COVID-19 VACCINES IN CANADA

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Declaration of Interests:

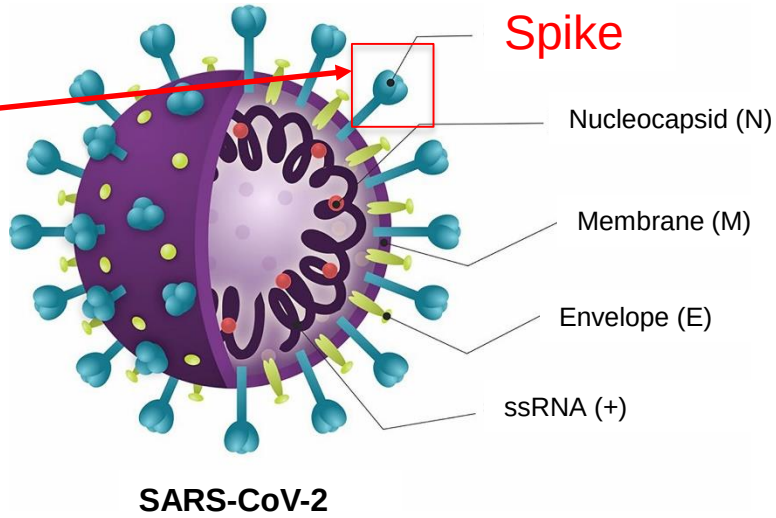
- Dr. Marina Salvadori- Nothing to declare
- Dr. April Killikelly- Nothing to declare

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

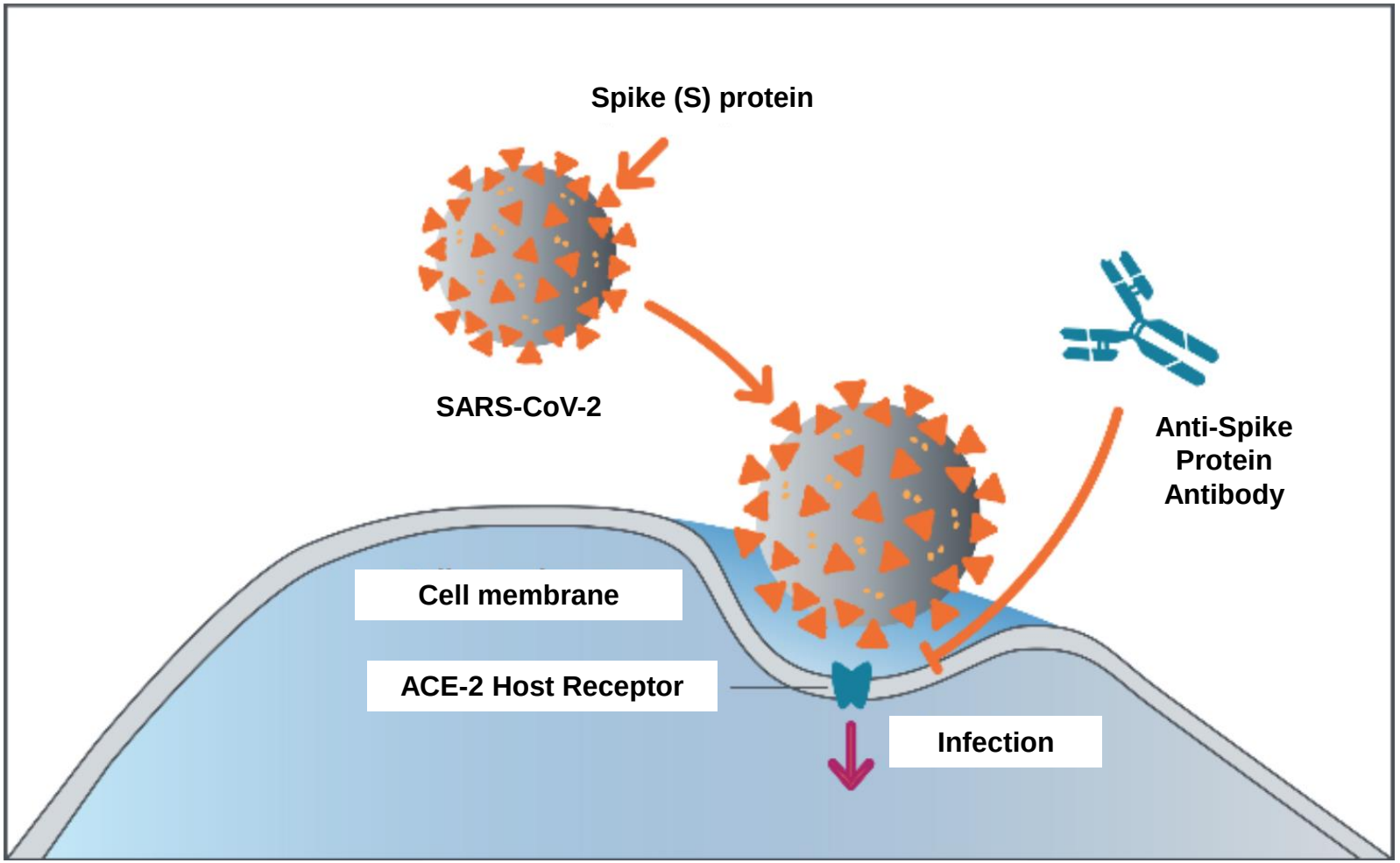
SARS-CoV-2 the virus that causes COVID-19



