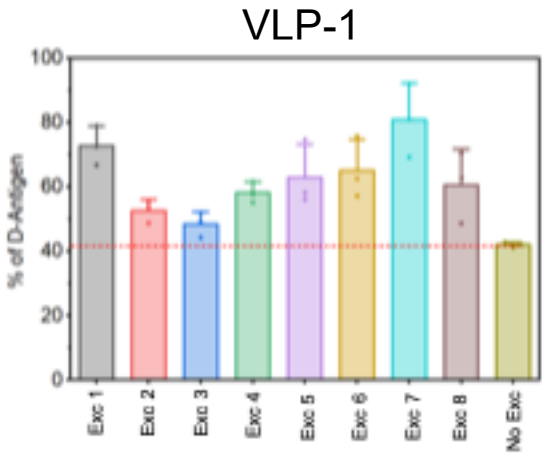
## Combinations generated by AI

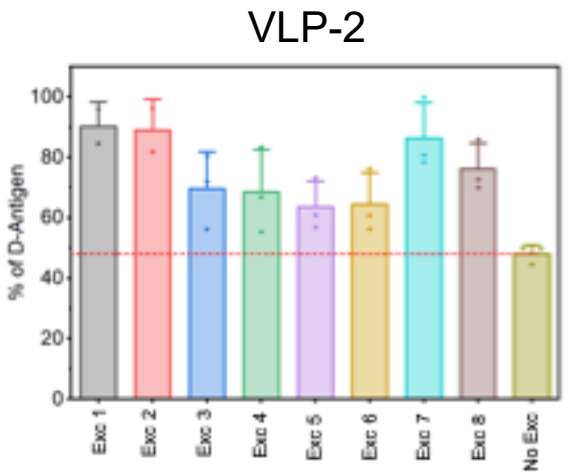


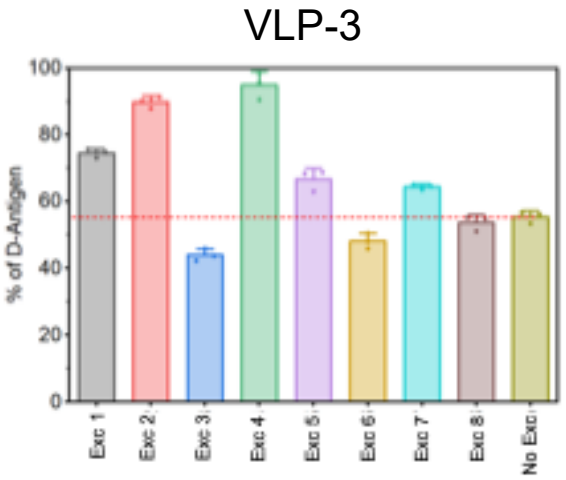

Based on the previous ELISA results, we subsequently applied an AI-driven screening approach to identify an optimal combination of excipients that could collectively stabilize all three VLPs in 96 well plate assay.

