

Single Injection Vaccines



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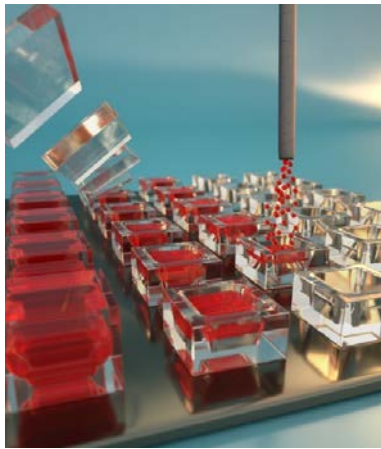


Global Vaccine and Immunization Research Forum (GVIRF)
Grand Hyatt, Incheon, Republic of Korea
March 29, 2023



Sustainable polymer based solutions for controlled delivery and stability of biologics and small molecules important for public health

Pulsatile drug delivery: **long-acting vaccines and therapeutics**



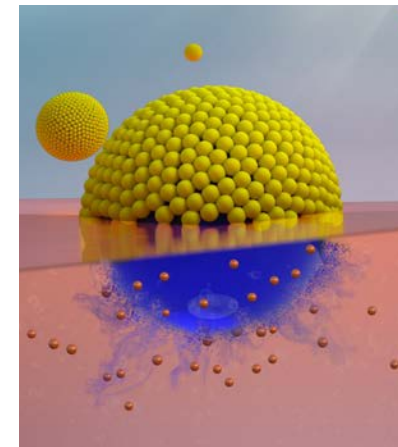
Science Trans. Med. 2020.
Science Adv. 2020 & 2022.
PNAS 2018.
Vaccine 2018.
Science 2017.

Microneedle based delivery: **vaccines and on patient record**



Nature Biotech 2023.
Science Trans. Med. 2019.

Heat-stable **micronutrient and probiotic delivery**



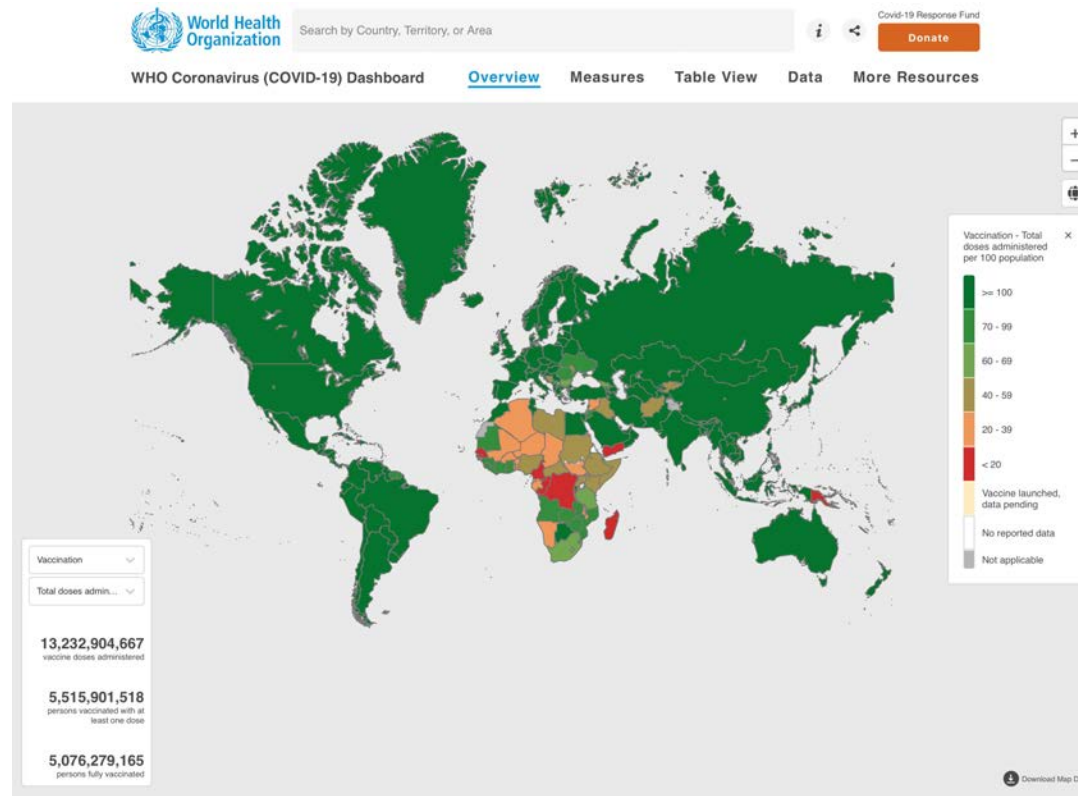
PNAS 2022.
Science Trans. Med. 2019.