- 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

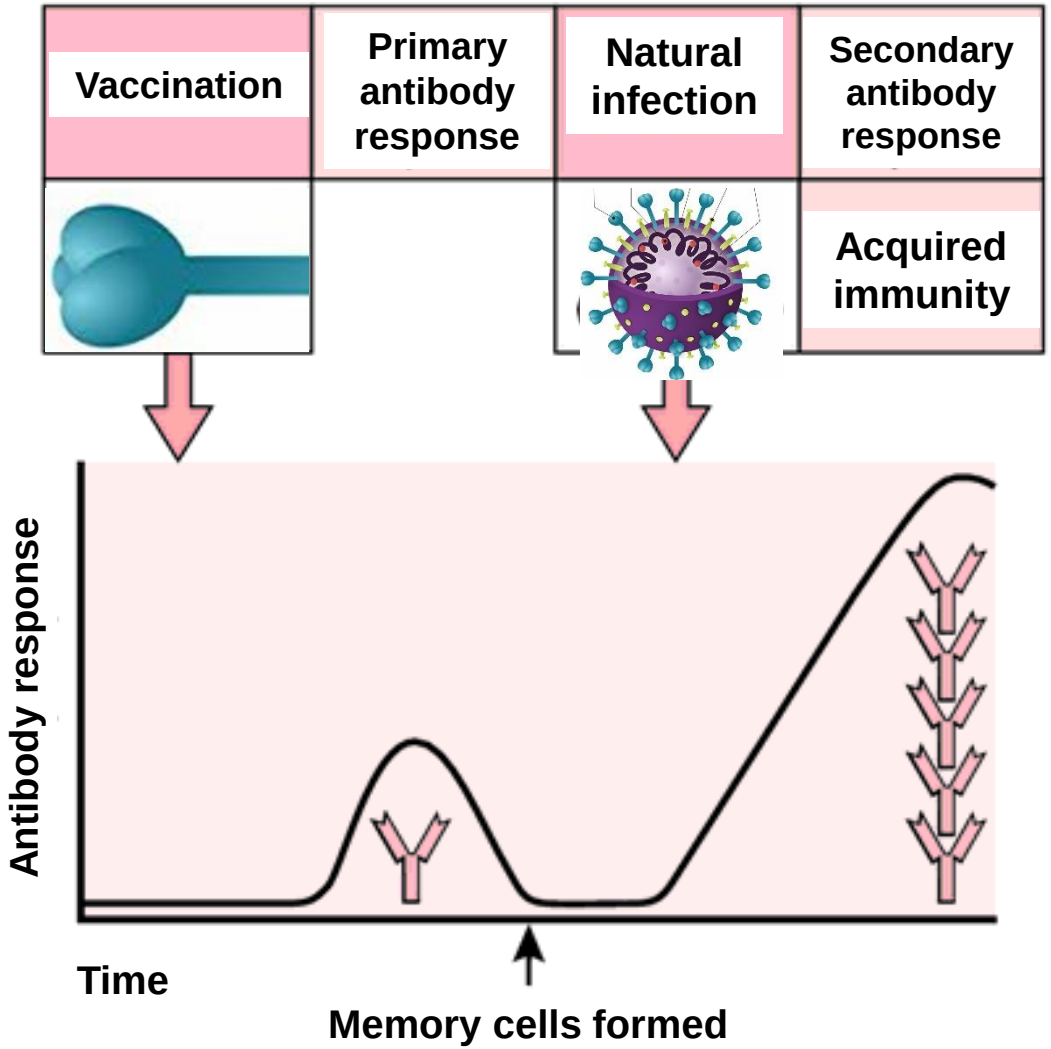
Spike mediates SARS-CoV-2 Infection



- 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-spike antibodies**

Image: Berkley Lights

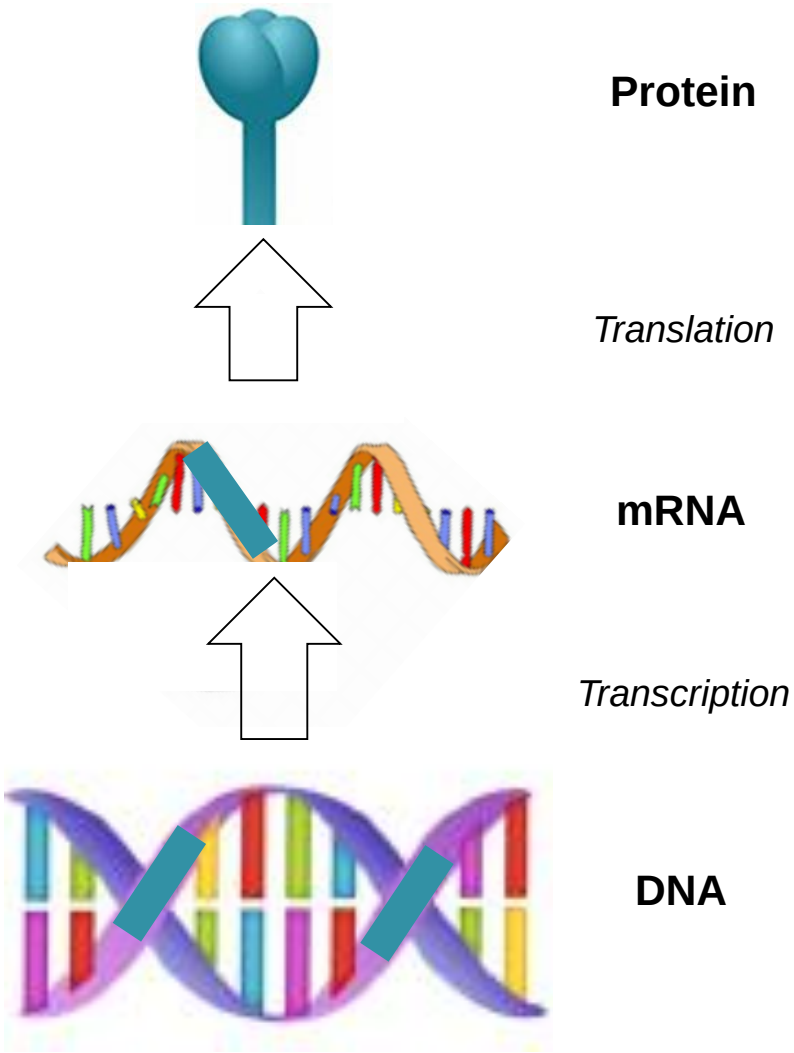
How to elicit anti-spike antibodies:



- 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

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 2: Translation

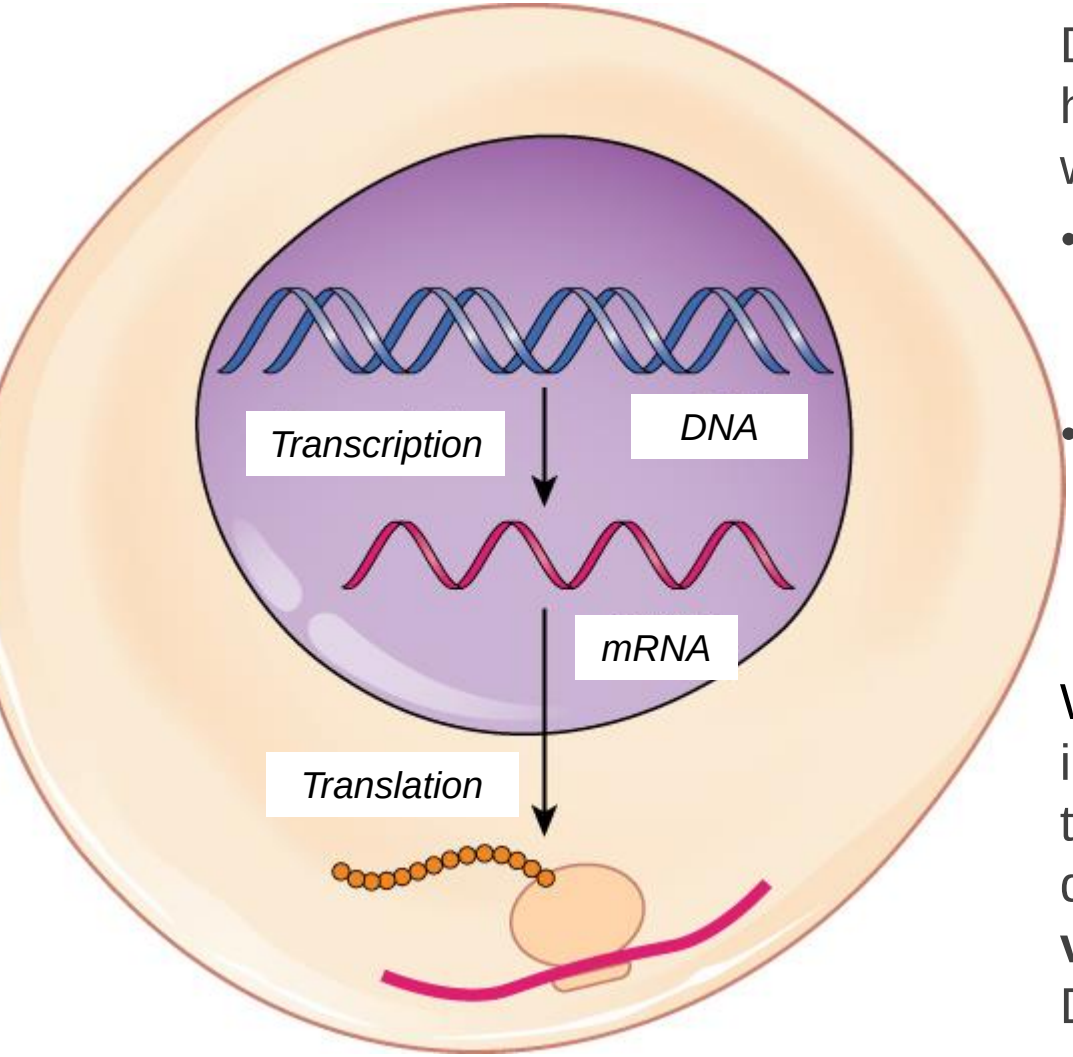
- mRNA molecules are **translated** into proteins

Step 1: Transcription

- Genes are **transcribed** into mRNA

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.