## 96-well plate mixing assay of VLPs with excipients



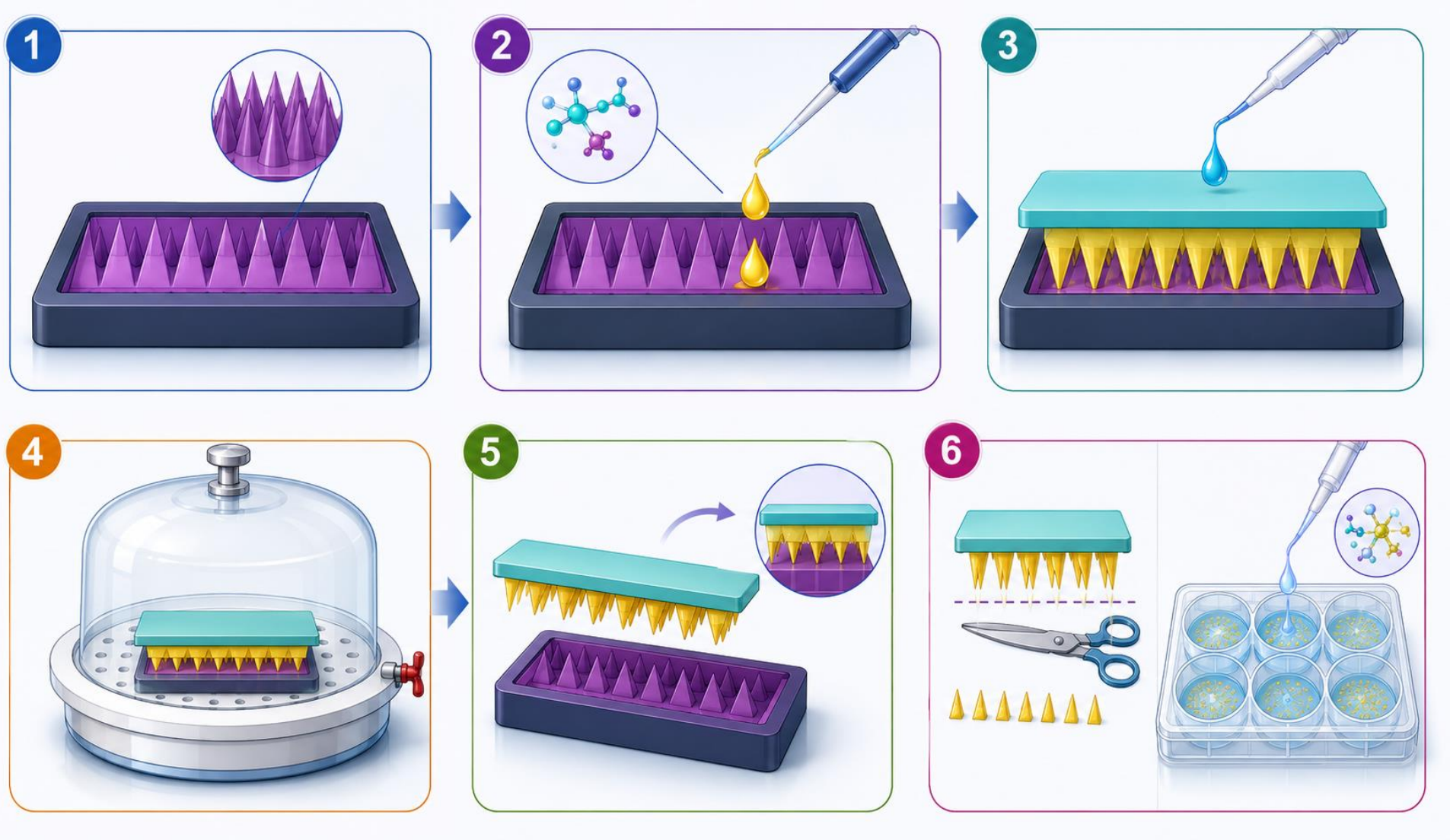



✓ *Using a 96-well plate–based mixing assay of VLPs with selected excipients, we achieved approximately 80-90% antigen stability.*

