INNOVATIVE VACCINE DELIVERY TECHNOLOGY:
NEW PARADIGMS FOR IMMUNOPROTECTIVE COUNTERMEASURES

Jonathan Seals

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Vaccines as Public Health/ Response Countermeasures

- Vaccines have been one of the most effective public health measures for reducing morbidity and mortality from infectious diseases in human history
- Vaccines are needed to play a key role in addressing emerging and re-emerging pathogens
- Development and registration of commercial vaccines is long (10-15 years) and costly ($2B)
- Vaccine technology has changed little in 200 years
- Innovative technologies have the potential to fundamentally change the delivery of vaccines for both public health and commercial vaccines

Evolving Vaccine Technologies

Immunogen Technology	Development	Manufacturing/ Scale-up	Regulatory	Administration	Supply Chain
Killed/ Live Attenuated Biologicals	Custom	Large Expensive Dedicated Batch	Large safety and efficacy database	Injectable Multi-dose vial Single-dose syringe	Cold Chain Lyo
Subunit Recombinant Adjuvants VLPs Vectors Engineered Nucleic Acids Synthetics	Platforms*	Smaller* Modular Multi-product Production Tech Continuous	Expedited?*	Nasal Oral Mucosal Patches Devices	Stabilized* Formulations

*Potential Cost and Time Savings

Supporting Vaccine Innovation

- BARDA's mission is to develop and deliver medical countermeasures for public health emergencies, including natural and man-made biothreats
- BARDA partners with commercial vaccine developers and manufacturers in this mission
- The time and cost of traditional vaccine development is a significant detriment for public health emergency interests
- BARDA actively seeks and supports innovative technologies that will facilitate the availability of vaccines for commercial and public health use

Immunogen Production and Formulation

	Description	Strengths	Liabilities	Time to FIH
Live Attenuated Pathogen	Natural variant that causes mild disease but has immunogenic cross-protection against disease-causing organism	Elicits strong protective response	Time to develop; rigorous testing to ensure against reversion	12-24 mo
Inactivated Pathogen	Organism treated to prevent infection and replication	Straightforward development path; requires minimal discovery	Complex composition may contain components that cause adverse reactions; process must ensure 100% inactivation	12-24 mo

Immunogen Production and Formulation

	Description	Strengths	Liabilities	Time to FIH
Subunit	Enriched or purified immunogenic component from pathogen	More defined vaccine composition may reduce adverse events	May not produce a robust protective response	12-18 mo
Recombinant	Protein antigen produced by engineering of host cell production system	Safer and more cost-effective production of protein antigens	May not produce a robust protective response	9-18 mo
Novel Adjuvants	Non-immunogenic component added to increase immunogenicity of vaccine antigen	May enhance protective response and have dose- and/or antigen-sparing effect	Increase vaccine reactogenicity and adverse responses	NA

Immunogen Production and Formulation

	Description	Strengths	Liabilities	Time to FIH
Virus-like particles	Protein antigen produced to self-assemble into non-infectious protein particle	Safe; particle may produce adjuvant effect	Manufacturing consistency; not all antigens may self-assemble	6-12 mo
Viral Vectors	Gene for protein antigen delivered to host via an engineered non-pathogenic virus	Production of antigen not required; host may produce adjuvant effect	Anti-host immunogenicity may interfere with booster or use of host for subsequent vaccine	6-12 mo

Immunogen Production and Formulation

	Description	Strengths	Liabilities	Time to FIH
Engineered Attenuated Pathogens	Pathogen genes selectively modified to reduce replication and/or pathogenicity	Vaccine retains protein composition for eliciting robust protective response	Must retain ability to grow in culture for manufacturing	6-12
Nucleic Acids	DNA or RNA delivered directly to cells for antigen production	Production of antigen not required; rapid production of nucleic acid	Inefficient transport of nucleic acid to cell and/or nucleus	3-9
Synthetic Production	Peptide antigen produced by chemical synthesis	Immunogen produced rapidly	Weak immune response requires adjuvant or conjugation to carrier	3-9 mo

Most Advanced Stage of Development in ID Product*

Preclinical	Phase 1	Phase 2	Phase 3	Licensed Product
Engineered Synthetic	DNA RNA	Vectored	Particle	Attenuated Inactivated Subunit Recombinant Adjuvant

*Some technologies are in more advanced stages for cancer products

Innovative Routes of Vaccine Administration

Mucosal -Nasal -Oral -Other	Ease of administration; targeting mucosal immunity may improve efficacy in some cases	Selective applicability
Skin patch -Microneedles -Soluble micro-structures	Ease of administration; may enhance immunogenicity in some cases; potentially more stable formulation	Limited commercial activity

Current Status and Future Prospects

- Vaccine technology that has remained relatively unchanged for 200 years is beginning to undergo a renaissance that may enable future vaccines to address contemporary threats
- Impetus comes from need to respond quickly to emerging and re-emerging diseases
- Government investment is needed to address public health threats and to overcome inertia of large commercial investment in current technology
- BARDA is seeking and investing in products and technologies to advance this evolution