Image Open Oregon State

VACCINE PLATFORMS

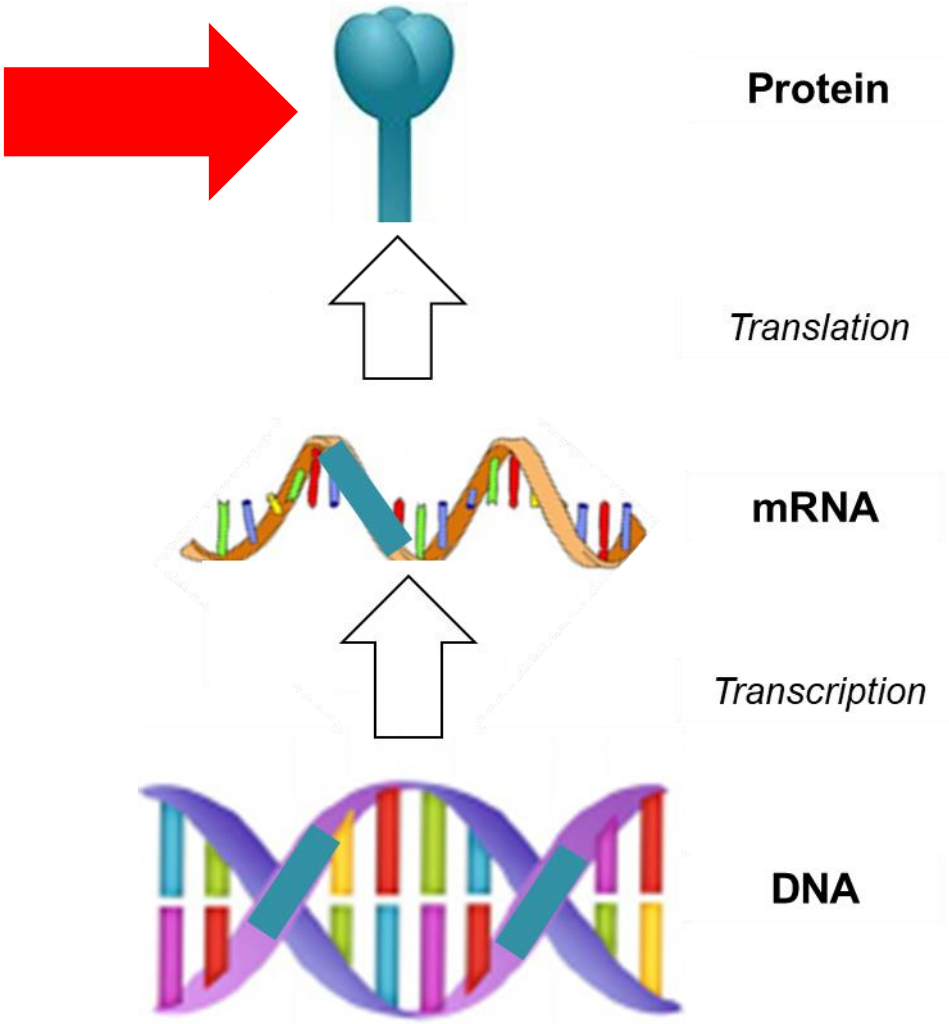
Protein, mRNA and Viral Vector

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:

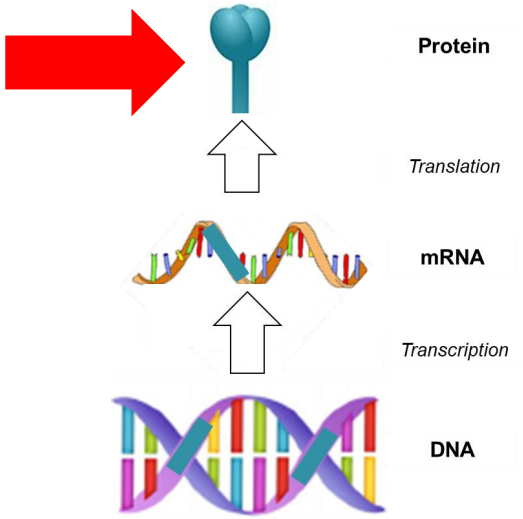
- Deliver vaccine antigens as proteins which directly elicit an immune response.
- An established technology
- Elicit a strong antibody response
- Commonly use adjuvants
- Generally slower manufacturing timelines

