COVID-19 VACCINES IN CANADA

Dr. Marina Salvadori and Dr. April Killikelly

Declaration of Interests- Dr. Marina Salvadori

- Nothing to declare

Declaration of Interests- Dr. April Killikelly

- Nothing to declare

OBJECTIVES

- To describe the platform technologies used by candidate vaccines against SARS-CoV-2 / COVID-19.

- To discuss mRNA vaccines in development by Pfizer/BioNTech and Moderna against SARS-CoV-2 / COVID-19.

Presentation Recorded on December 12th 2020

Every attempt has been made to present the most current information however information about COVID-19 vaccines is rapidly evolving and the information presented here may be out of date.

Please check the Public Health Agency of Canada website for the most up to date information.

https://www.canada.ca/en/public-health.html

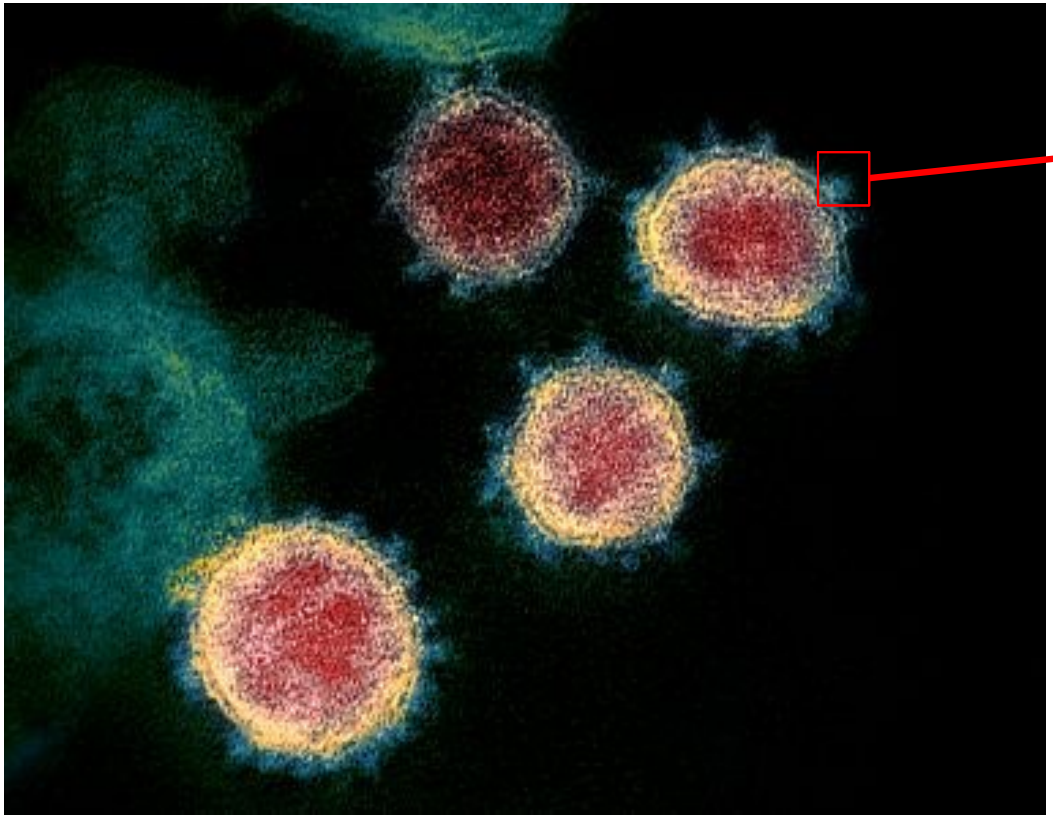
Vaccine Platforms

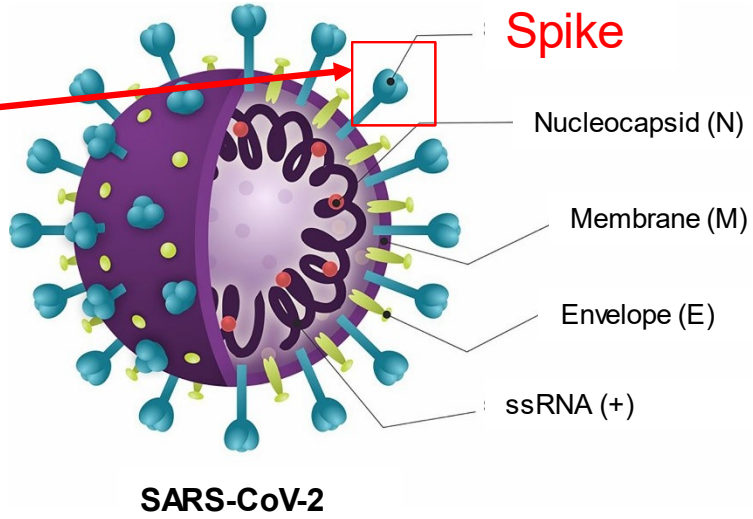
- Canada has made agreements in principle with 7 vaccine developers to supply Canadians with doses of vaccine if their vaccine candidate is assessed to be safe and efficacious by Health Canada

