

Johns Hopkins Engineering

Immunoengineering

Immunoengineering Cancer: Vaccines

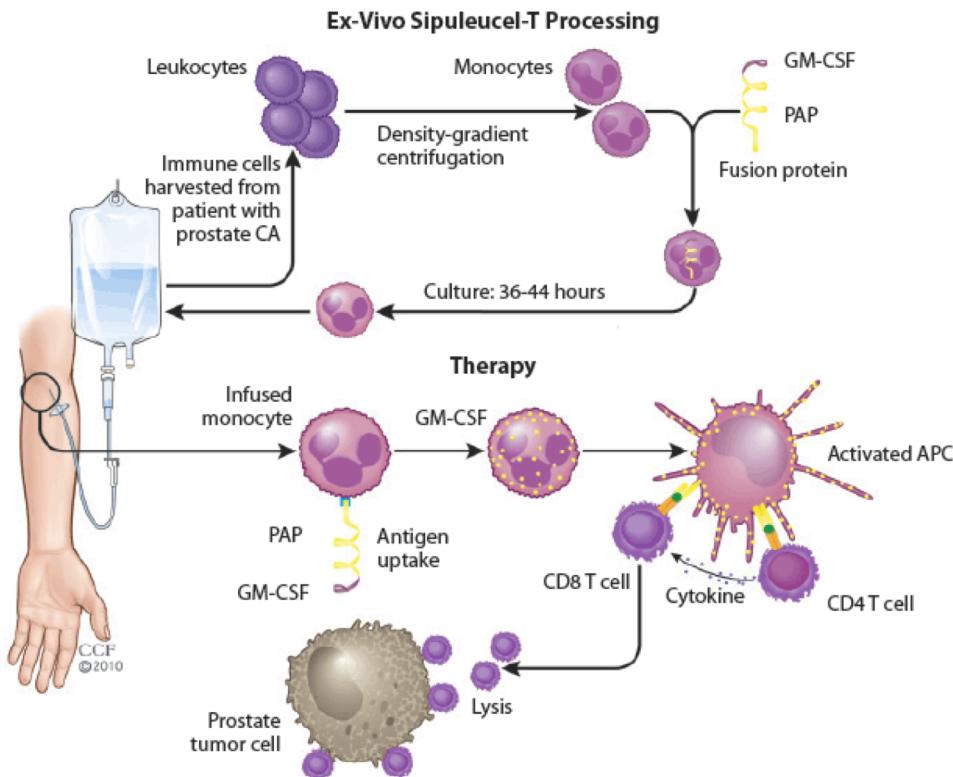


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Cancer Vaccines

- Two broad types: prophylactic vs. therapeutic
- Types of cancer vaccines
 - Tumor cell
 - Dendritic cell vaccines
 - Protein/peptide
 - Genetic
- Two components: antigen and adjuvant

Sipuleucel-T (Provenge)



Garcia et al. "Immunotherapy in Castration-Resistant Prostate Cancer: Integrating Sipuleucel-T Into Our Current Treatment Paradigm". *Oncology* 25(3).

Why is a delivery system advantageous?

