COVID-19 VACCINES IN CANADA

Dr. Marina Salvadori and Dr. April Killikelly
Declaration of Interests:

• Dr. Marina Salvadori- Nothing to declare
• Dr. April Killikelly- Nothing to declare
OBJECTIVES

• To describe SARS-CoV-2 spike protein as a vaccine antigen

• To discuss the similarities and differences between vaccine platform technologies that may be available in Canada
SARS-COV-2 VACCINE ANTIGENS: THE SPIKE PROTEIN
SARS-CoV-2 the virus that causes COVID-19

- Spike is a viral protein antigen on the surface of SARS-CoV-2

(L) Image: Transmission electron microscope image shows SARS-CoV-2, the virus that causes COVID-19, isolated from a patient in the U.S. Source: National Institutes of Health
(R) Image: de Andrade Santos et al, Review in Frontiers in Microbiology Aug 2020
Spike mediates SARS-CoV-2 Infection

- Spike mediates contact between the virus and the host cell to cause infection.
- One way to prevent infection is to block the interaction between spike and ACE-2 via the production of **anti-spine antibodies**.
How to elicit anti-spike antibodies:

- Vaccination with spike protein elicits a primary immune response that forms immunological memory.

- Upon natural infection, immunological memory is called upon to mount a protective immune response.

**Table:****

<table>
<thead>
<tr>
<th>Vaccination</th>
<th>Primary antibody response</th>
<th>Natural infection</th>
<th>Secondary antibody response</th>
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</thead>
</table>

**Image:** Modified from Janeway Immunobiology
How to deliver SARS-CoV-2 spike protein: From Gene to Protein

Proteins are made through a 2 step process:

Step 1: Transcription
- Genes are **transcribed** into mRNA

Step 2: Translation
- mRNA molecules are **translated** into proteins

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Image Adapted from Qin et al. [The Current Status and Challenges in Computational Analysis of Genomic Big Data](#)
How to deliver SARS-CoV-2 spike protein: From Gene to Protein

Different steps to create a protein happens in different locations within a cell:

- **Transcription (DNA->mRNA)** happens inside the *nucleus* of the cell
- **Translation (mRNA->protein)** happens inside the *cytosol* of the cell

Without help, material does pass into the cytosol or the nucleus of the cell. Vaccine developers have developed **lipid nanoparticle** and **viral vector technology** to allow DNA and mRNA to pass through membranes.
VACCINE PLATFORMS
Protein, mRNA and Viral Vector
Vaccine Platforms

• Canada has made agreements in principle with 7 vaccine developers to supply Canadians with doses of vaccine if their vaccine candidate is assessed to be safe and efficacious by Health Canada

• The vaccines in development for which Canada may have first access use three different technologies:
  – Protein subunit (including Virus Like Particles (VLPs))
  – Messenger RNA (mRNA)
  – Viral vectors
Protein Subunit Vaccines:

Subunit Protein Vaccines:

- Deliver vaccine antigens as proteins which directly elicit an immune response.
- An established technology
- Elicit a strong antibody response
- Commonly use adjuvants
- Generally slower manufacturing timelines

COVID-19 Protein Subunit vaccines:
Novavax
Sanofi
Virus-Like Particle Vaccines (VLP)

VLP Vaccines
- Deliver vaccine antigens as proteins which directly elicit an immune response.
- An established technology
- Elicit a strong antibody response
- Commonly use adjuvants
- Generally slower manufacturing timelines

COVID-19 VLP vaccines:
Medicago
Messenger RNA (mRNA) Vaccines:

- Lipid nanoparticles are used to deliver mRNA directly into cells
- mRNA coding for spike protein are then translated
- New technology
- Elicitation of antibodies and T-cells
- Fast manufacturing timeline

mRNA vaccines:

- Moderna
- Pfizer/BioNTech

Image: [Opportunities and Challenges in the Delivery of mRNA-Based Vaccines](#)
COVID-19 Viral Vector Vaccines

Viral Vector Vaccines:
- Modified adenovirus used as a vector to deliver spike genes (DNA) into the cell
- Elicitation of antibodies and T-cells
- Potential for interference from pre-existing adenoviral immunity

COVID-19 VLP vaccines:
Janssen/Johnson & Johnson
AstraZeneca/University of Oxford
Assessing Vaccine Efficacy