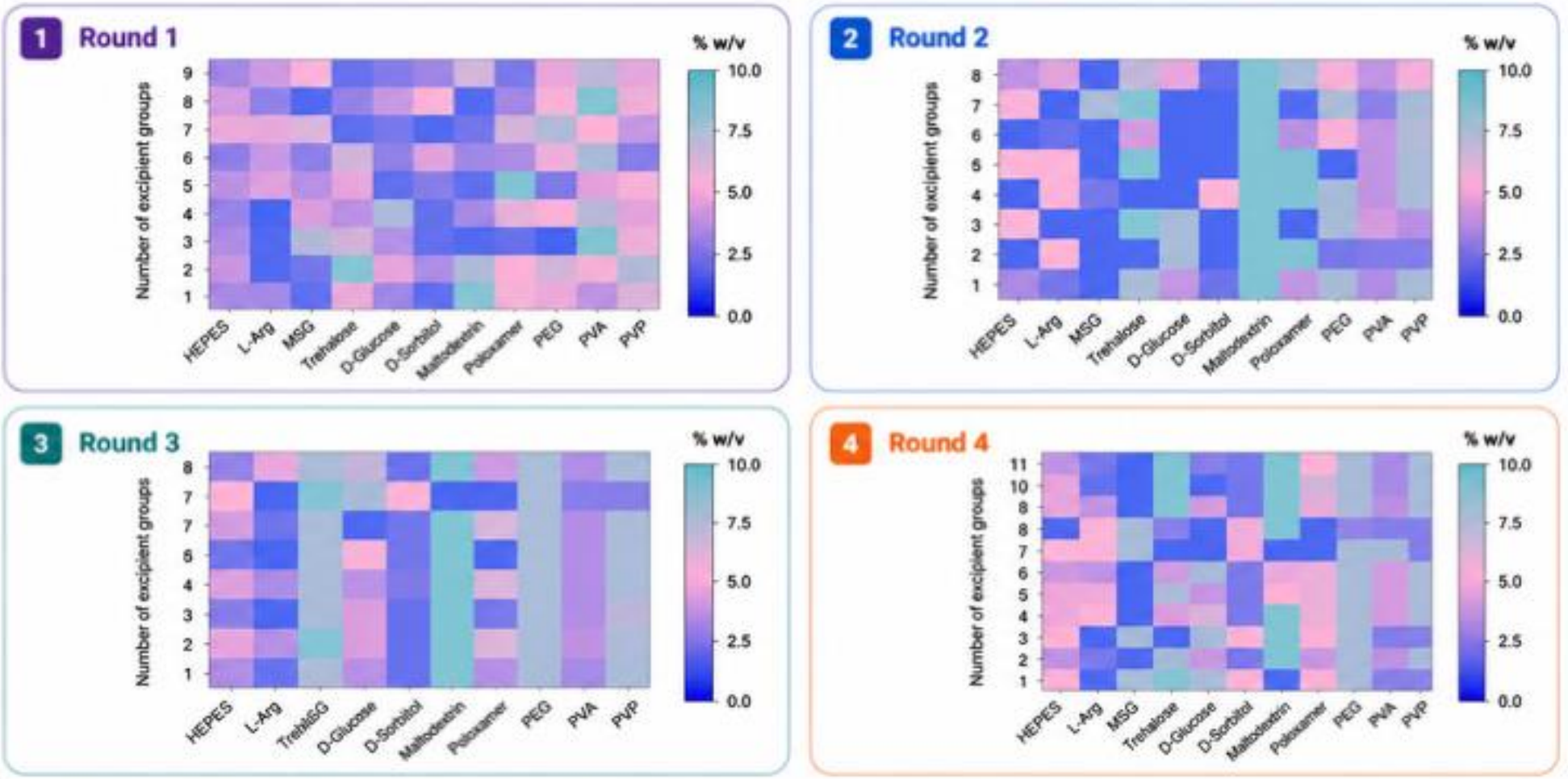
# Schematic Representation of MAP Fabrication




**Steps:**

1. PDMS mold
2. Addition of VLP I,II,III mixture with excipients
3. Addition of backing layer
4. Vacuum drying for 24 h
5. Peel out the patch
6. Cut down the needles and dissolve in buffer