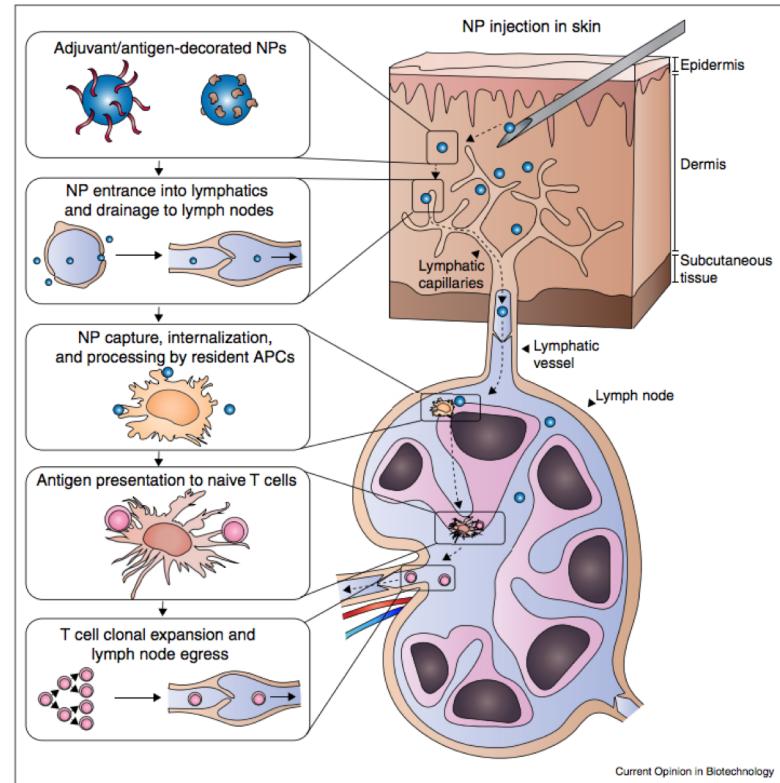
- Soluble antigen rapidly diffuses in and out of LNs
- Antigen without adjuvant → tolerance
 - Co-delivery enables both are delivered to the same APC
- Delivery systems can enable sustained release (like prime and boost injection)
- Concentrate payloads to allow much lower doses of immunostimulatory molecules

Particle-Based Vaccines

- Method to deliver tumor antigen and adjuvant to APCs
- Soluble peptide/DNA/RNA delivery is not effective
- Advantages of particles
 - Protect antigen from degradation
 - Combine antigen and adjuvant in one vehicle
 - Incorporate targeting
 - Can modulate particle parameters to vary pharmacokinetics, targeting, uptake pathway, etc.
 - Long-term release

Particle Size Dependence

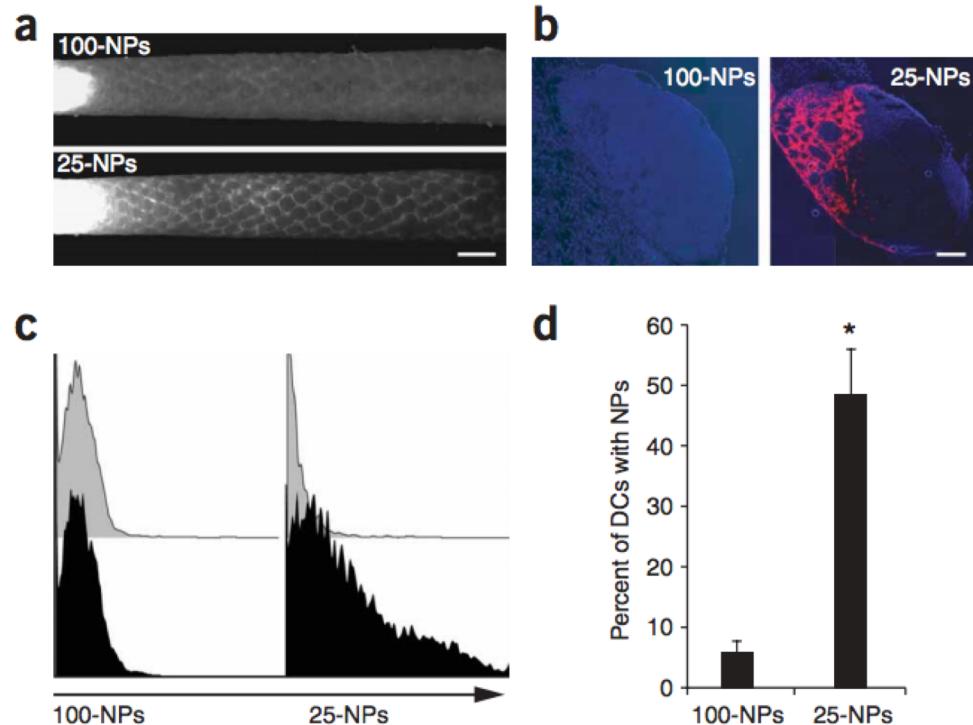
- Nanoparticles more adept at draining to lymph nodes than microparticles
- Ultra-small NPs (<10 nm) and soluble antigen rapidly diffuse in and out of LNs
- Intermediate-sized NPs (10-100 nm) efficiently drain to LNs and are retained there
- Microparticles (>500 nm diameter) require cellular transport by APCs to be delivered to lymph nodes, otherwise trapped at injection site



