

# Johns Hopkins Engineering

## Immunoengineering

### Immunoengineering—Pathogens

#### Biomaterial Vaccine Design



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WHITING SCHOOL  
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# Biomaterials can be engineered to improve existing therapies

Pathogenic Immunoengineering applications we will look at:

- **Vaccines**
- Antibiotics

# What Makes an Effective Vaccine?

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We know a vaccine needs:

- Danger signal
- Antigen

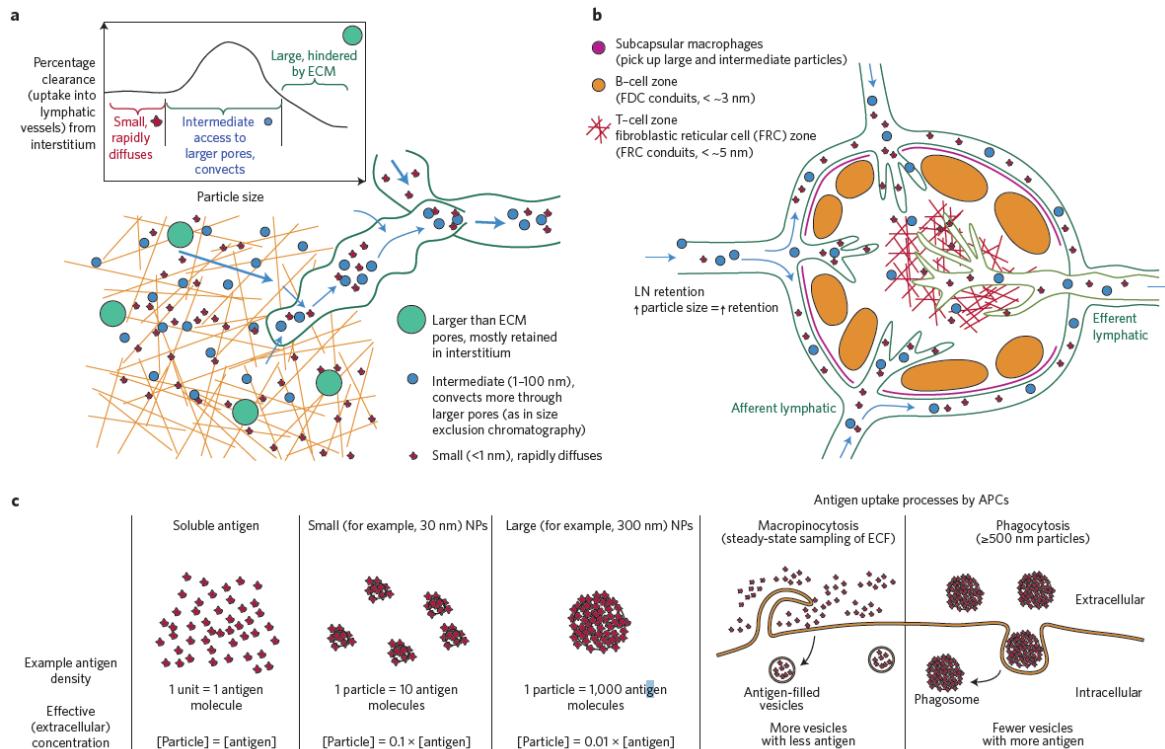
# Challenges to Vaccine Delivery

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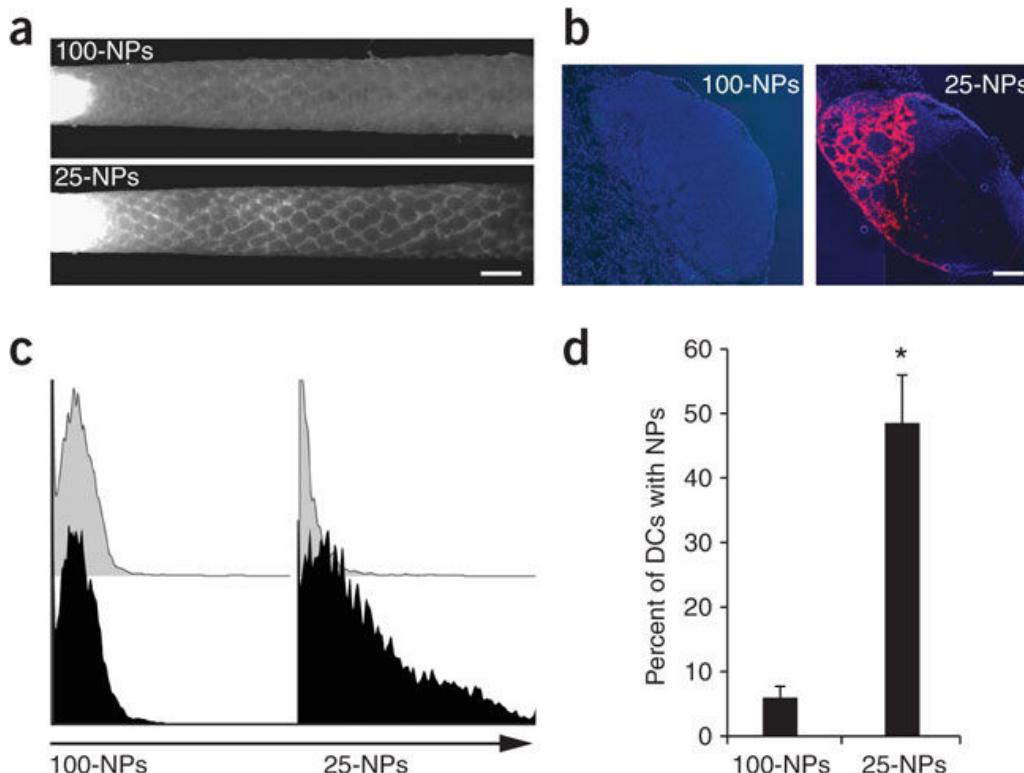
- Delivery to correct APCs
- Co-delivery of antigen and adjuvant
- Dosing of vaccine
- Robust response
- Cost and packaging
- Administration of vaccine