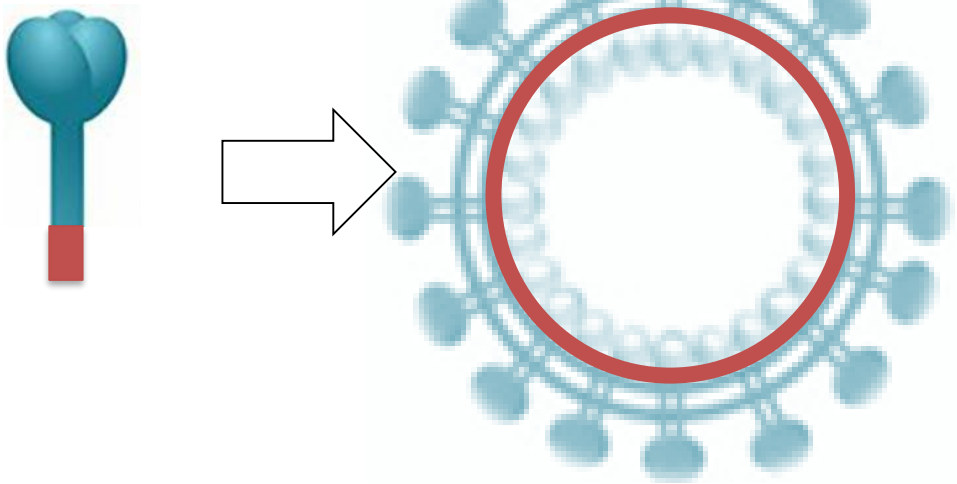
COVID-19 Protein Subunit vaccines:

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

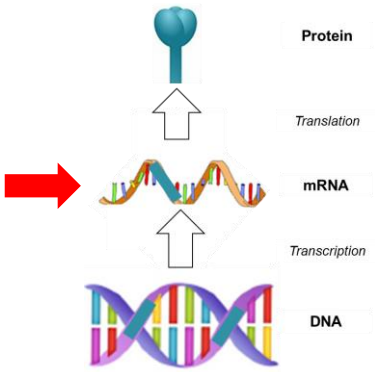
COVID-19 VLP vaccines:

Medicago

Image Micro and Nanotechnology in Vaccine Development

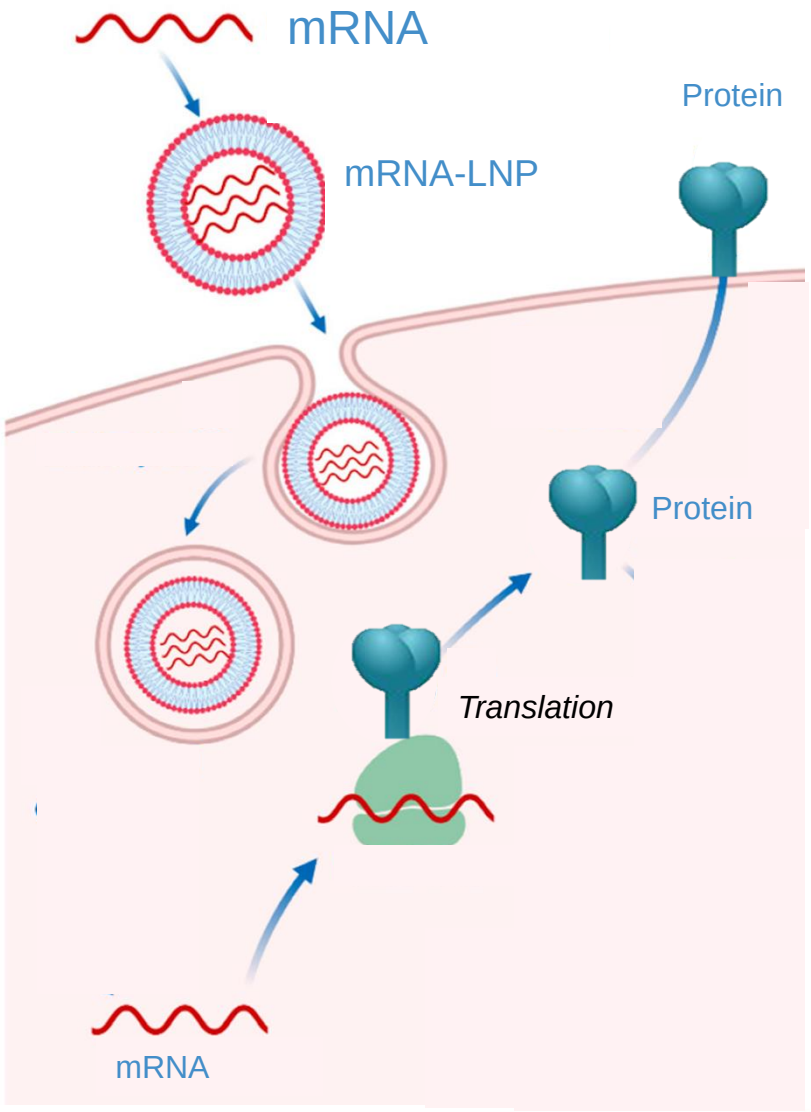
Messenger RNA (mRNA) Vaccines:

Cellular and Humoral Immune Responses



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



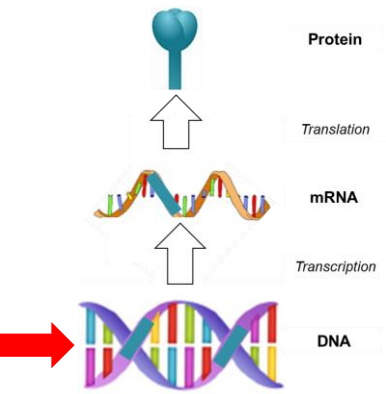
mRNA vaccines:

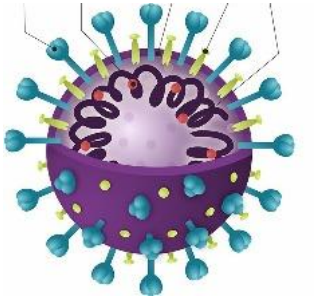
Moderna

Pfizer/BioNTech

Image: Opportunities and Challenges in the Delivery of mRNA-Based Vaccines

COVID-19 Viral Vector Vaccines

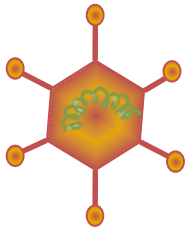




SARS-CoV-2

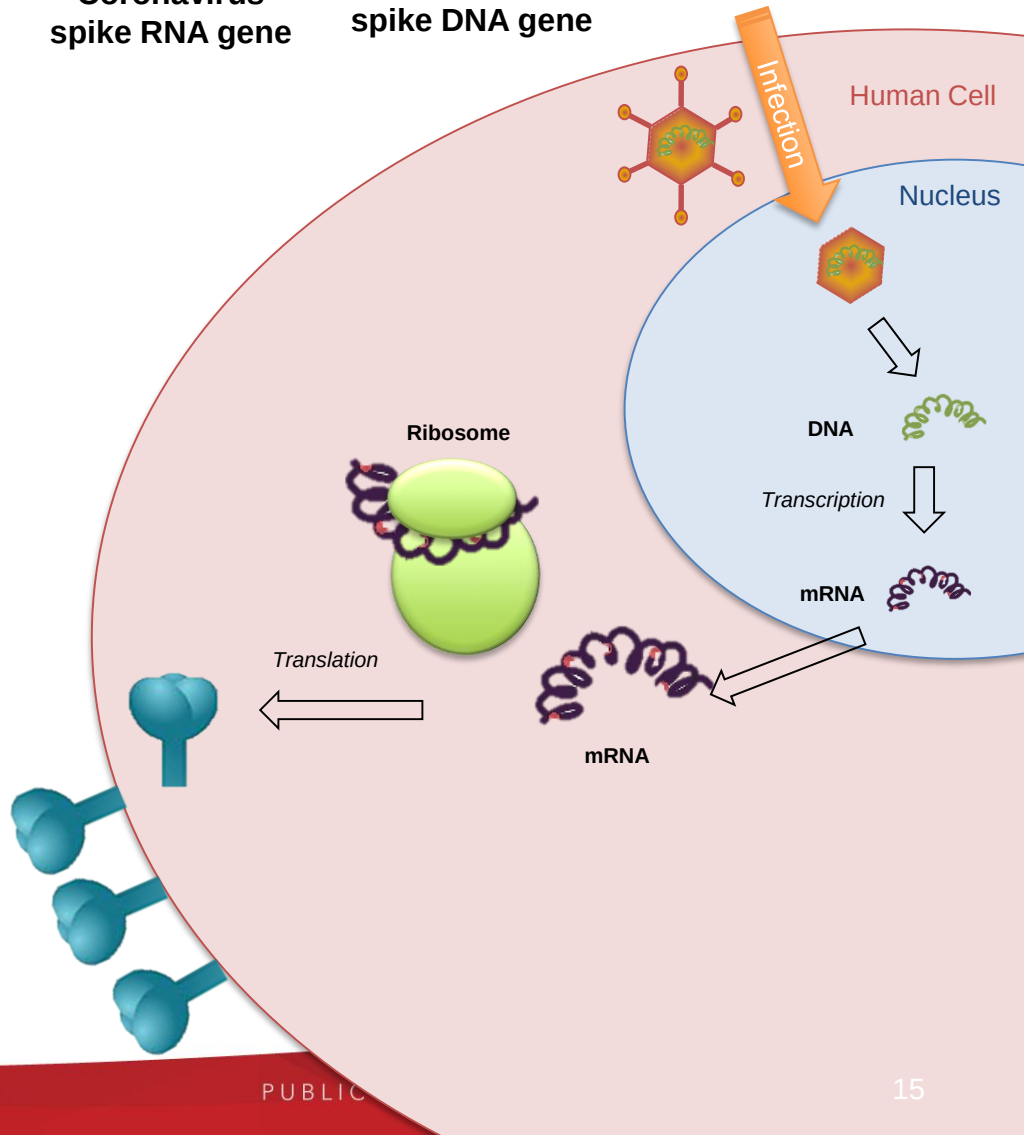