- 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**

SARS-COV-2 VACCINE ANTIGENS: THE SPIKE PROTEIN

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

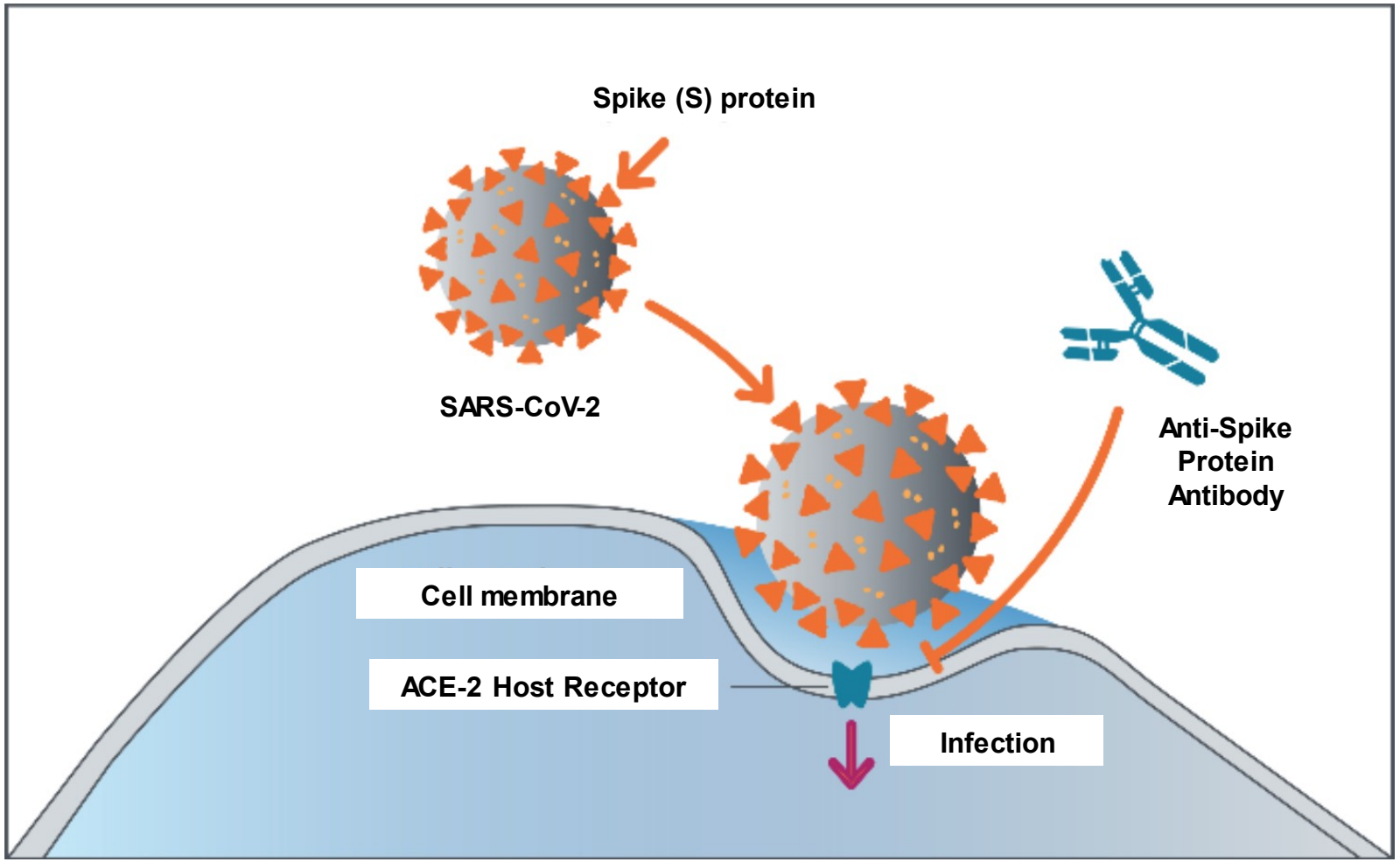




- Spike is a viral protein antigen on the surface of SARS-COV-2