# Sequential rounds of AI-guided excipient screening for the stabilization of VLPs in MAPs



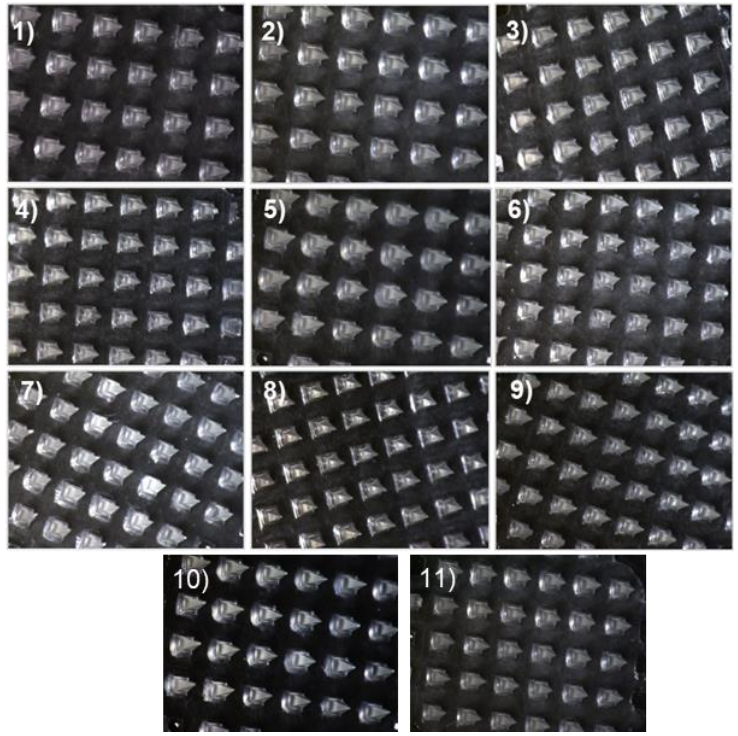

## Key highlights

- Graphs 1-4 shows data generated through AI.
- Following each round of AI screening, MAPs were fabricated using different groups.
- ELISA was conducted after dissolutions of needles to evaluate D-antigen recovery.

AI guided screening refines excipient combinations to enhance VLP stabilization

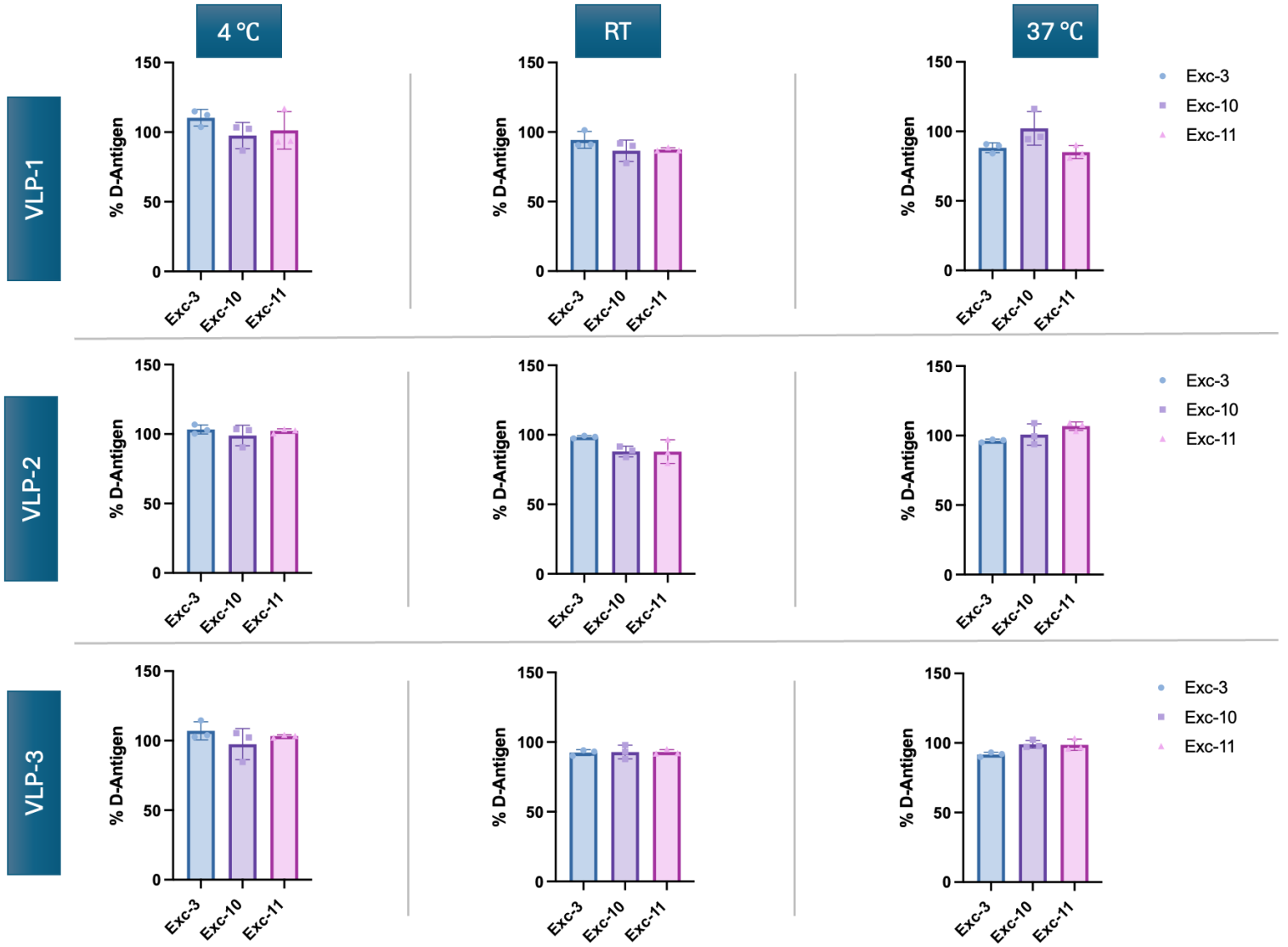
# Identification of lead excipients group to stabilize all VLPs following AI-guided Screening