COVID-19 Infections and Vaccinations



Globally, as of 11:31am CET, 16 March 2023, there have been 760,360,956 confirmed cases of COVID-19, including 6,873,477 deaths, reported to WHO. As of 14 March 2023, a total of 13,232,904,667 vaccine doses

COVID-19 Infections and Vaccinations



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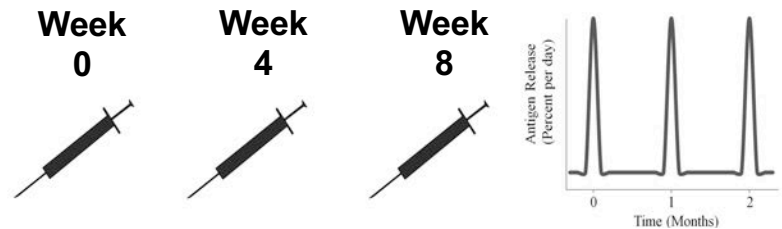
Single injection vaccine delivery for *self-boosting, long-acting and durable vaccines*

Approach: Develop a microparticle platform that confers immunity after a single injection by mimicking current vaccination regimens

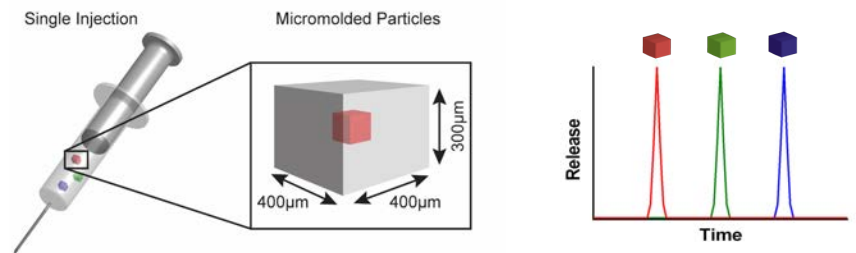
Advantages:

1. Reach herd immunity quicker due to improved compliance
2. Obtain higher and more sustained titers
3. Decrease the chances of variant's having a chance to occur due to 1 and 2