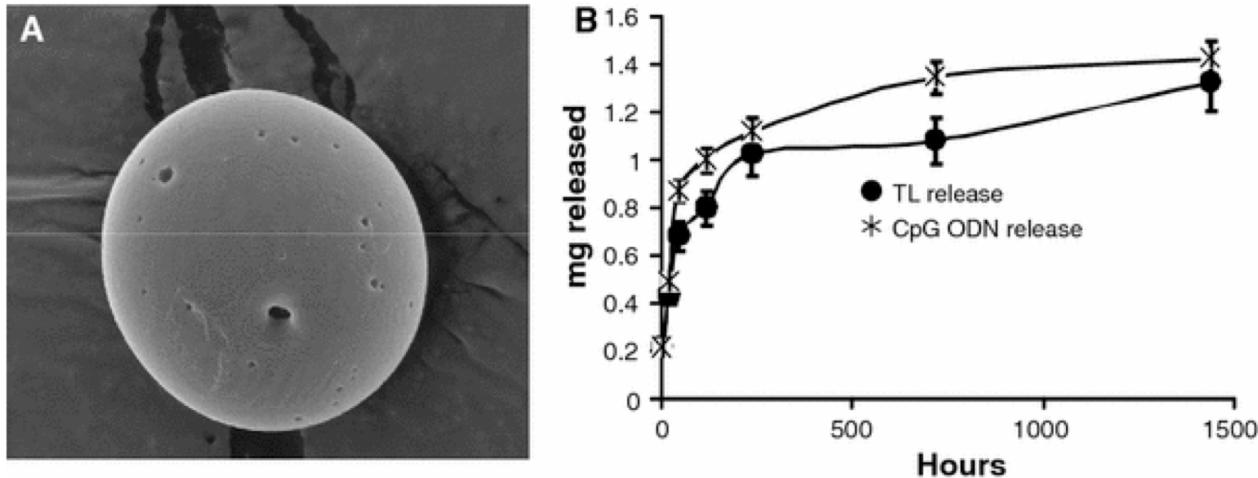
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Size Dependence

- Particles 20-200 nm in diameter drain to lymph nodes
- Particles smaller than 1000 nm can be taken up by DCs