# Particle Vaccine Design

- Lymph node trafficking
- Cellular uptake
- Cellular processing



# Particle Size for Vaccine

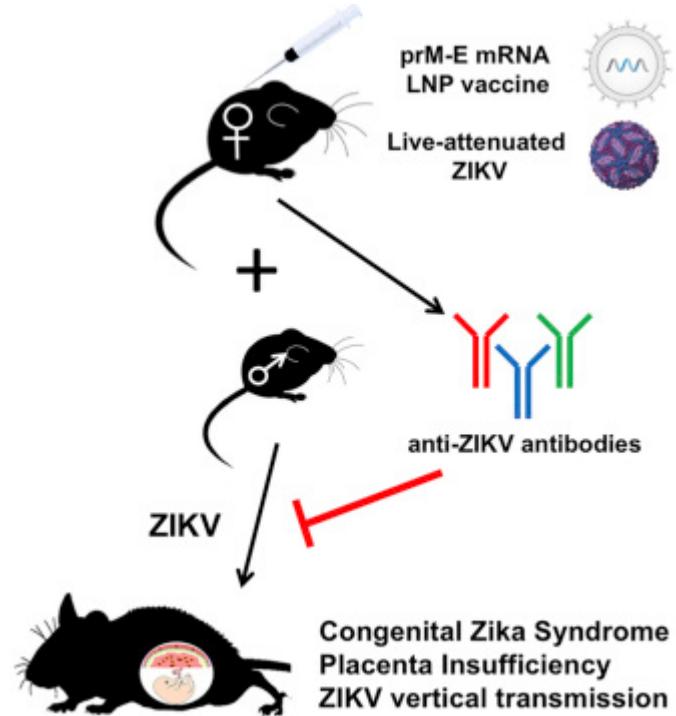


Reddy, Sai T., et al. "Exploiting lymphatic transport and complement activation in nanoparticle vaccines." *Nature biotechnology* 25.10 (2007): 1159.

# Lipid Nanoparticle mRNA Vaccine

mRNA vaccines are attractive because:

- Safety and plasticity – produce any protein
- Cost effective and scalable
- Small doses needed