Current Vaccination Schedule

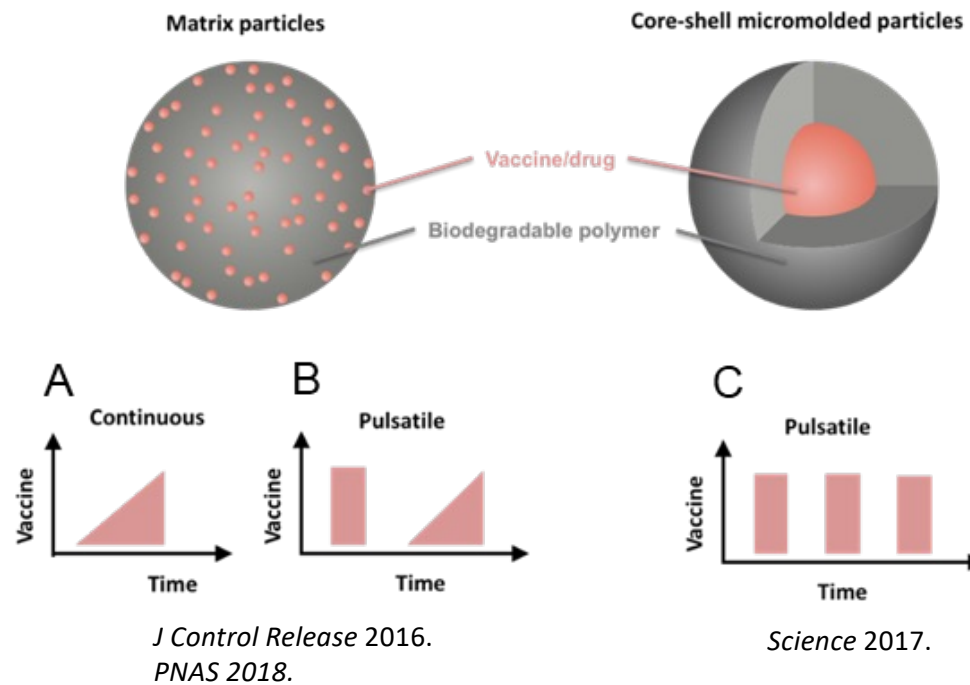


Single-injection Vaccination

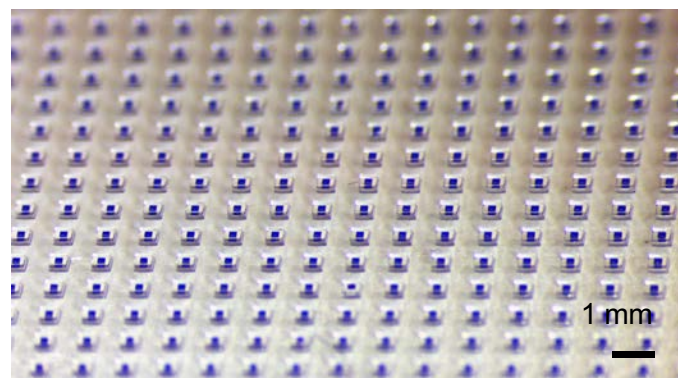
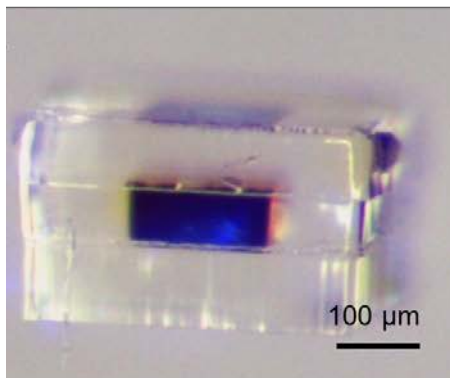
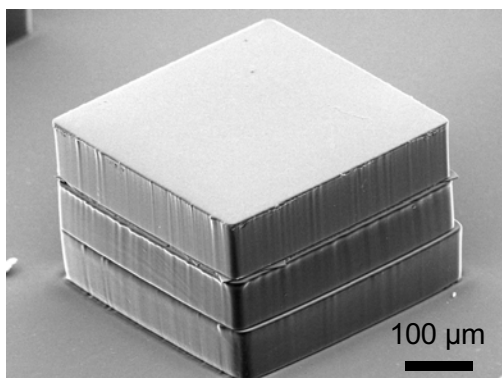
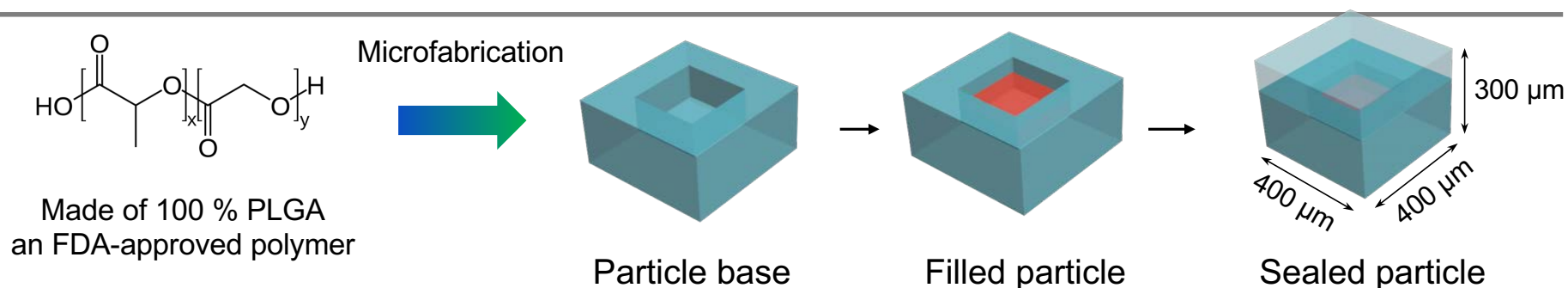


Pulsatile Drug Delivery Platform

Hypothesis: Microparticles with a core-shell structure will exhibit pulsatile release after a material-dependent delay



Micromolded particles using PLGA



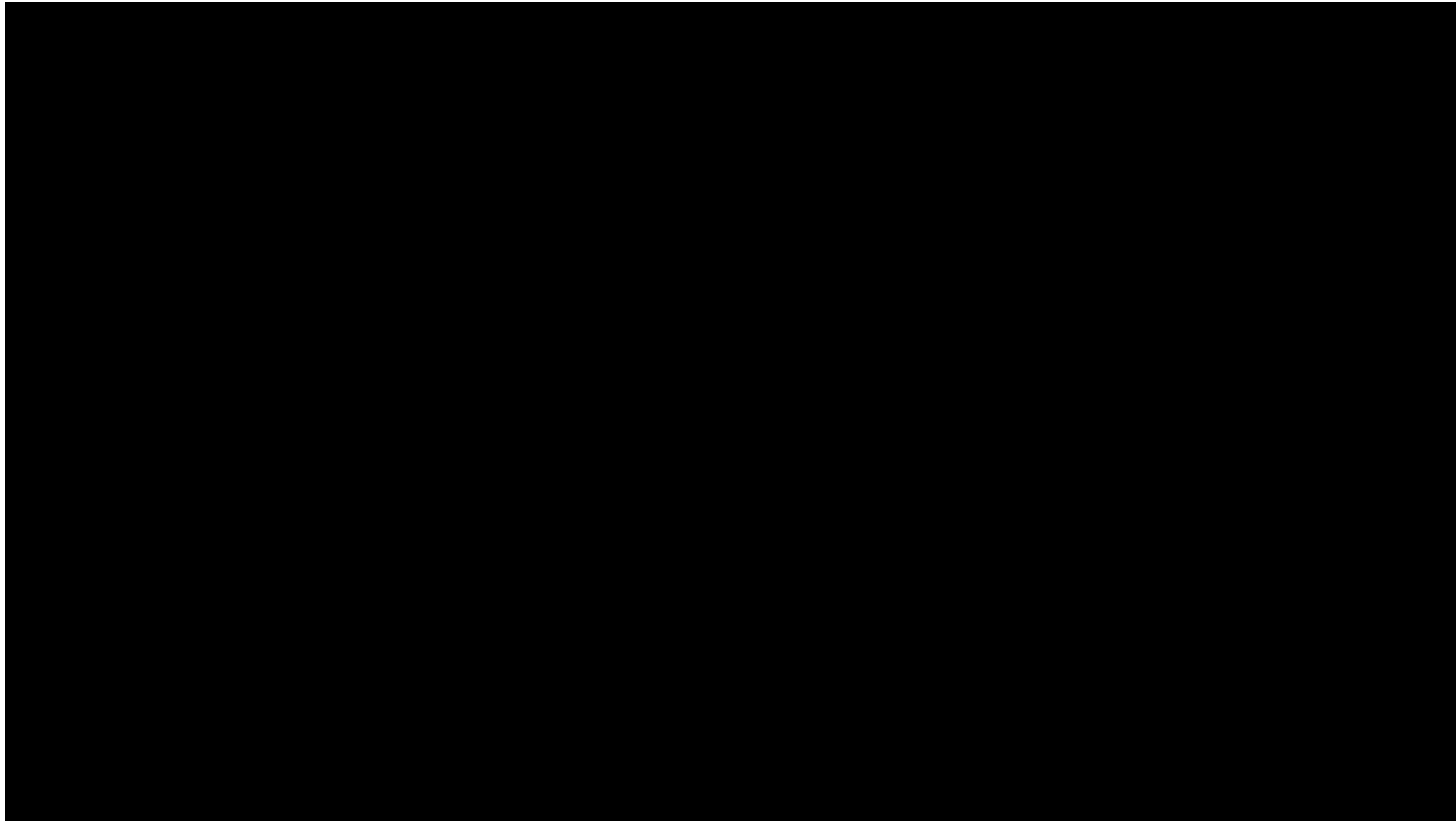
We could encapsulate a wide range of vaccines, including [inactivated viruses](#), [recombinant proteins](#), [nucleic acids](#), etc.