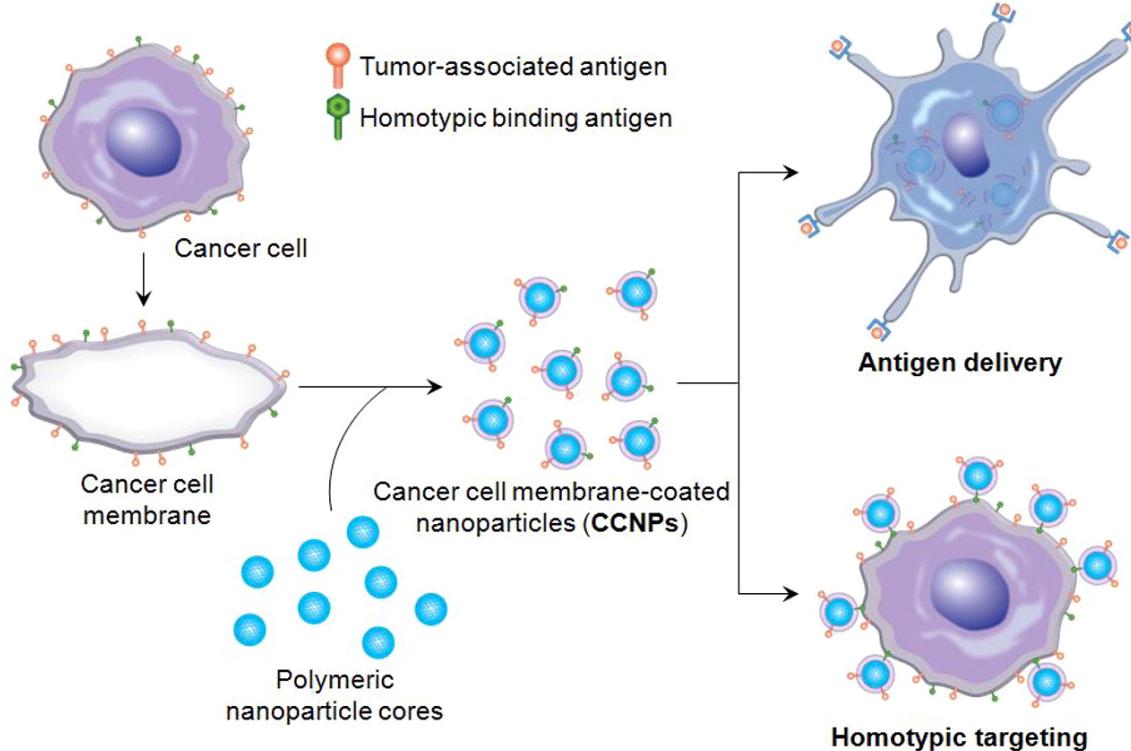


Co-delivery of Antigen and Adjuvant

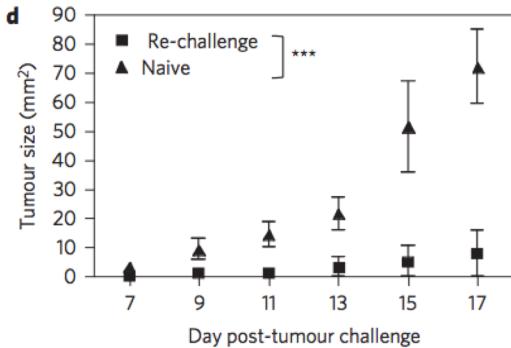
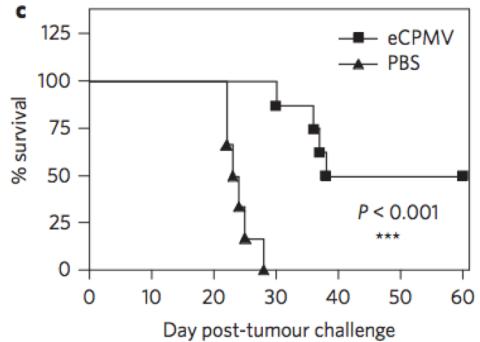
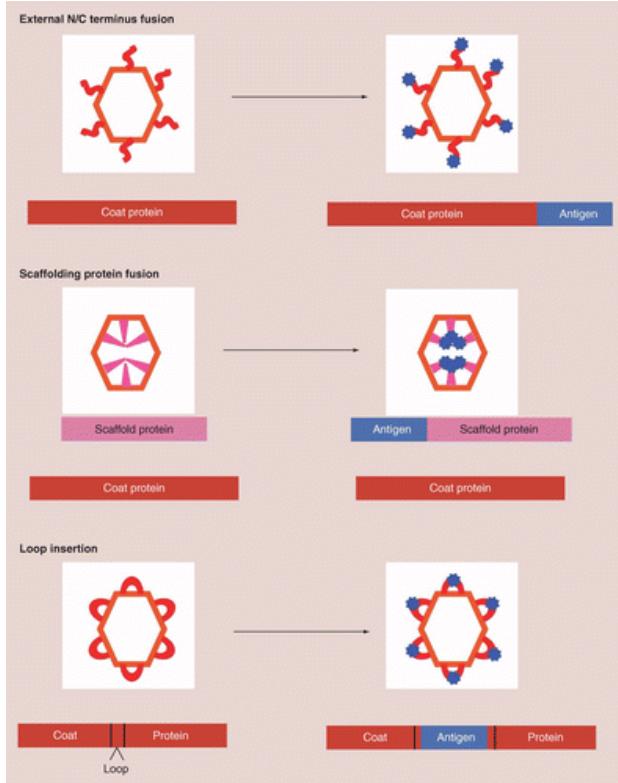


- PLGA microparticles loaded with antigen (TL = tumor lysate) and adjuvant (CpG ODN)
- Sustained release of both factors