# What Delivery Kinetics are Desirable?

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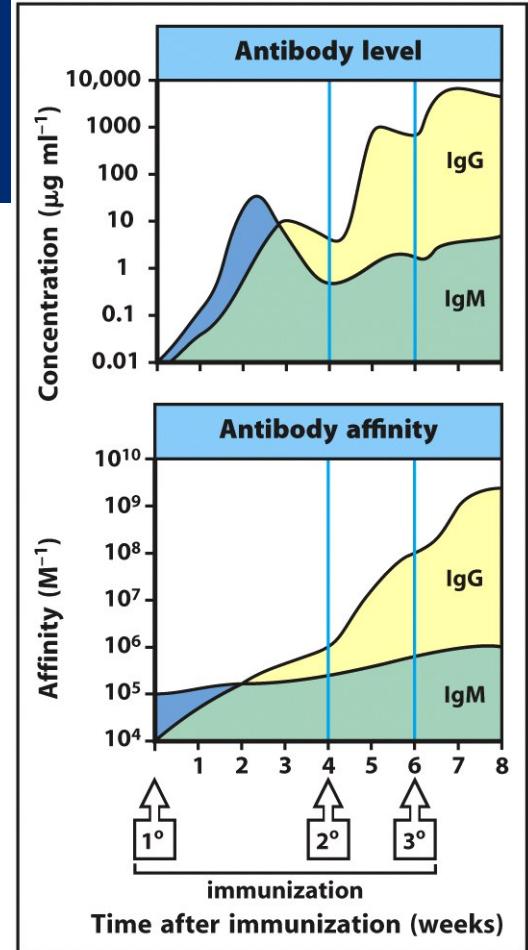
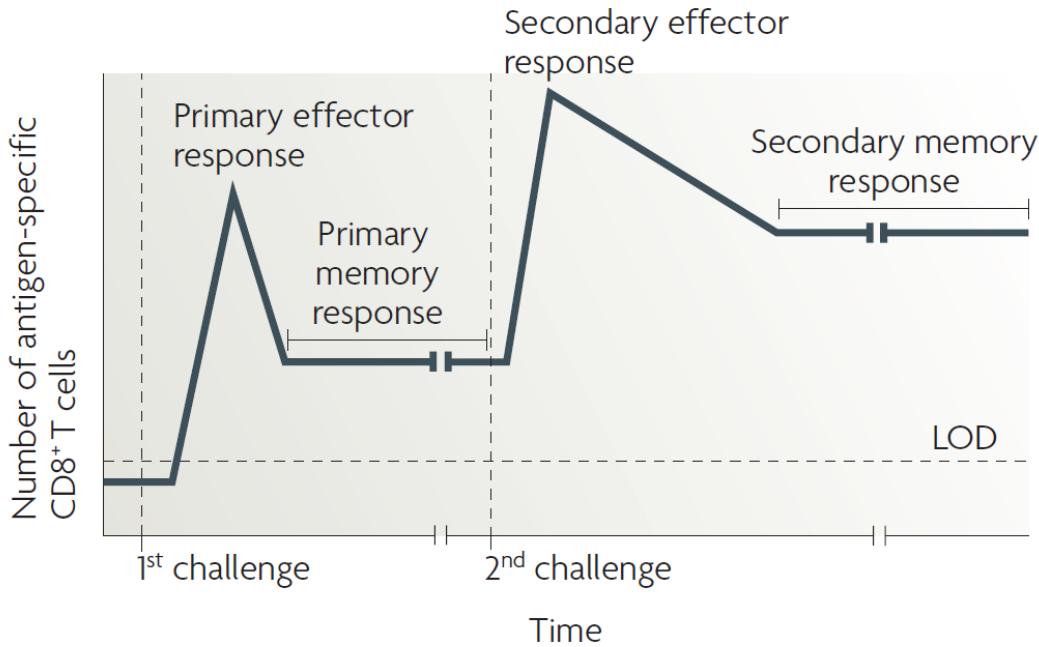
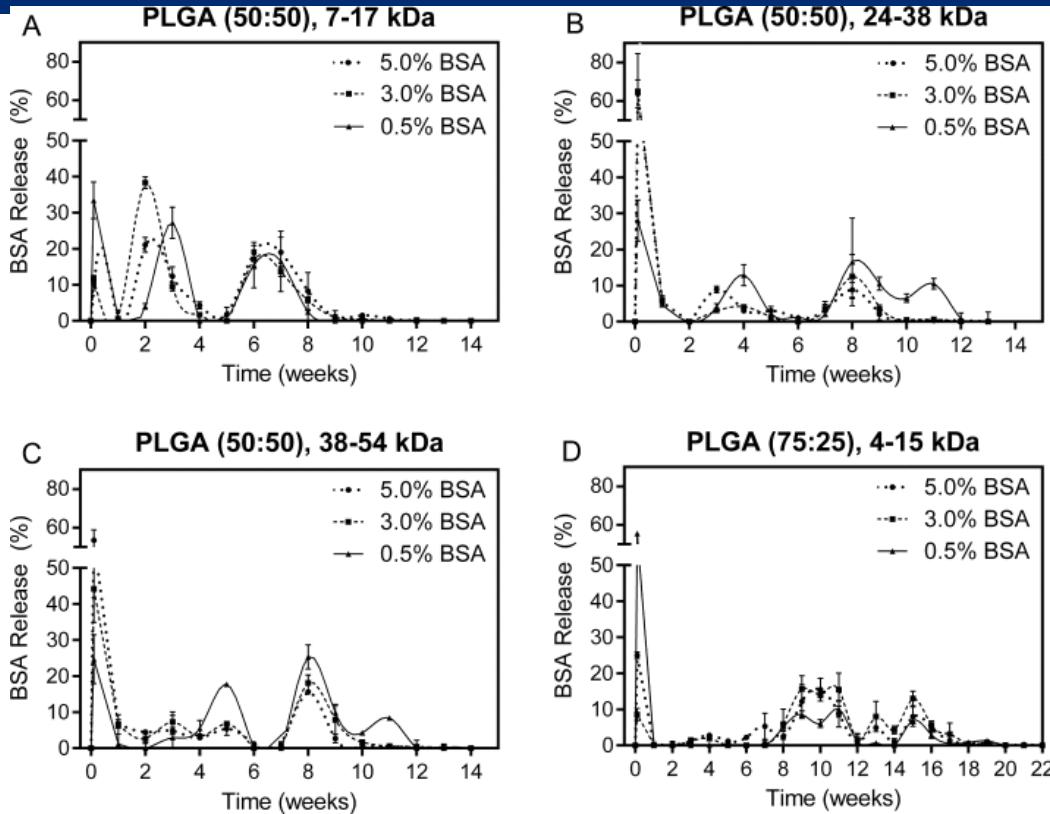