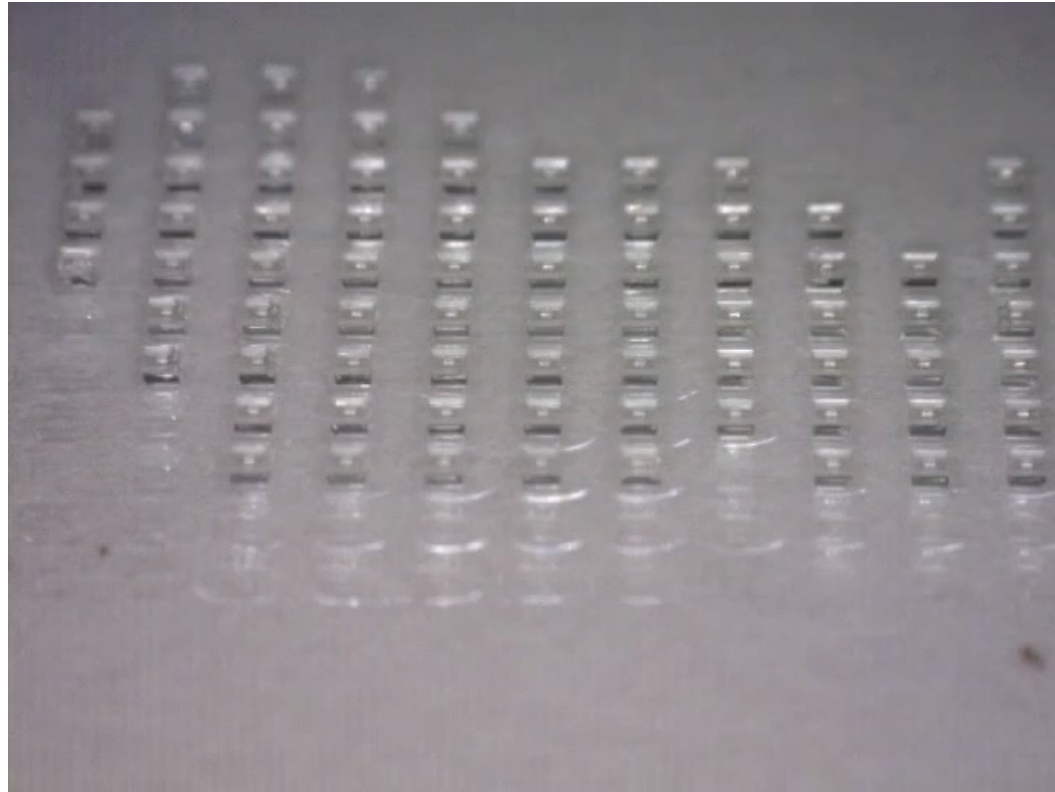
Massachusetts Institute of Technology

“Fabrication of fillable microparticles and other complex 3D microstructures.”
Science, 2017, 357, 1138