MAPs fabrication




- The microneedles were dissolved in an appropriate buffer, and the released antigen was quantified using ELISA.
- The percentage of D-antigen retention was calculated relative to the corresponding soluble VLP control formulation.

# Thermostability of VLP-loaded MAPs after one month

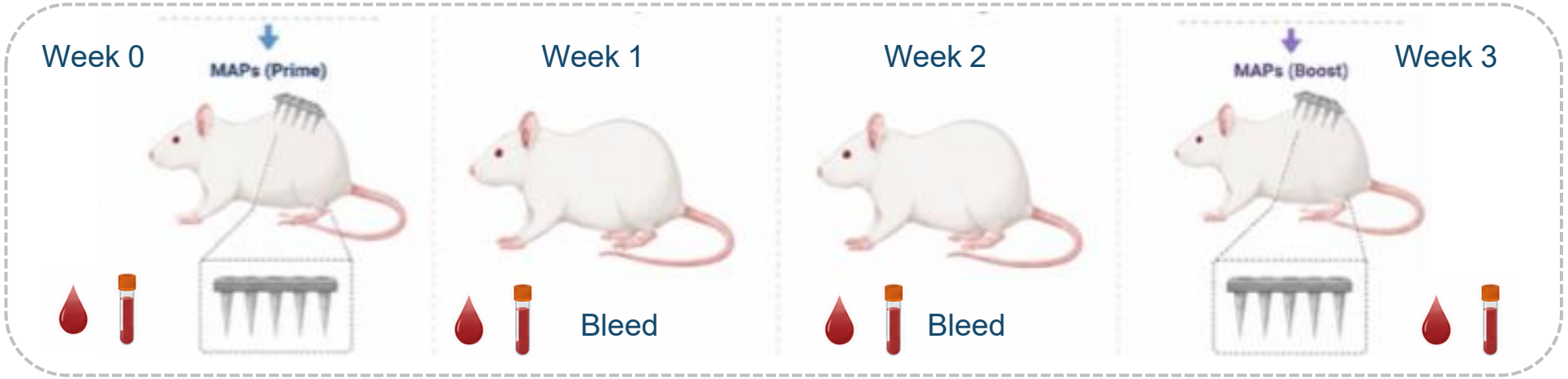


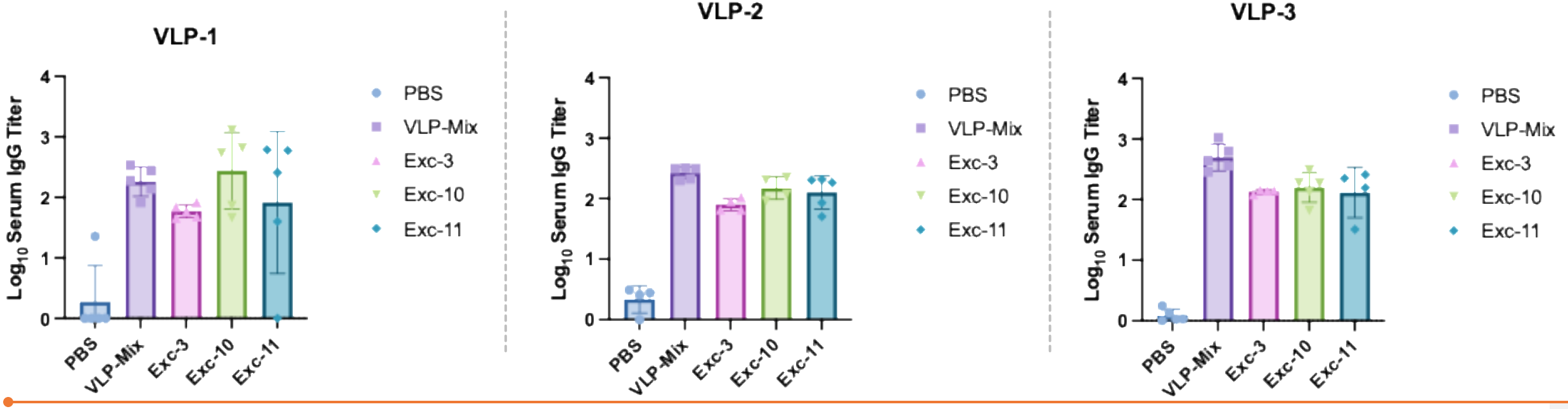

## Key highlights

- Three different excipients were used to make MAPs.
- MAPs stored for one month.
- Storage conditions:
  4 °C, RT and 37 °C.
- After one month, MAPs dissolved in buffer.
- D-antigen quantified using ELISA

VLP-1, VLP-2 and VLP-3 stable