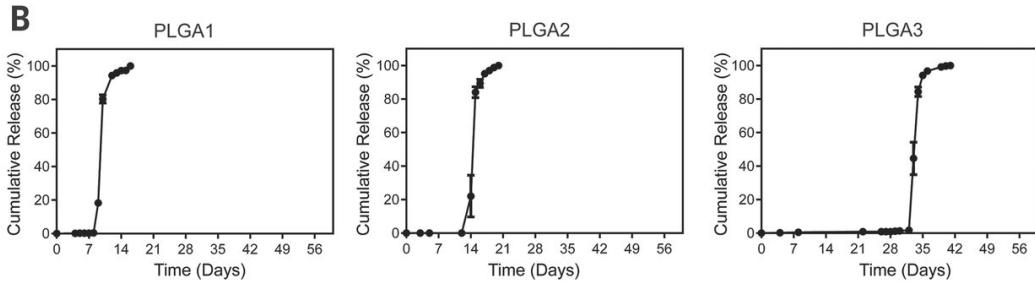
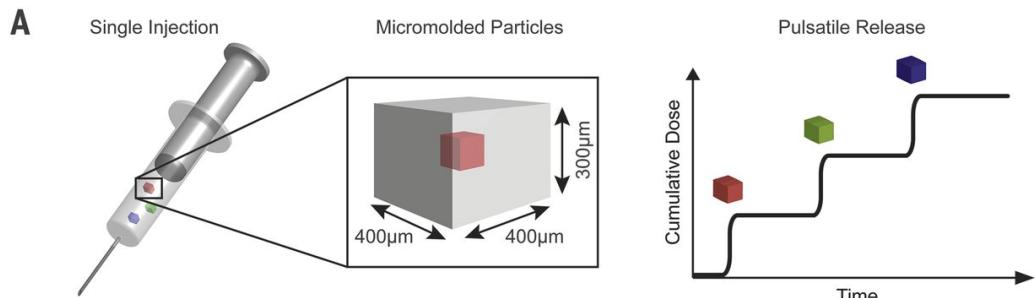
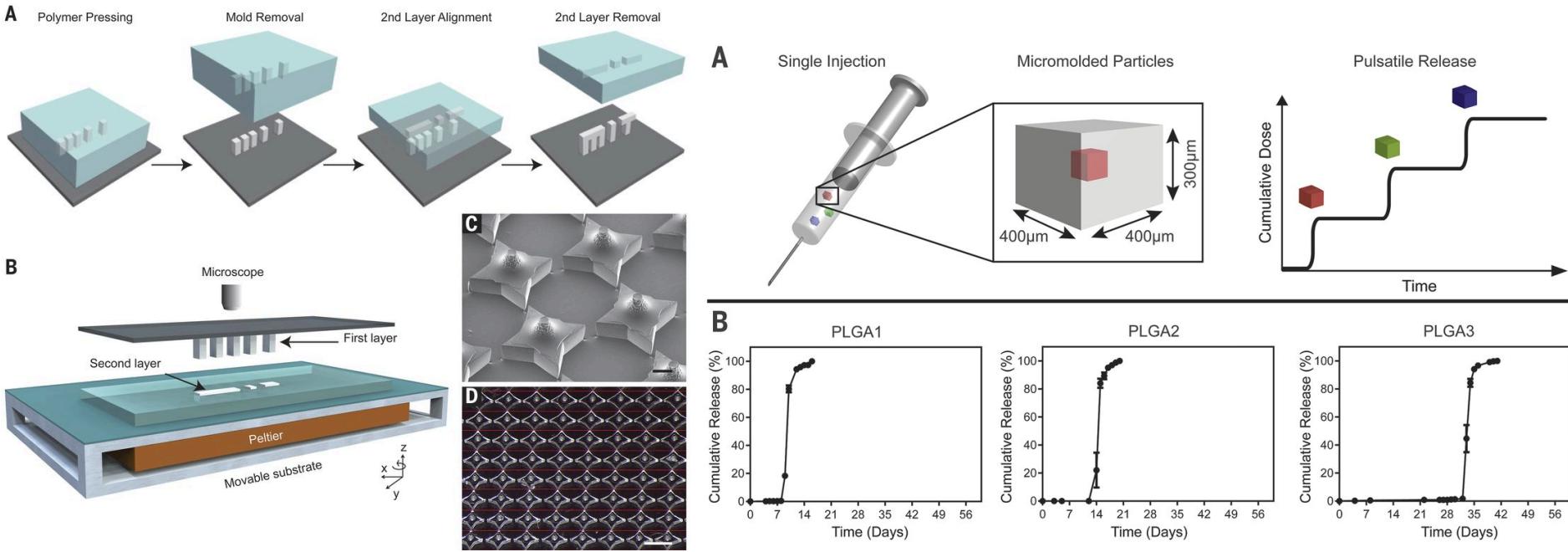
Figure 11.19 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

# Pulsatile Vaccine Release

1. Release from particle surface
  2. Diffusion through porous particle
  3. Release from structural degradation
- Change:
    - polymer composition
    - MW
    - Antigen loading