Cancer Cell Membrane Coated NPs

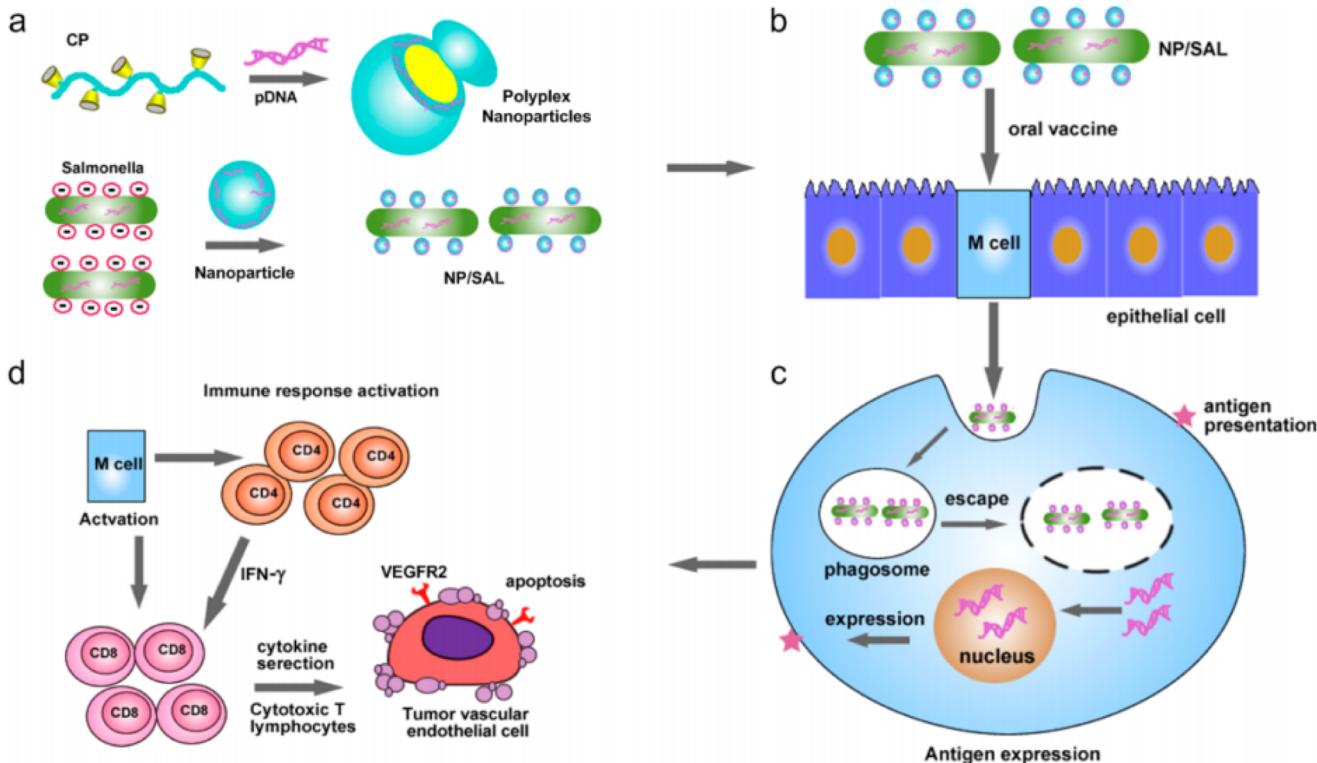


Virus-like Particles (VLPs)



Lizotte et al. "In situ vaccination with cowpea mosaic virus nanoparticles suppresses metastatic cancer" *Nature nanotechnology* 11, (2016): 295- 304.