# Preliminary Immunogenicity Results Following Prime Immunization



# Conclusions

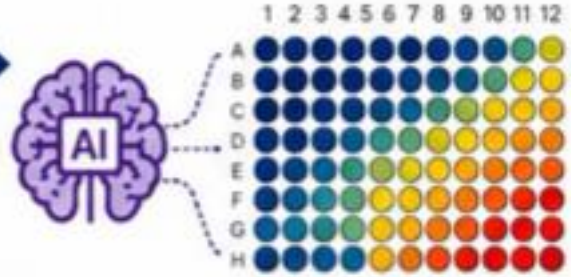
## 1 CHALLENGE

Polio VLPs are sensitive to drying during MAP fabrication

- D-antigen loss during drying and MAP fabrication
- Need for thermostable formulations
- Preserving immunogenicity is critical for efficacy

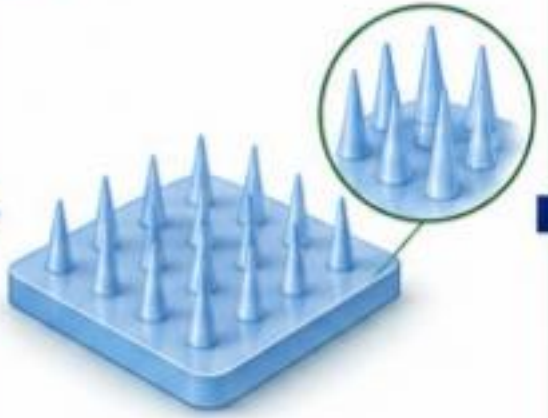
## 2 AI-DRIVEN SOLUTION

AI-assisted excipient screening identified stabilizing formulations




- 96-well plate vacuum-drying screening platform
- AI algorithm ranked combinations for maximum stability
- Optimal excipient combinations selected for VLP-1, VLP-2, VLP-3