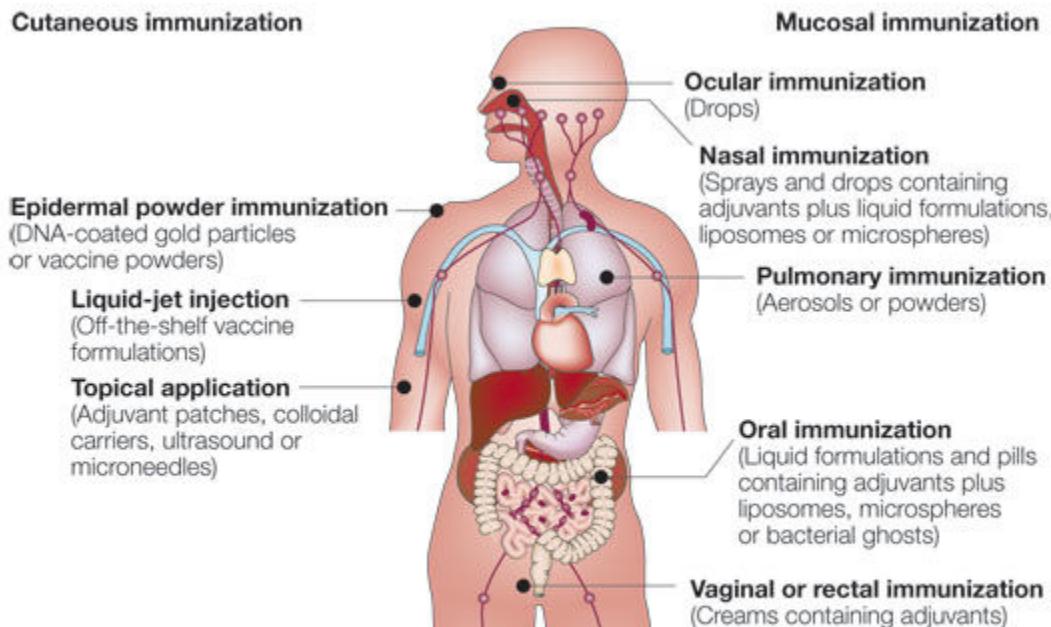


# Pulsatile Vaccine Release: Carriers



# Methods of Vaccine Administration

- Patient compliance
- Safety
- Efficacy
- Immunological implications



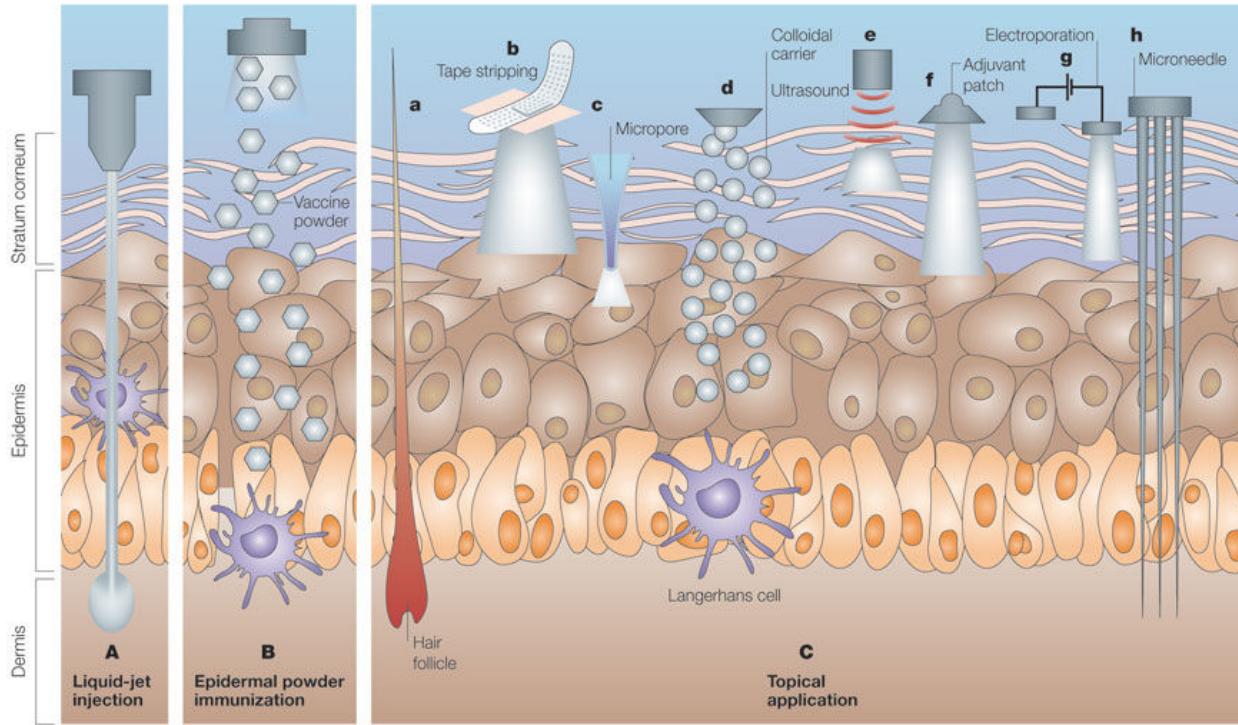
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Nature Reviews | Immunology

# Immunization Without Needles

Method	Advantages	Limitations
<b><i>Cutaneous immunization</i></b>		
Liquid-jet injection	Long history of use, ability to work with existing formulations, and success with many forms of vaccine	Issues associated with cross-contamination when using MUNJIs, high cost of device, and occasional pain and bleeding
Epidermal powder immunization	Use of powders facilitates storage, strong data for DNA vaccines, and natural targeting of Langerhans cells	High cost of device, occasional bleeding, limited clinical data for non-DNA vaccines, and limited clinical history
Topical application	Ease of access, natural targeting of Langerhans cells, generation of mucosal and systemic immunity, and high patient compliance	Strong adjuvants or permeabilizing agents required, some permeabilization methods require expensive devices, and most delivery methods have limited clinical history
<b><i>Mucosal immunization</i></b>		
Oral	Ease of administration, high patient compliance, no complex devices necessary in most cases, primary site of infection of many pathogens, and long history of use for live attenuated pathogens	Gastrointestinal deactivation of vaccines, high doses required, variability of response, and mixed clinical data
Nasal	Easier access to mucosal membrane than for oral delivery, low cost, and one of the main sites of infection for airborne pathogens	Short contact time, enzymatic activity of nasal tissue, adjuvants required, safety concerns with earlier nasal vaccine, and limited applicability in patients with upper respiratory-tract infections
Pulmonary	Large surface area, one of the main sites of infection for airborne pathogens, and history of use for measles vaccine	Strong adjuvants required, high cost of some devices, and interference from upper respiratory-tract infections
Vaginal or rectal	High relevance for HIV and causative agents of other sexually transmitted diseases	Poor patient compliance for general applications, and strong adjuvants required