Non-Replicating Vector Vaccine

Adenovirus



Coronavirus spike RNA gene

Coronavirus spike DNA gene



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

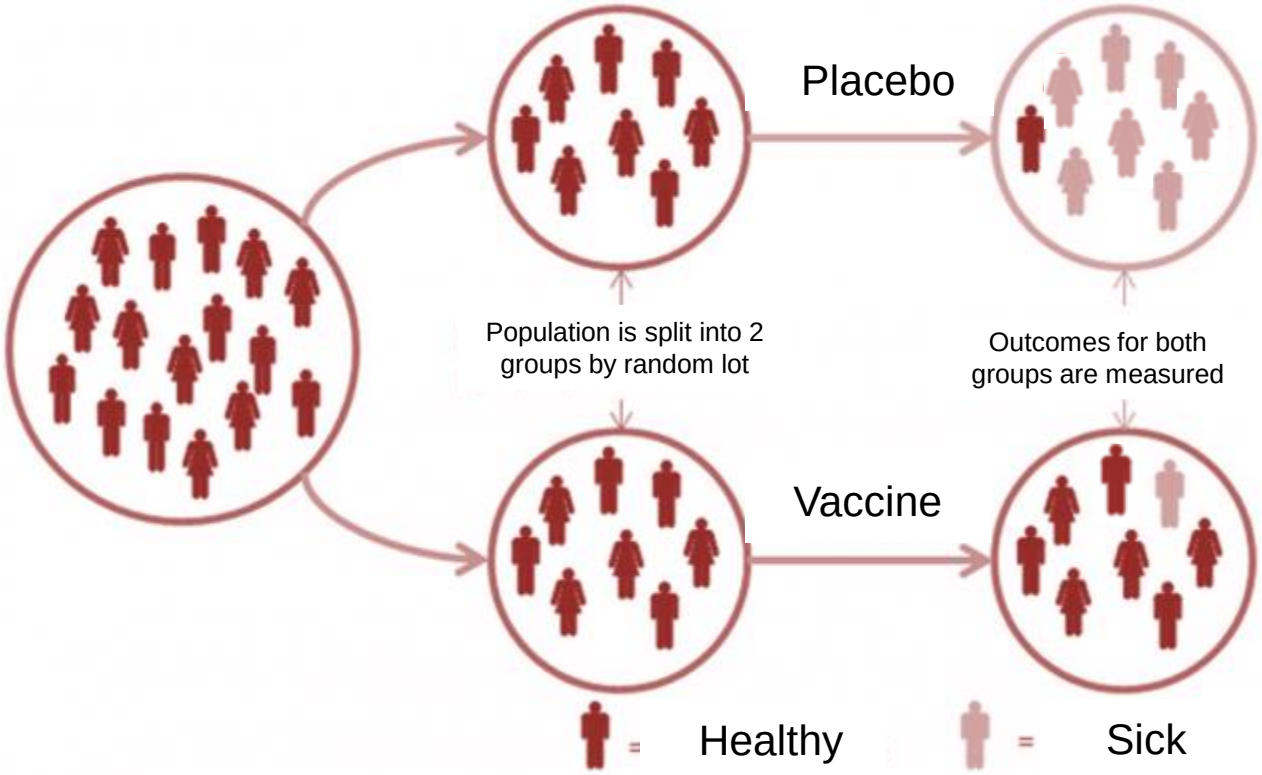
COVID-19 VLP vaccines:

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



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

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

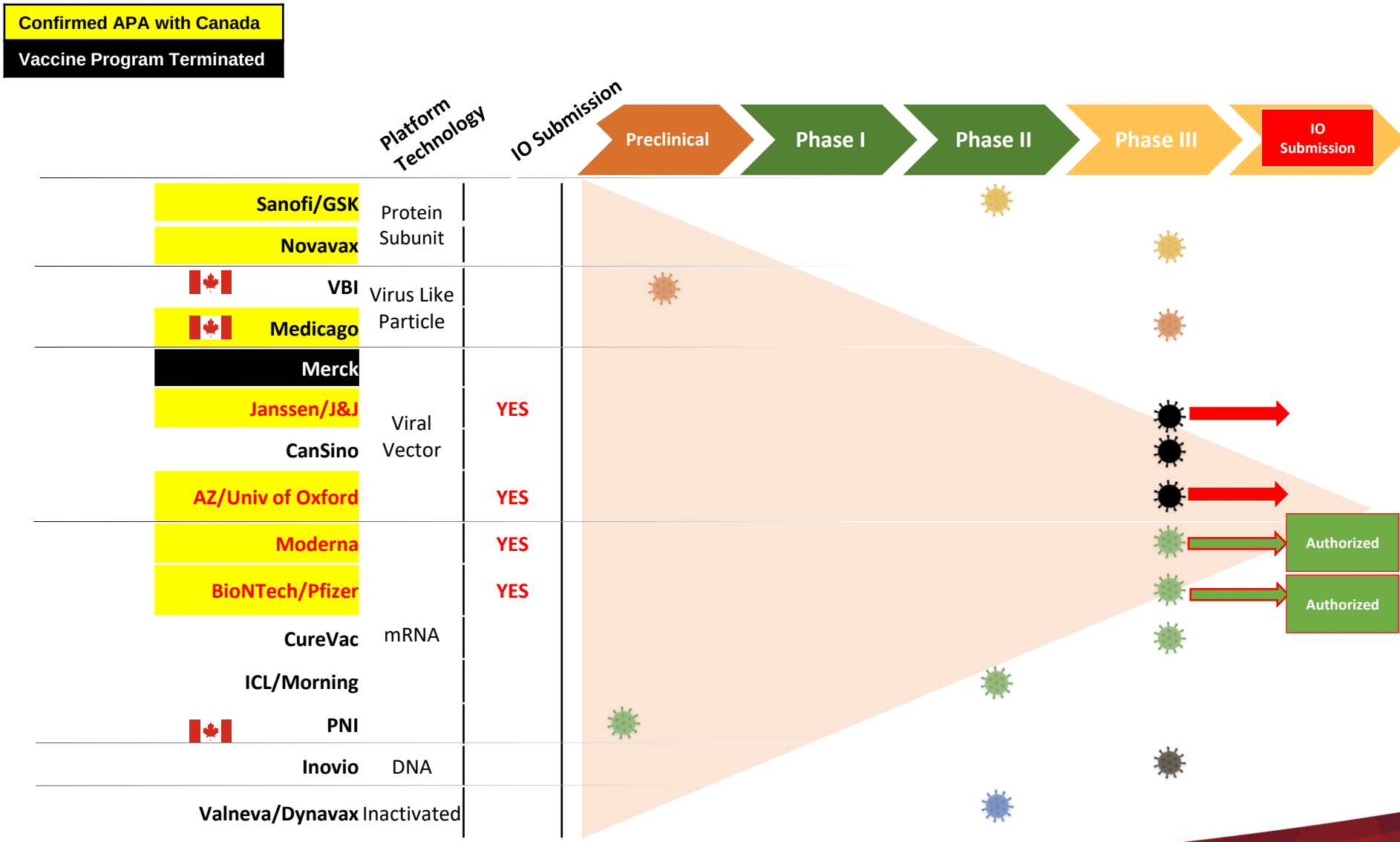
Vaccine Efficacy:

The vaccinated group would experience **86% fewer disease cases** than they would have if they had not been vaccinated.

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

Updated 2021-01-29

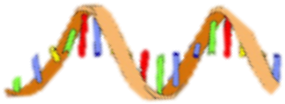
COVID-19 Vaccine Development Landscape:



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

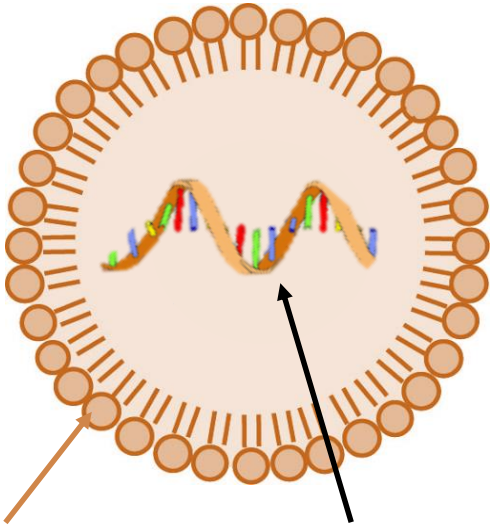
mRNA Vaccines: Moderna and Pfizer/BioNTech

SARS-CoV-2 Spike mRNA



- 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).

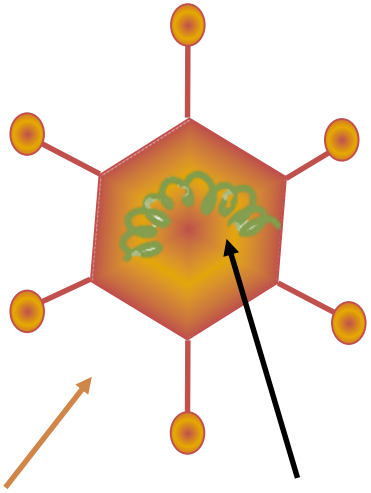
Image adapted from : **Solid Lipid Nanoparticles: A Potential Approach for Dermal Drug Delivery**

Viral Vector Vaccine: AstraZeneca (Janssen/J&J)

SARS-CoV-2 Spike DNA

- 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)

SARS-CoV-2 Spike Protein

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

Protein-based Vaccine

+ ***Adjuvant***

- ***Matrix M (Novavax)***
- ***AS03 (Sanofi)***

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

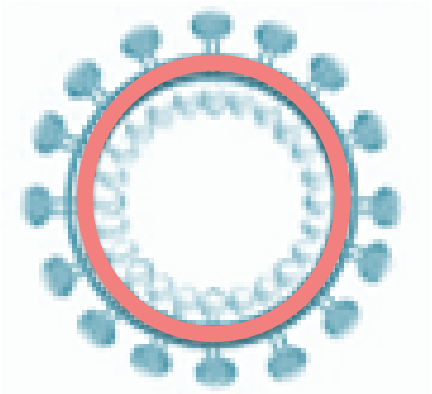
Protein-Based Vaccines:
Virus-Like Particle Vaccines (Medicago)

SARS-CoV-2 Spike Protein

- 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)***

Image Micro and Nanotechnology in Vaccine Development

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

https://www.canada.ca/en/public-health/services/canadian-immunization-guide.html

National Advisory Committee on Immunization Statements

https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci.html