## 3 KEY OUTCOMES



- ✓ Exc-3, Exc-10 and Exc-11 selected
- ✓ ≥90% D-antigen recovery after MAP fabrication
- ✓ Stability maintained at 4°C, RT and 37°C
- ✓ Robust IgG responses after prime immunization

## 4 NEXT STEPS

- Post-boost immunogenicity studies
- Neutralization antibody evaluations
- Long-term stability assessment
- Advance toward combination vaccine MAPs

# Beyond Vaccination: Expanding the Potential of MAPs

**Influenza MAP**


**MRV-MAP**

**Polio-VLP MAP**

**Platform Validated**

- Safety
- Tolerability
- Delivery

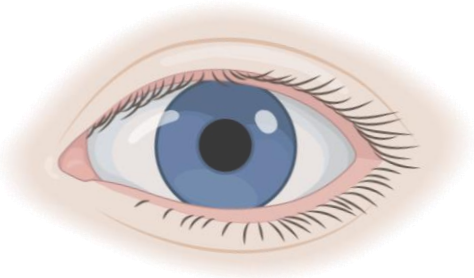
**NEW FRONTIERS**

**Ocular Delivery of Biologics**

mRNA delivery

# Dissolving Ocular Microneedle Contact Lens

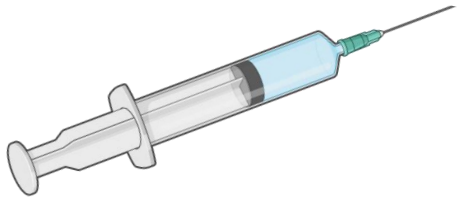
***Breaking the Ocular Barrier for Targeted Biologic Delivery***