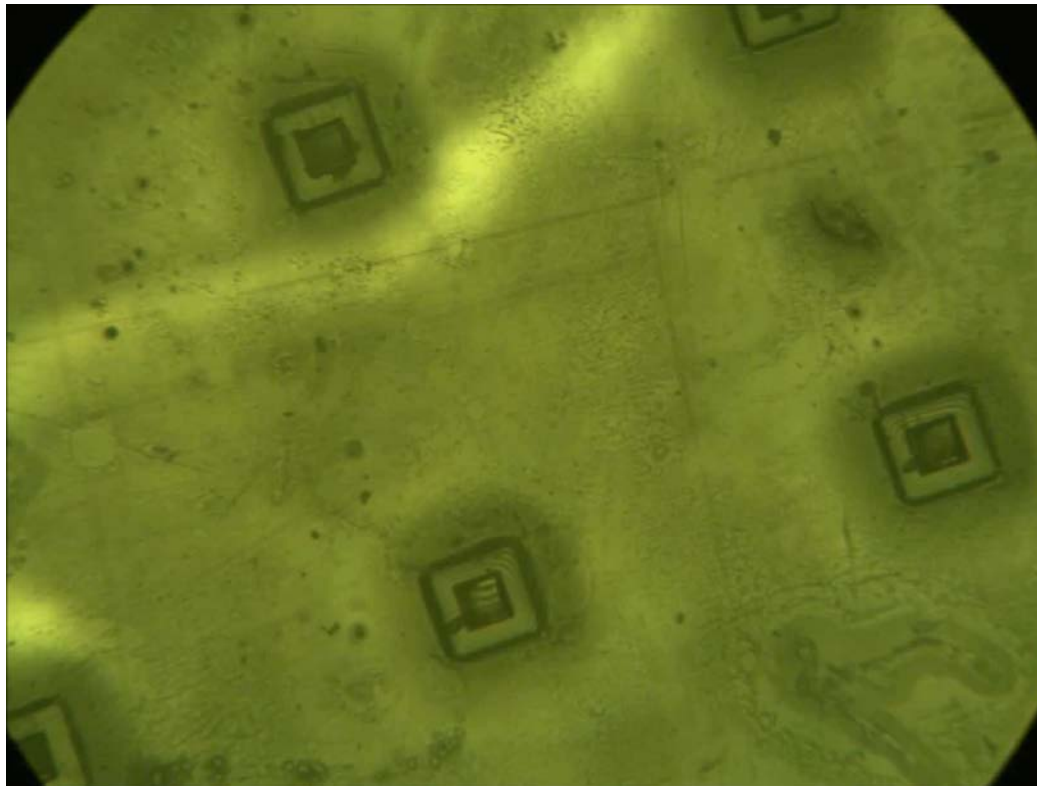
Microparticle Fabrication



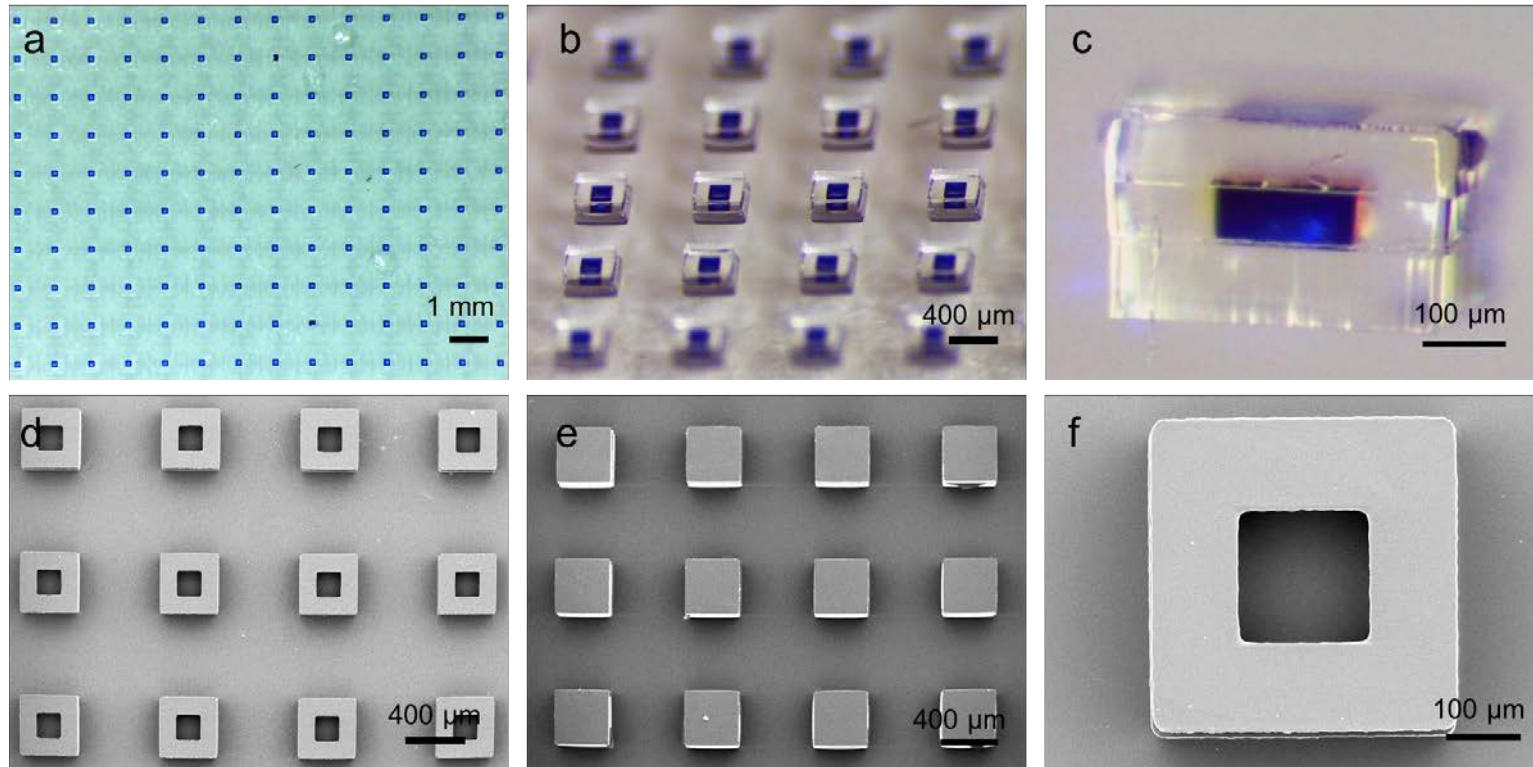
Microparticle Filling



Microparticle Sealing

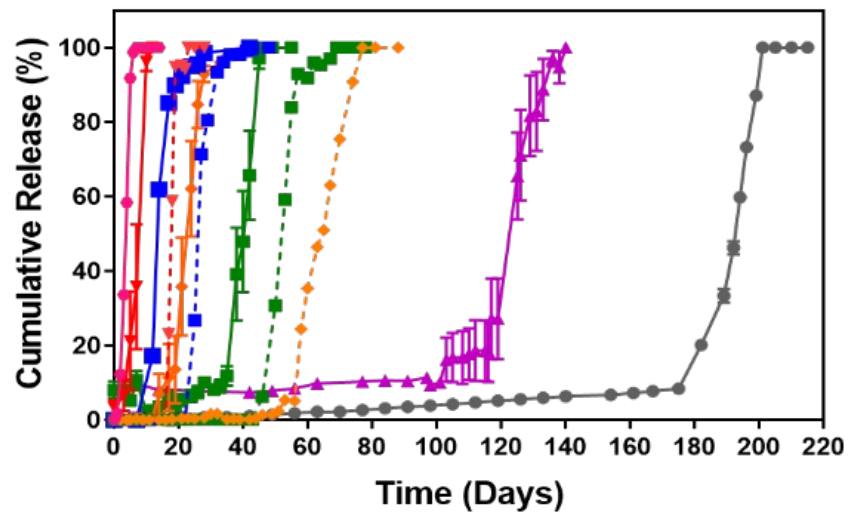


STING PLGA-MPs

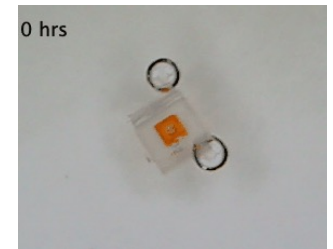
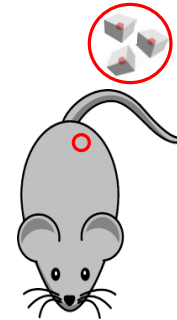


In vivo release kinetics library

Particle library that covers pulsatile release at ~1, 2, 4, and 6 months in mice

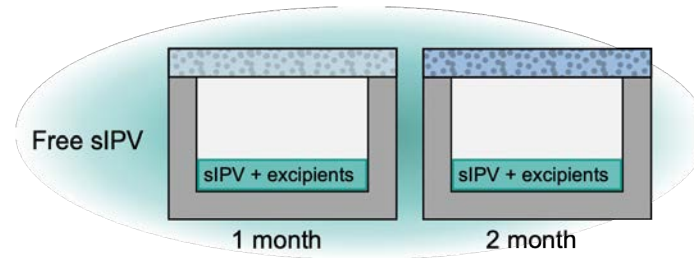
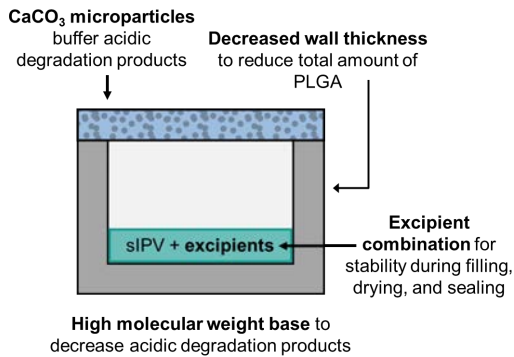


- PLGA 50:50, 4.4 kD, Acid