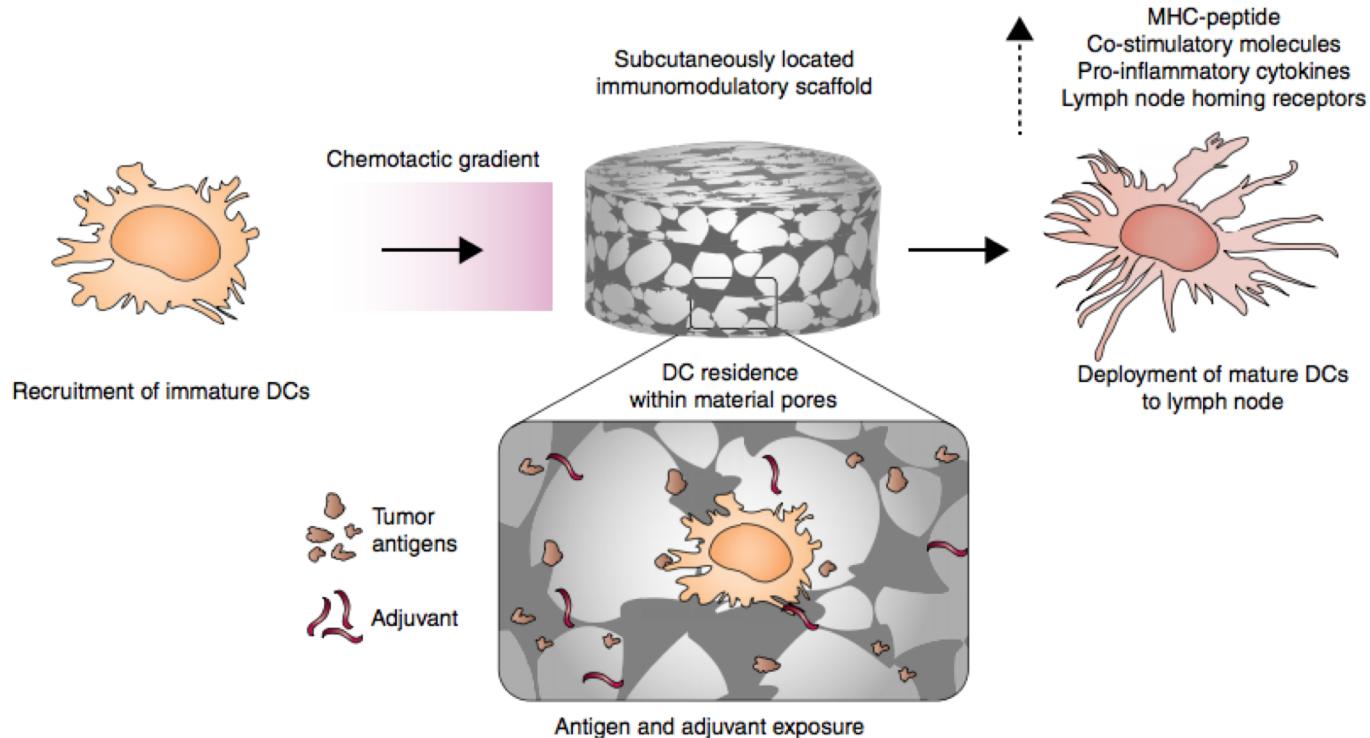
Genetic Vaccines



Scaffolds for DC Programming

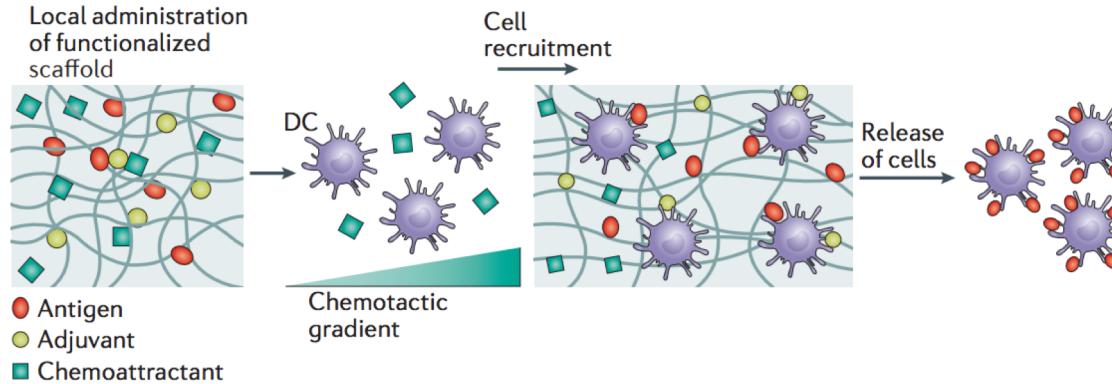
- Create "artificial lymph node" that recruits APCs
- Scaffold/hydrogel releases tumor antigen, adjuvant, and factors to enhance APCs
- APCs mature and then migrate to the lymph node to activate T cells