OCULAR DELIVERY

## THE CHALLENGE

1

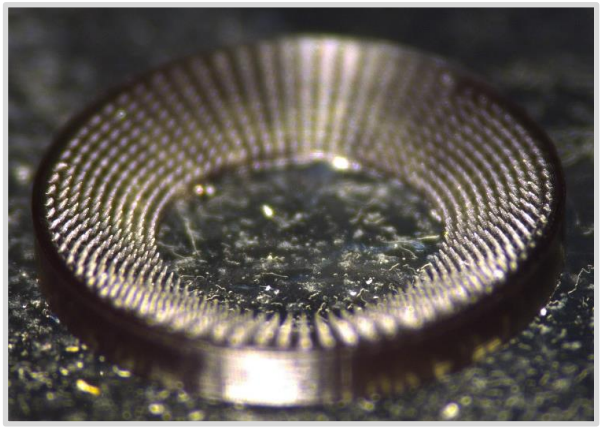


Invasive, retinal detachment, hemorrhage risk

2

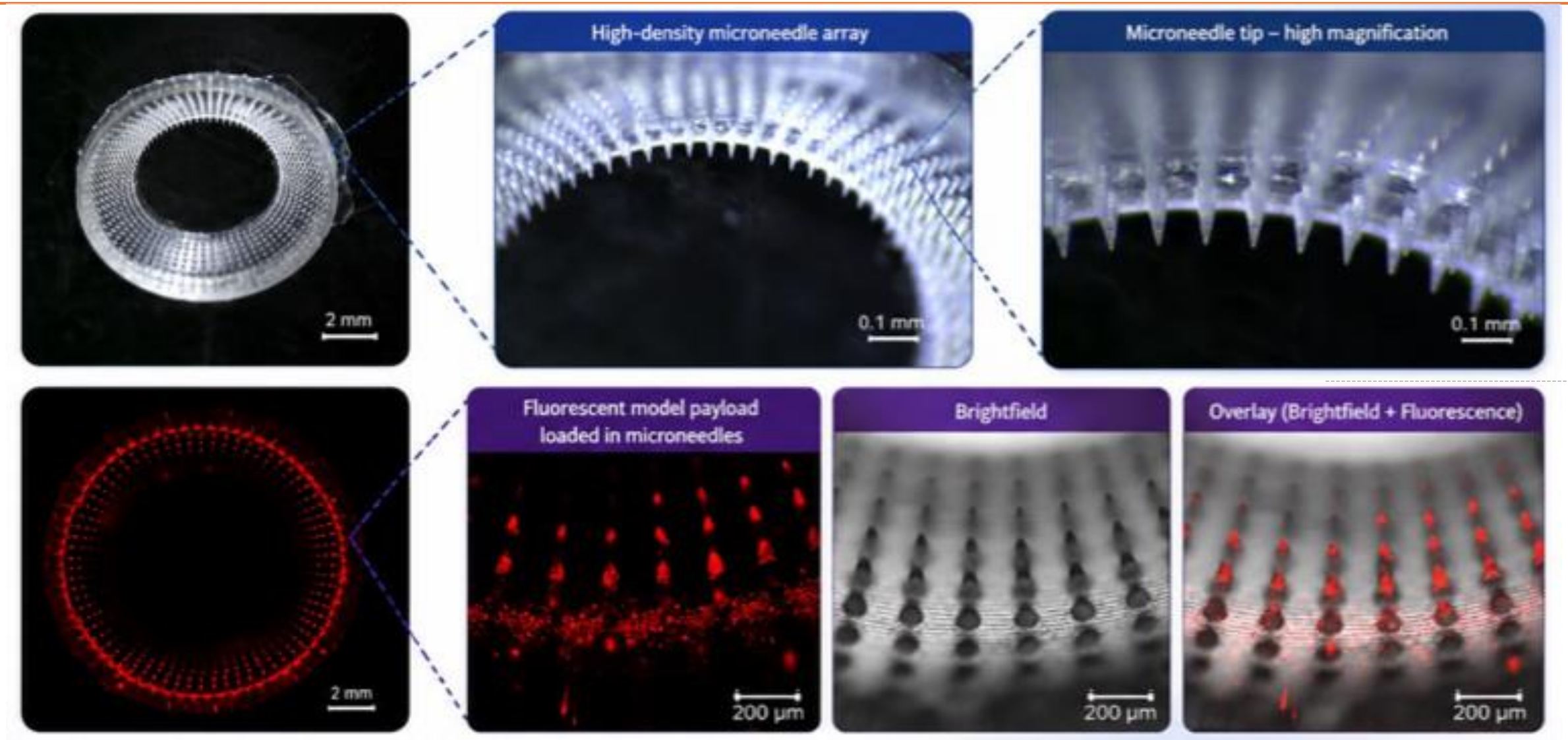
Low bioavailability, poor permeability into corneal

## OUR SOLUTION



MICRONEEDLE LENS

# Microneedle Contact Lens



# Thank You!

## Advancing the Future of Pediatric Vaccination

Needle-Free | Thermostable | Accessible | Patient-Centric


### ACKNOWLEDGMENTS

Bill & Melinda Gates Foundation

Fulbright-Nehru Postdoctoral Fellowship

Massachusetts Institute of Technology

### RESEARCH TEAM

- Prof. Robert Langer
- Dr. Ana Jaklenec
- Langer Lab Team
- Collaborators & Technical Support Staff

### SPECIAL THANKS

Special thanks to

Shuai Liu

Jinbi Tian

Taewon Jeon

### WORKSHOP ACKNOWLEDGMENT

We gratefully acknowledge the organizers of this workshop

U.S. Food and Drug Administration (FDA)

University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI)

IQ Pediatric Consortium

European Paediatric Formulation Initiative (EuPFI)

*For organizing the workshop "Shaping the Future of Pediatric Formulation Development"*

### LET'S STAY CONNECTED

sonika24@mit.edu

Connect with me on LinkedIn