 - ▼— PLGA 50:50, 12 kD, Acid
 - PLGA 50:50, 30 kD, Ester
 - ◆— PLGA 50:50, 12 kD, Ester
 - PLGA 50:50, 61 kD, Ester
 - ▲— PLGA 75:25, 95 kD, Ester
 - PLGA 85:15, 214 kD, Ester
 - PLGA 50:50, 30 kD, Ester, + 10% CaCO₃
 - ▼— PLGA 50:50, 12 kD, Acid, + 10% CaCO₃
 - PLGA 50:50, 61 kD, Ester, + 10% CaCO₃
 - ◆— PLGA 50:50, 12 kD, Ester, + 10% CaCO₃
- Average ± SEM, n=7-22



Burst release at day 4
37°C in PBS buffer

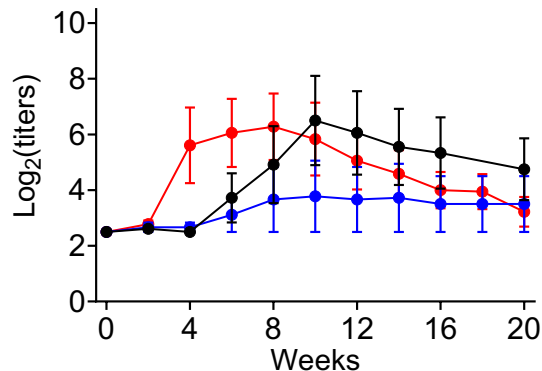
Self-boosting Sabin inactivated polio vaccine (sIPV)