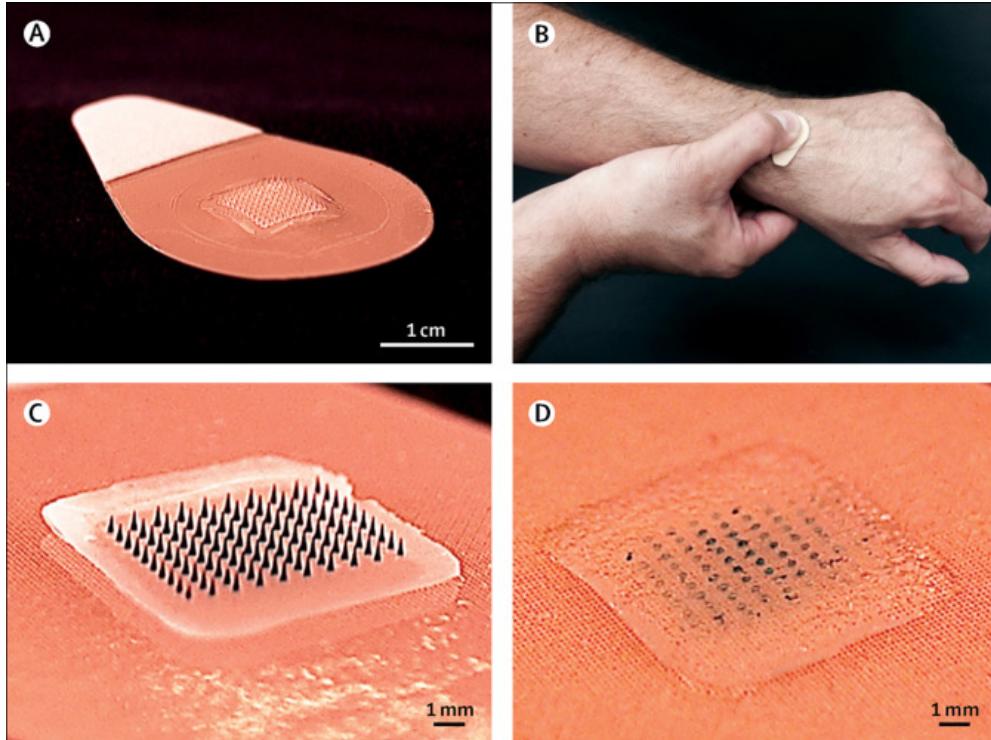
MUNJI, multi-use-nozzle jet injector.

# Methods of Cutaneous Vaccine Delivery



# Biomaterial Example: Microneedle Patches for Influenza Vaccine

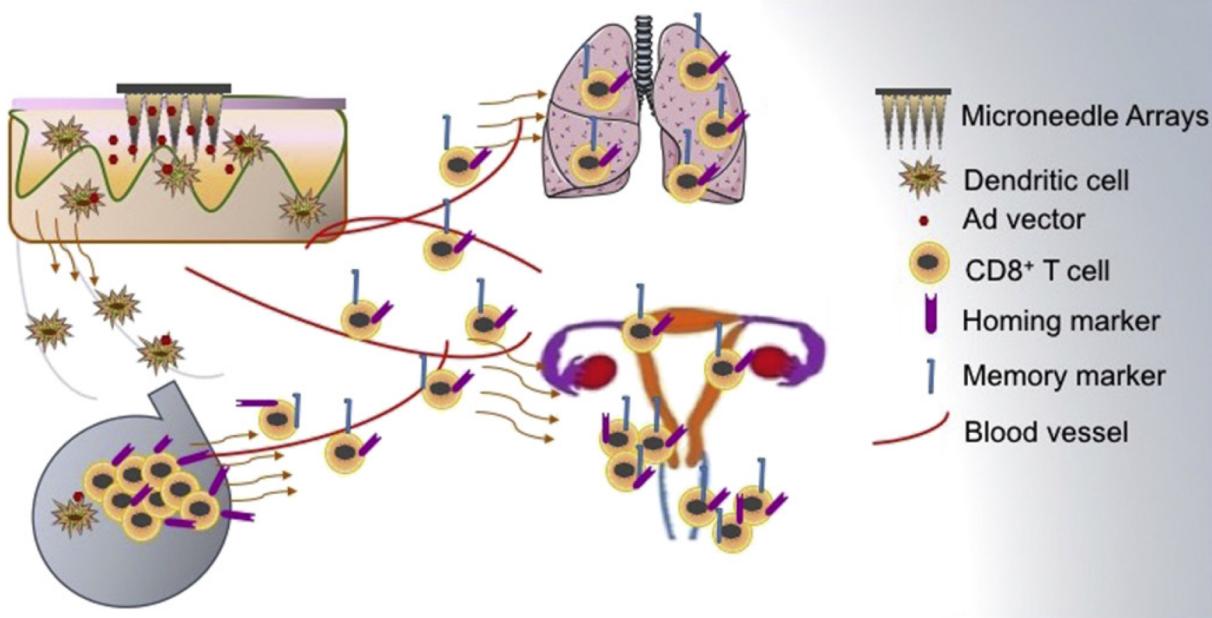
- Administration
- Cost
- Packaging
- Safety



Rouphael, Nadine G., et al. "The safety, immunogenicity, and acceptability of inactivated influenza vaccine delivered by microneedle patch (TIV-MNP 2015): a randomised, partly blinded, placebo-controlled, phase 1 trial." *The Lancet* 390.10095 (2017): 649-658.