- **Vaccine Efficacy**: How well a vaccine protects vaccinated vs unvaccinated people from disease *in a clinical trial*
- **Vaccine Effectiveness**: How well a vaccine protects vaccinated vs unvaccinated people from disease *in the real world*
- Randomized controlled trials (RCTs) are the best method to assess vaccine efficacy

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Image adapted from: **Test, Learn, Adapt: Developing Public Policy with Randomised Controlled Trials**

- Population is split into 2 groups by random lot
- Outcomes for both groups are measured

**Incidence of Disease in Placebo Group**: (7/8)

**Incidence of Disease in Vaccine Group**: (1/8)

**Vaccine Efficacy**: The vaccinated group would experience **86% fewer disease cases** than they would have if they had not been vaccinated.
COVID-19 Vaccine Development Landscape:

**Confirmed APA with Canada**

- **Vaccine Program Terminated**

### Platform Technology

- **Sanofi/GSK**
  - Protein
- **Novavax**
  - Subunit
- **VBI**
  - Virus Like Particle
- **Medicago**
  - Virus Like Particle
- **Merck**
  - Viral Vector
- **Janssen/J&J**
  - Viral Vector
- **CanSino**
  - Viral Vector
- **AZ/Univ of Oxford**
  - mRNA
- **Moderna**
  - mRNA
- **BioNTech/Pfizer**
  - mRNA
- **CureVac**
  - mRNA
- **ICL/Morning**
  - mRNA
- **PNI**
  - DNA
- **Inovio**
  - DNA
- **Valneva/Dynavax**
  - Inactivated

### IO Submission

- Preclinical
- Phase I
- Phase II
- Phase III
- IO Submission

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*APA or other agreements outlining vaccine supply in principle. Amounts listed here may cover multiple mechanisms of access.*

Developed by the Secretariat to the National Advisory Committee on Immunization (NACI)

*Updated 2021-01-29*
mRNA Vaccines: Moderna and Pfizer/BioNTech

- Vaccine antigen is mRNA coding for a gene for SARS-CoV-2 spike protein
- mRNA is very unstable

mRNA Lipid Nanoparticle

- mRNA LNPs are made of two parts-
  - mRNA
  - Lipids
- The lipids allow the mRNA to enter into the cell
- Like oil and water, lipids don’t mix well with water so the mRNA lipid nanoparticle vaccines have special frozen and ultrafrozen storage and handling requirements (ie: no shaking).

Image adapted from: [Solid Lipid Nanoparticles: A Potential Approach for Dermal Drug Delivery](image-url)
Viral Vector Vaccine: AstraZeneca (Janssen/J&J)

- Vaccine antigen is DNA coding for a gene for SARS-CoV-2 spike protein
- DNA is more stable than RNA but can’t get into the cell or the nucleus without help

Viral Vectored Vaccine

- Viral Vector Vaccines are made of two parts-
  - DNA
  - Non-replicating vector virus (Adenovirus)
- Adenovirus carries the vaccine antigen DNA into the cell and into the nucleus of the cell
- Adenoviruses are much more complex than lipid particles and have features to allow them to be stable at higher temperatures (fridge or room temperature)
Protein-Based Vaccines: (Novavax, Sanofi)

• Vaccine antigen is the SARS-CoV-2 spike protein

Protein-based Vaccine

• Protein-based Vaccines can be made of two parts-
  • Protein antigen
  • Adjuvant
• To elicit strong immune responses, protein-based vaccines commonly use adjuvants

• Matrix M (Novavax)
• AS03 (Sanofi)
Protein-Based Vaccines: Virus-Like Particle Vaccines (Medicago)

- Vaccine antigen is the SARS-CoV-2 spike protein
- Insertion at base of spike allow virus-like particle (VLP) formation

VLP Vaccines

- VLP Vaccines can be made of two parts-
  - Protein antigen in a VLP
  - Adjuvant

+ Adjuvant
  - AS03 (Medicago)
Key Messages for COVID-19 Vaccine Candidates:

- SARS-CoV-2 spike protein antigens have been demonstrated to induce protective efficacy against COVID-19 in randomized controlled trials.

- Canada has negotiated agreements in principle to supply vaccine to Canadians with 7 companies who are using three different vaccine platforms:
  - Protein subunit (including virus-like particle)
  - mRNA
  - Viral vector

- Different vaccine technology platforms use different methods to deliver their antigen and may have different components, but they all aim to deliver the spike protein to elicit protective immune responses.
Additional Resources

Authorized COVID-19 vaccines in Canada:
https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/vaccines.html

Canadian Immunization Guide

National Advisory Committee on Immunization Statements