Scaffolds for DC Programming



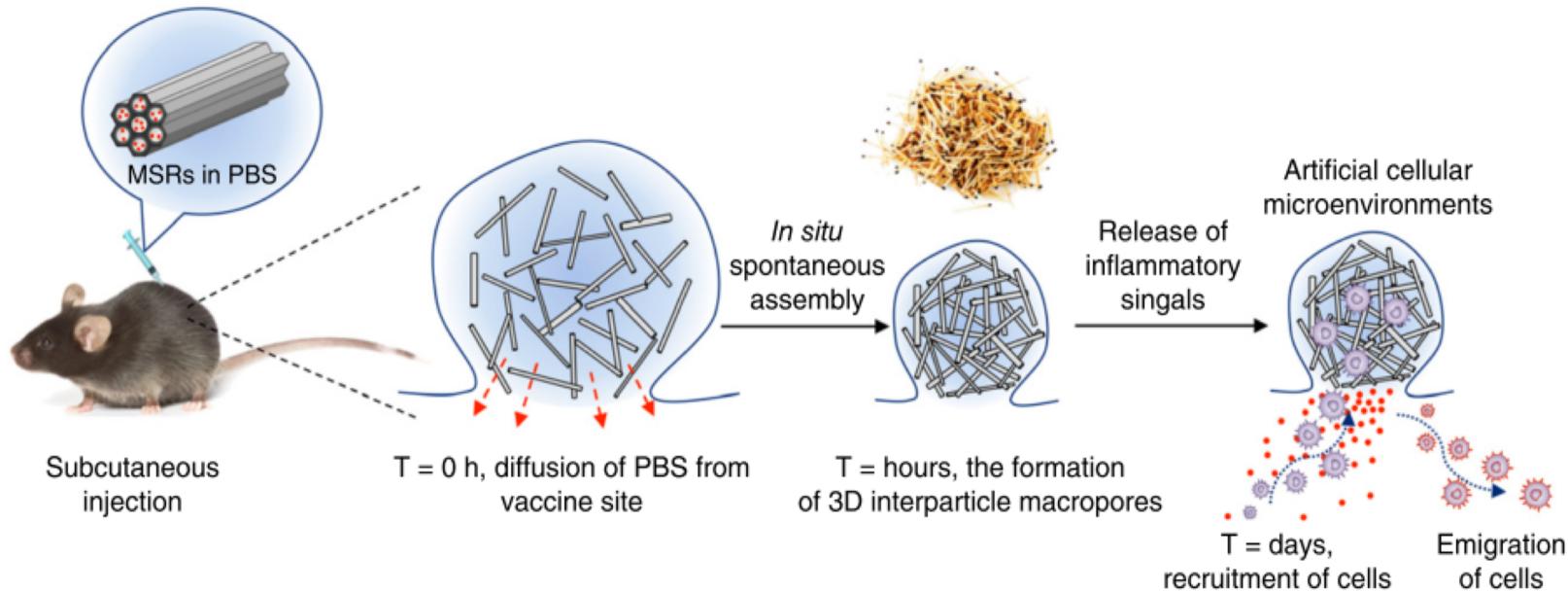
Current Opinion in Biotechnology

Scaffold Biomaterial Parameters



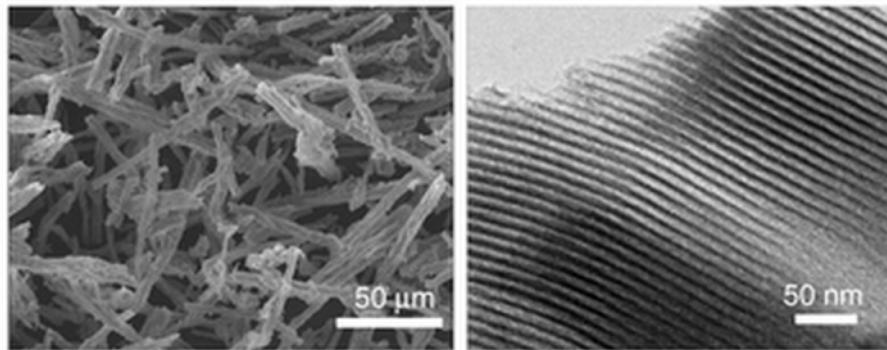
Characteristics of material formulation	Methods of administration	Biomolecules integrated	Incorporation strategies
<ul style="list-style-type: none">• Biocompatibility• Biodegradability• Structural integrity• Porosity• Rigidity	<ul style="list-style-type: none">• Implantation• Injection	<ul style="list-style-type: none">• Chemokines• Adhesion molecules• Activating ligands• Antibodies• Cytokines• Lymphogenic factors	<ul style="list-style-type: none">• Physical entrapment• Ionic interaction• Hydrophobic interaction• Covalent coupling

