New Technologies for Accessible, Durable and Broadly Protective Coronavirus Vaccines

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Agenda

• Current State of Vaccines for COVID
• Gaps in Existing COVID-19 Vaccines
• IDRI Technology to Address COVID-19 Vaccine Gaps
  • Thermostability
  • Durability
  • Breadth of Protection
• Other Solutions for COVID-19
  • GMP Manufacturing
  • Allogenic NK Cell Therapy
## Current COVID-19 Vaccine Landscape

### Vaccine Types and Characteristics

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Type</th>
<th>Dosing</th>
<th>Storage</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer/BioNTec</td>
<td>mRNA + LNP</td>
<td>2 doses, 3 weeks apart</td>
<td>-20C</td>
<td>95%</td>
</tr>
<tr>
<td>Moderna</td>
<td>mRNA + LNP</td>
<td>2 doses, 4 weeks apart</td>
<td>4C for 30d, -20C for 6 months</td>
<td>95%</td>
</tr>
<tr>
<td>Johnson and Johnson</td>
<td>Human Adenovirus</td>
<td>Single Dose</td>
<td>4C for 3 months</td>
<td>61-72%</td>
</tr>
<tr>
<td>Oxford / AstraZeneca</td>
<td>Chimp Adenovirus</td>
<td>2 doses</td>
<td>4C for 6 months</td>
<td>79%</td>
</tr>
<tr>
<td>Sputnik V</td>
<td>Human Adenovirus</td>
<td>2 doses, 3 weeks apart</td>
<td>-20C</td>
<td>92%</td>
</tr>
<tr>
<td>CanSinoBio</td>
<td>Human Adenovirus</td>
<td>Single Dose</td>
<td>4C</td>
<td>65%</td>
</tr>
<tr>
<td>Sinovac</td>
<td>Inactivated Virus</td>
<td>2 doses, 2 weeks apart</td>
<td>4C</td>
<td>50-84%</td>
</tr>
</tbody>
</table>

Current COVID-19 Vaccine Challenges

Access
• Requirement for deep cold storage of mRNA vaccines have put them out of reach for many at US and abroad

Durability
• Immune protection may wane after several months with current vaccine candidates, necessitating regular boosters

Breadth
• Current vaccines’ efficacy may be less against emerging viral variants
IDRI Technology: Thermostable RNA Vaccines and Potent Vaccine Adjuvants
Thermostable RNA Vaccine
# New Technologies for Accessible, Durable and Broadly Protective Coronavirus Vaccines

## Addressing Gaps in Current RNA Vaccines

<table>
<thead>
<tr>
<th>Limitation</th>
<th>Current RNA Vaccines</th>
<th>IDRI RNA Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Storage / Distribution</strong></td>
<td>Requirement for deep cold chain.</td>
<td>NLC formulation allows for lyophilization and long-term stability at room temperature.</td>
</tr>
<tr>
<td><strong>Potency</strong></td>
<td>Elicit immunity at levels similar to recovered patients, which may allow re-infection.</td>
<td>Self amplifying RNA allows higher potency; input RNA 100-1000 fold lower than mRNA vaccines gives equal potency.</td>
</tr>
<tr>
<td><strong>Duration of Immunity</strong></td>
<td>Modest immunogenicity may be associated with short durability</td>
<td>Self-adjuvanting RNA vaccine platform may increase duration and breadth of immunity</td>
</tr>
<tr>
<td><strong>Adaptability</strong></td>
<td>RNA sequence encapsulated within delivery vehicle making adaptations to novel tumor antigens challenging</td>
<td>RNA decorated on outside of NLC, allows easy substitution of genetic sequence; can be rapidly modified for new strains</td>
</tr>
</tbody>
</table>
Alphavirus RNA Replicon Used to Deliver SARS-CoV-2 Spike Protein Sequences
A Tale of Two Doughnuts…

Moderna and Pfizer/BioNTec LNP

IDRI’s NLC

3/30/21
Lipid-Based Nanoparticle Delivery

Lipid Nanoparticles (LNPs)
- Encapsulated RNA
- Complex to manufacture and scale
- Each target RNA must be encapsulated with delivery formulation

From Tam et al 2013, PMID 24300520

IDRI Nanostructured Lipid Carriers (NLCs)
- Enhanced stability/bioavailability
- Externally bound RNA
- Protection of RNA from degradation
- Potential for stockpiling
- Scalable manufacturing
- Self-adjuvanting
Advantages of IDRI’s RNA Vaccine Platform

Thermostable at Room Temperature for >8 months

Efficient RNA delivery into cell cytoplasm

![Graph showing SEAP expression and LNP vs. NLC comparison]

- LNP vs. NLC comparison
  - 10 µg IDRI RNA replicon/mouse, delivered i.m.

- Relative Luminescence Units
  - Days post-immunization

- ns

![Image of gel lanes showing RNA stability at different temperatures]
Potent Vaccine Adjuvants
IDRI Adjuvants Enable Broad Coronavirus Protection

SARS-CoV2 RBD Protein + IDRI / 3M adjuvant (3M052-Alum) generated higher nAb titers to mutant COVID strains compared with mRNA vaccine, and also conferred strong protection across coronaviruses.
Conclusions

• Amazing progress has been made in speeding several COVID vaccines through the clinical development pipeline

• However, the majority of the population both at home and abroad lack access to COVID-19 vaccines

• A focus on next-generation vaccine technologies can address current gaps in COVID-19 vaccines while helping prepare for the next inevitable pandemic
The Promise of Innate Immune Enhancement

**Infectious Diseases**
A new generation of innate immune enhancers has revolutionized vaccinology and the prevention of infectious diseases.

**Cancer**
Innate immune stimulants are now recognized as effective therapeutic agents against cancer, and important adjuncts to immunotherapy.

**Chronic Diseases**
Targeting the innate immune system has shown promise in early studies for diabetes, autoimmune disease, and Alzheimer's.
IDRI Takes Products from the Bench to the Clinic

- IDRI is a trusted, and experienced provider of cGMP services:
  - Pioneering the latest methods to manufacture investigational products;
  - Translating our own immune-stimulating formulations into clinical products;
  - Supporting nonprofit/academic organizations and biotech startups;

- IDRI is an internationally approved supplier:
  - Compliant with the highest quality standards
  - Supported by internal QA and QC teams with years of industry experience.

- IDRI’s Clinical and Regulatory teams have enable dozens of rapid and effective early-phase clinical trials for IDRI and partners
Thank you

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