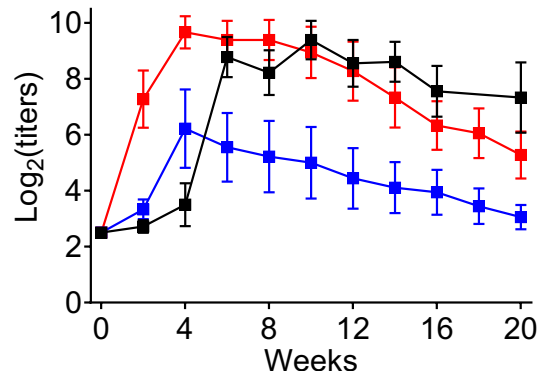
- 3X Free sIPV Injections
- 1X Unbuffered Particles
- 1X CaCO₃-doped Particles



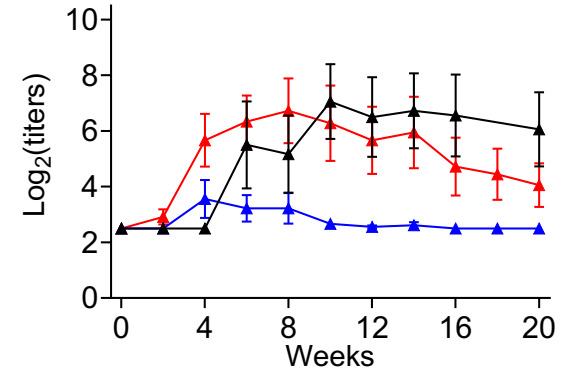
Type 1 neutralizing titers



Type 2 neutralizing titers



Type 3 neutralizing titers



injection timing
 ↑ ↑ ↑ ↑ ↑
 (Black, Red, Blue, Black, Black arrows)

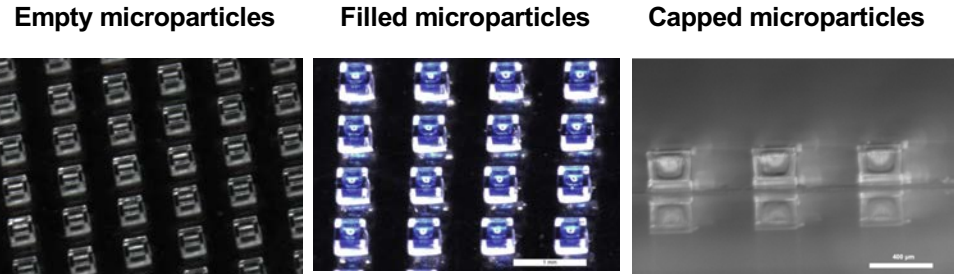
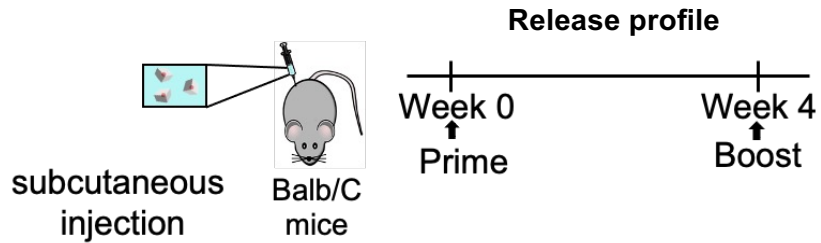
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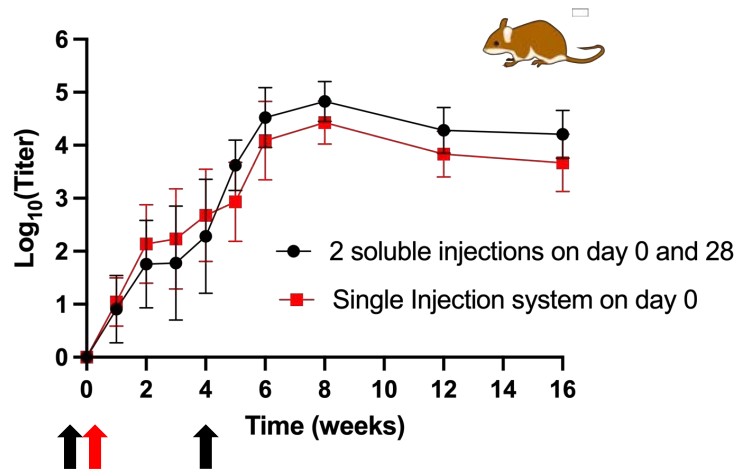


Self-boosting Hepatitis-B vaccine

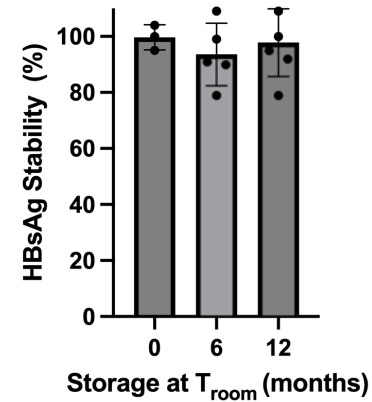
- Recombinant antigen HBsAg



Comparable performance to soluble injections

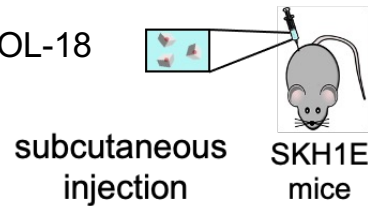


Antigen in microparticles retains 96% stability for at least 1 year storage at room temp.