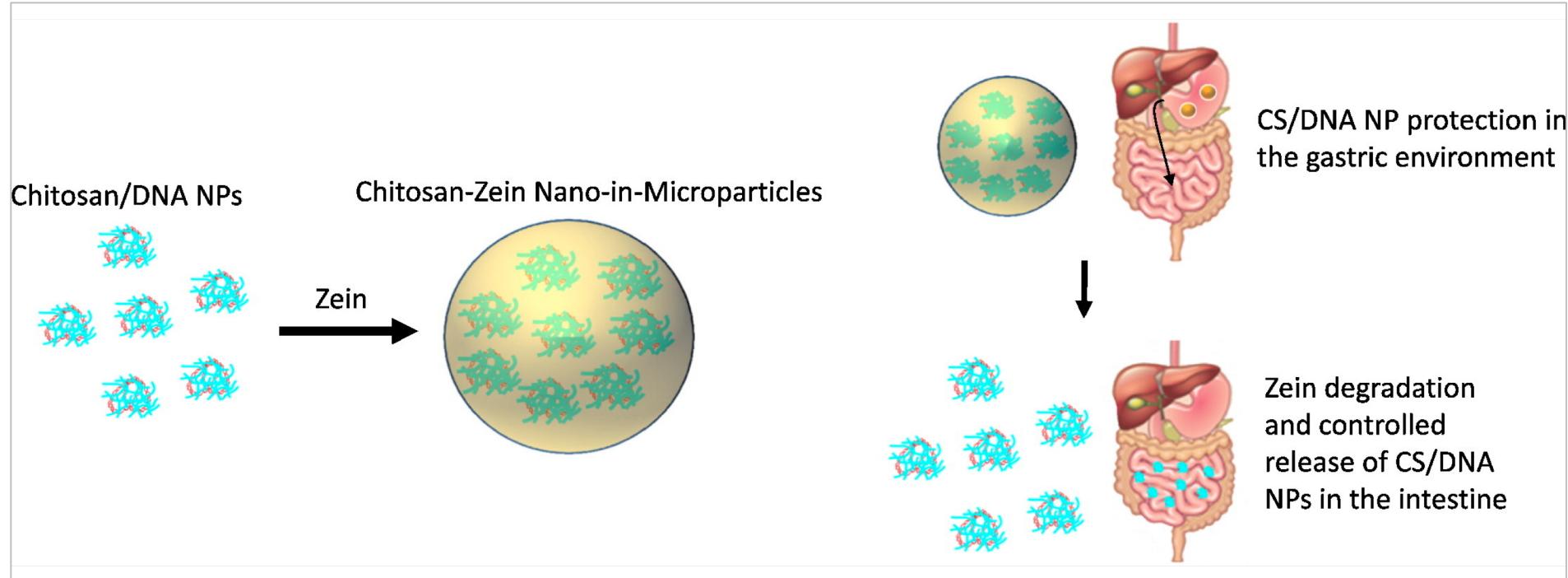
# Vaccine Delivery Modalities

- Live attenuated Vaccine
- Efficacy
- Mechanism



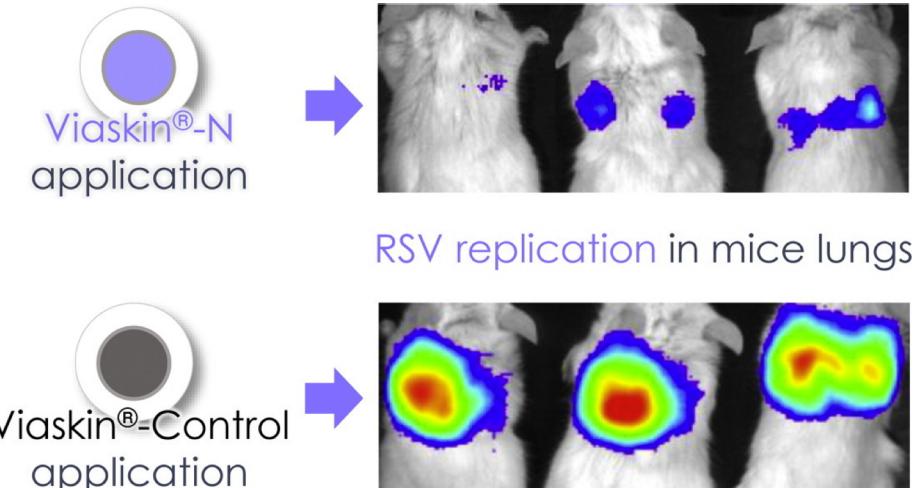
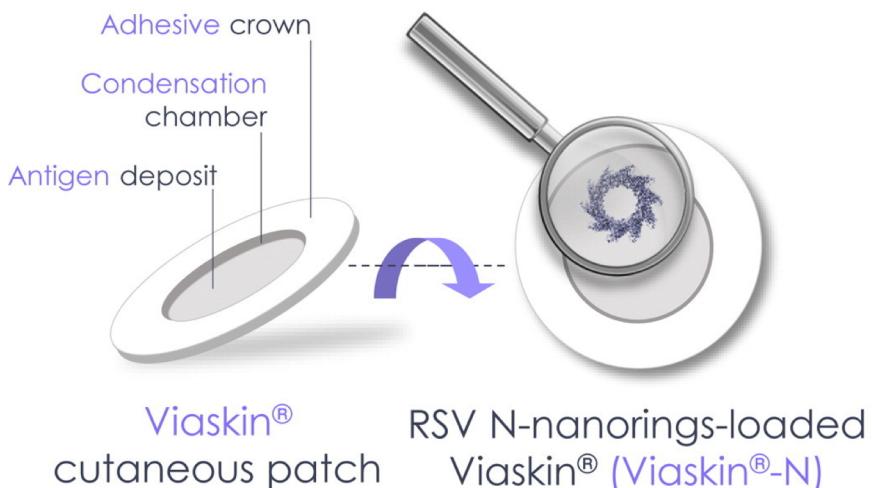
Zaric, Marija, et al. "Long-lived tissue resident HIV-1 specific memory CD8+ T cells are generated by skin immunization with live virus vectored microneedle arrays." *Journal of Controlled Release* 268 (2017): 166-175.

# DNA Vaccine Oral Delivery - Particles



# Vaccine Delivery Modalities

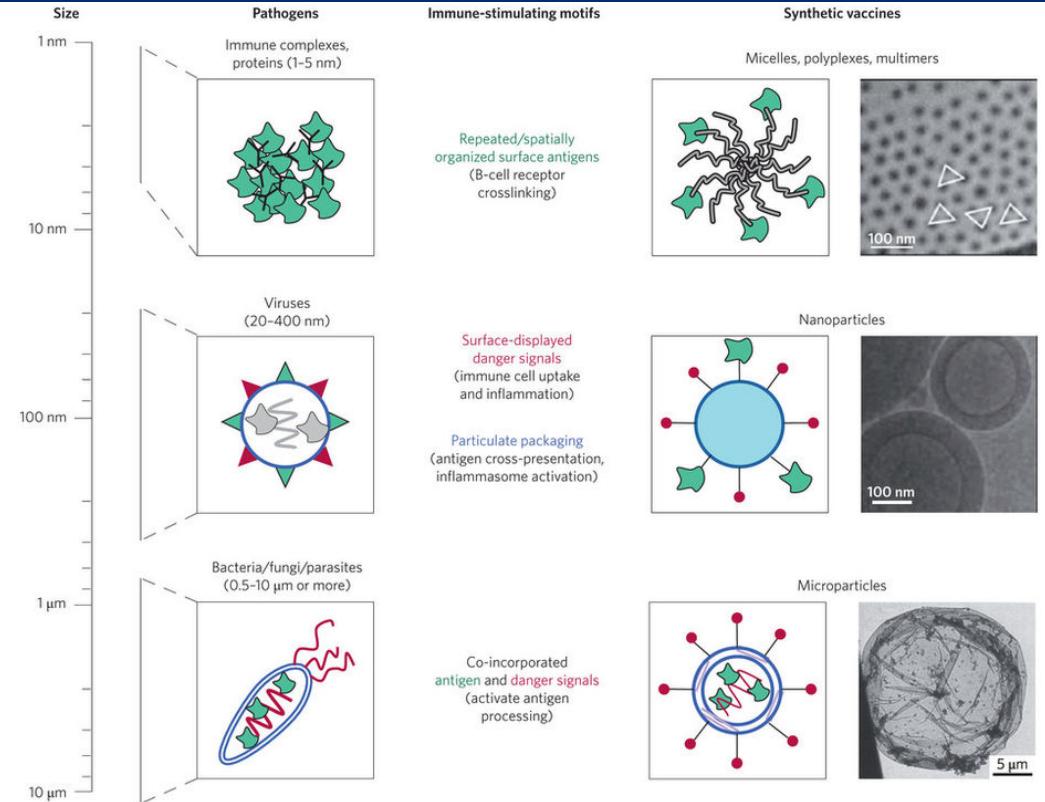
- Patient population considerations
- Combination technologies



Hervé, Pierre-Louis, et al. "Non-invasive epicutaneous vaccine against respiratory syncytial virus: Preclinical proof of concept." Journal of Controlled Release 243 (2016): 146-159.

# Bio-inspired Vaccine Design

- Generating antigenicity through size
- Mimicking surface structure and presentation



Irvine, Darrell J., zelody A. Swartz, and Gregory L. Szeto. "Engineering synthetic vaccines using cues from natural immunity." *Nature materials* 12.11 (2013): 978.

# Biomaterial Approaches Address Challenges in Vaccine Delivery

- Delivery to correct APCs
- Co-delivery of antigen and adjuvant
- Dosing of vaccine
- Robust response
- Cost and packaging
- Administration of vaccine



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