Scaffold-based Vaccines

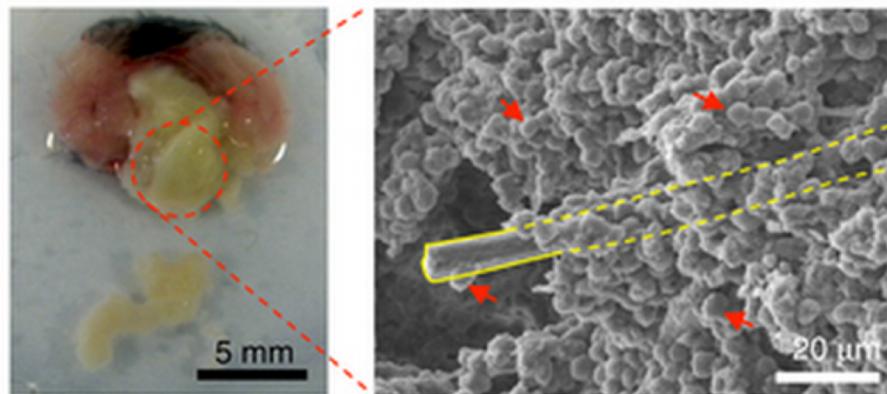


Kim et al. "Injectable, spontaneously assembling, inorganic scaffolds modulate immune cells *in vivo* and increase vaccine efficacy".
Nature Biotechnology, 33(1), (2014): 61-69.

Biophysical Properties of Mesoporous Silica Rods

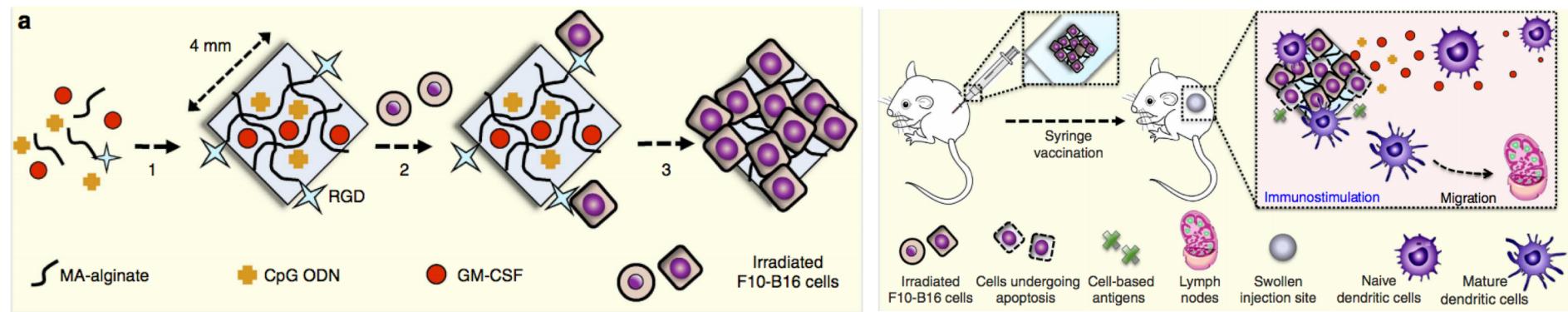


- Shape
 - High aspect ratio
 - Scaffold pore size large enough for cellular infiltration
 - Macropores create large surface area for cell contact



- Material
 - Mesoporosity allows encapsulation of OVA, CpG ODN, and GM-CSF
 - *In situ* assembly allows for injection instead of surgical implantation

Hydrogels for Vaccine Delivery



- Cryogel encapsulating GM-CSF (DC enhancing factor), CpG ODN (adjuvant), and irradiated tumor cells (antigen)



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