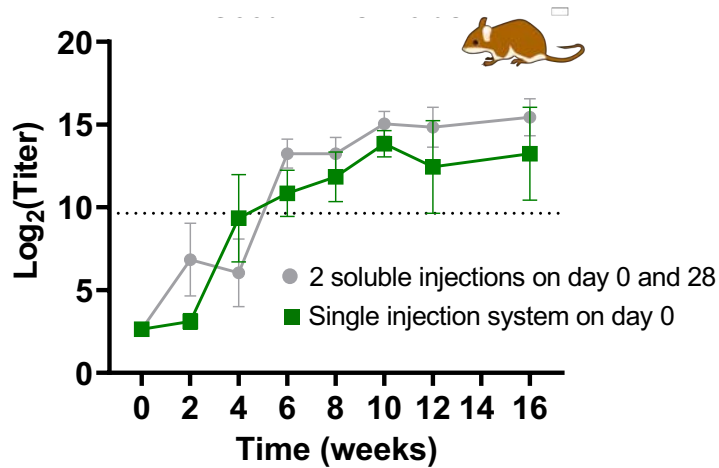


Self-boosting *Taenia solium* vaccine

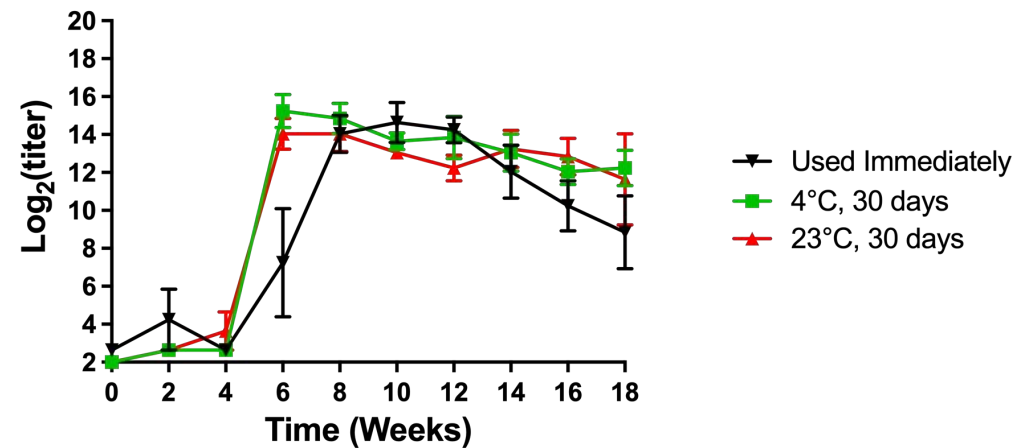
- Recombinant antigen TSOL-18



Comparable performance to soluble injections



Antibody titer induction of vaccine loaded microparticles after storage at different conditions



SELF BOOSTING VACCINES - POC

SEAL Platform	Immunogen + Adjuvant	Clinical Dose	Preclinical Model	Dose Studied	Delayed Release Window	Particles Required	Status	Readout
Poliovirus Serotypes 1–3	Sabin inactivated polio vaccine	T1: 1.5 DU T2: 50 DU T3: 50 DU	Wistar rat Cynomolgus macaque	Rat T1: 0.4 DU T2: 12.5 DU T3: 12.5 DU Cyno T1: 0.8 DU T2: 25 DU T3: 25 DU	1 and 2 months	Rat: 70 Cyno: 280	Rat: <i>Completed, noninferior</i> ✓ Cyno: Ongoing	Poliovirus neutralizing titers
Hepatitis B	Recombinant HBsAg (Hepatitis B surface antigen) + CpG oligonucleotide	20 µg	BALB/c mouse Rhesus macaque	Mouse 1.5 µg Rhesus 10 µg	1 month	Mouse: 20 Rhesus: 200	Mouse: <i>Completed, noninferior</i> ✓ Rhesus: Ongoing	anti-hepatitis B IgG
Taenia solium (tapeworm) infection in pigs	Recombinant antigen TSOL-18 + Quil-A	150 µg	SKH1E mouse Yorkshire swine	Mouse 0.75 µg Swine 135 µg	1 month	Mouse: 5 Swine: 600	Mouse: <i>Completed, noninferior</i> ✓ Swine: Planned	anti-TSOL 18 IgG
Influenza (CA09 H1)	Ferritin nanoparticle displaying influenza hemagglutinin + CpG oligonucleotide	60 µg	SKH1E mouse	Mouse: 10 µg	1–3 months	Mouse: 20	Ongoing	anti-CA09 HA IgG
SARS-CoV-2	mRNA lipid nanoparticles	30–100 µg	BALB/c mouse	Mouse: 1–10 µg	1 month	<i>Depends on formulation</i>	Formulation	Luminescence (firefly luciferase mRNA) anti-SARS-CoV-2 IgG



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