(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

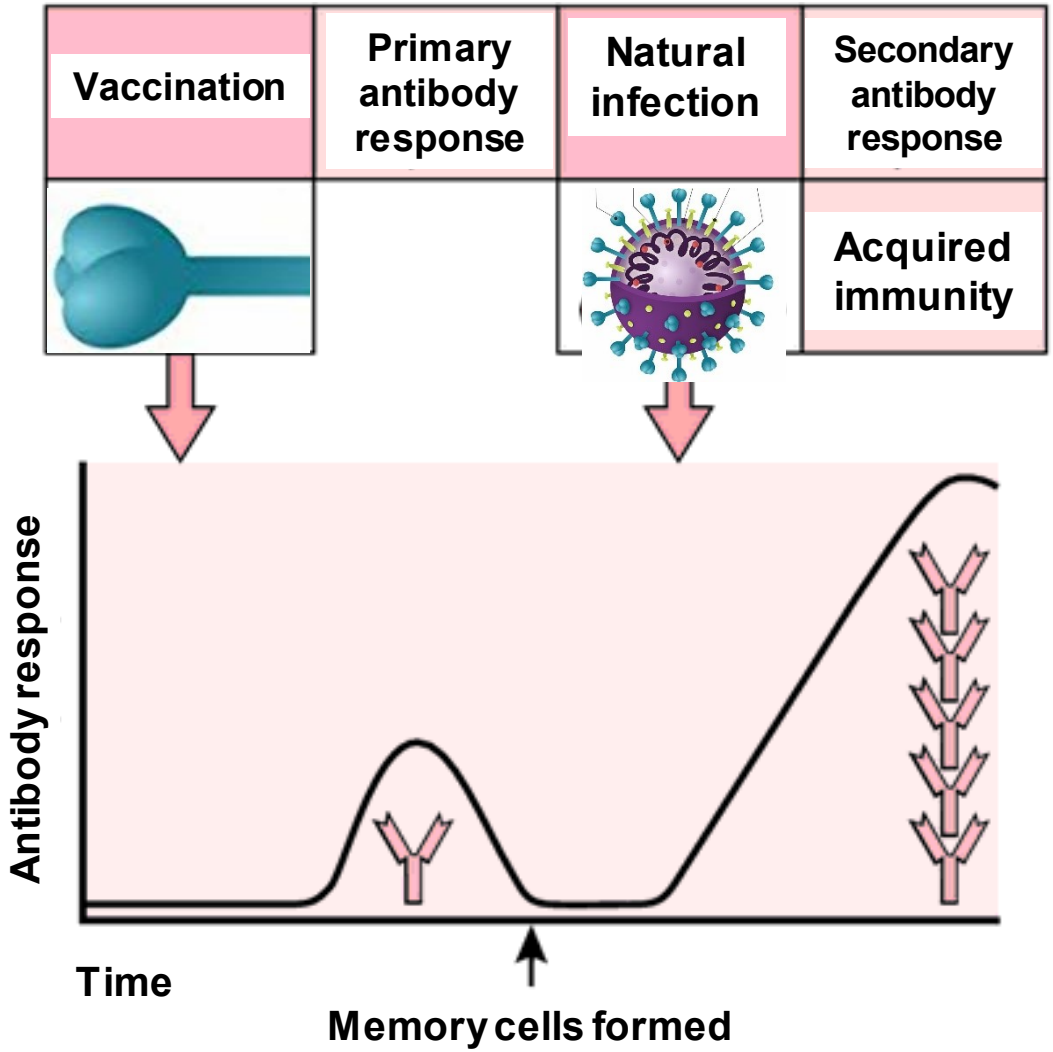
Spike mediates SARS-CoV-2 Infection



- 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

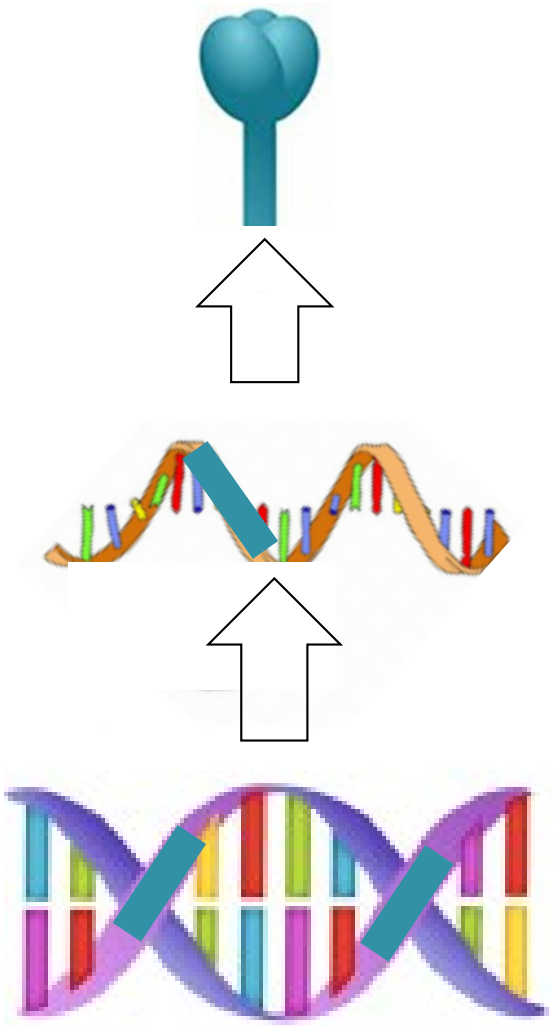
How to elicit anti-spike antibodies:



- 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

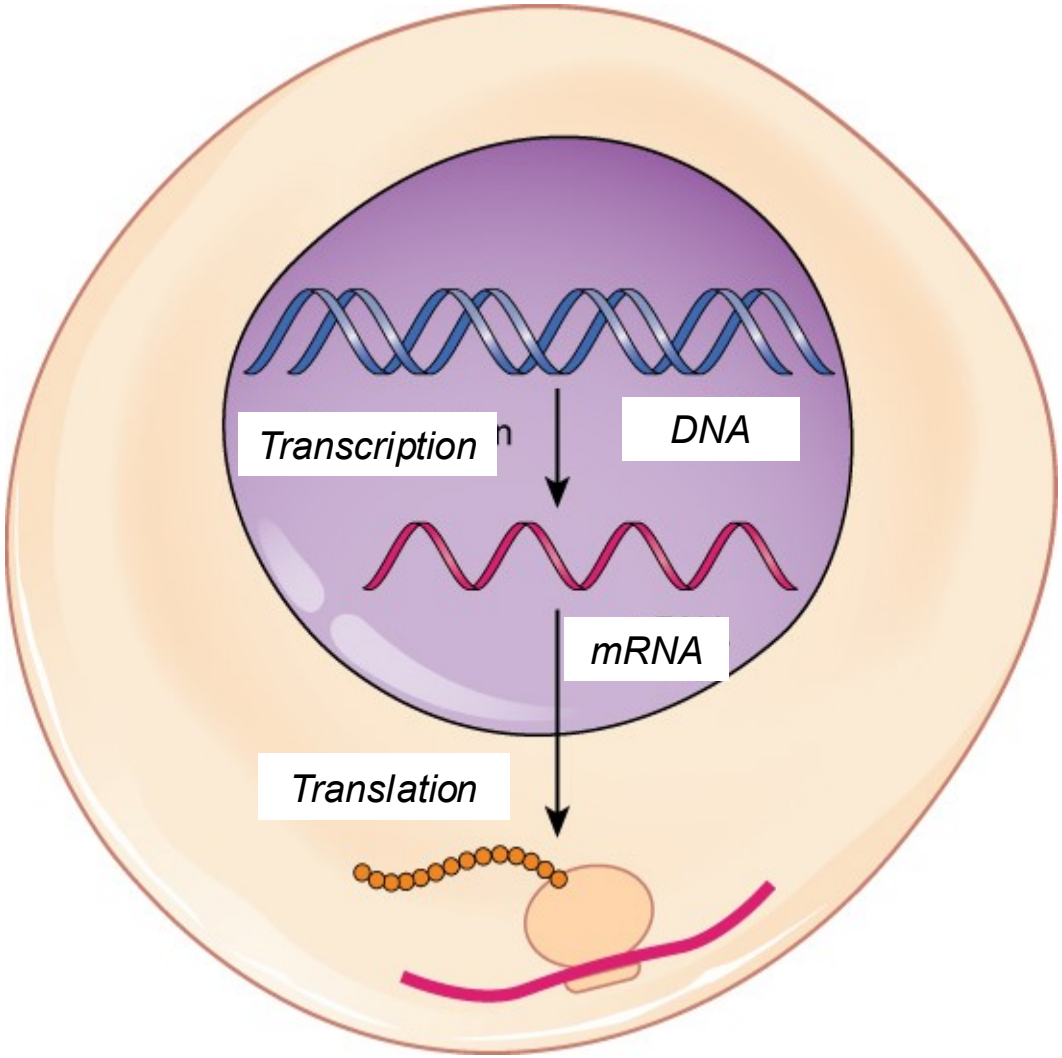


Image Open Oregon State

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

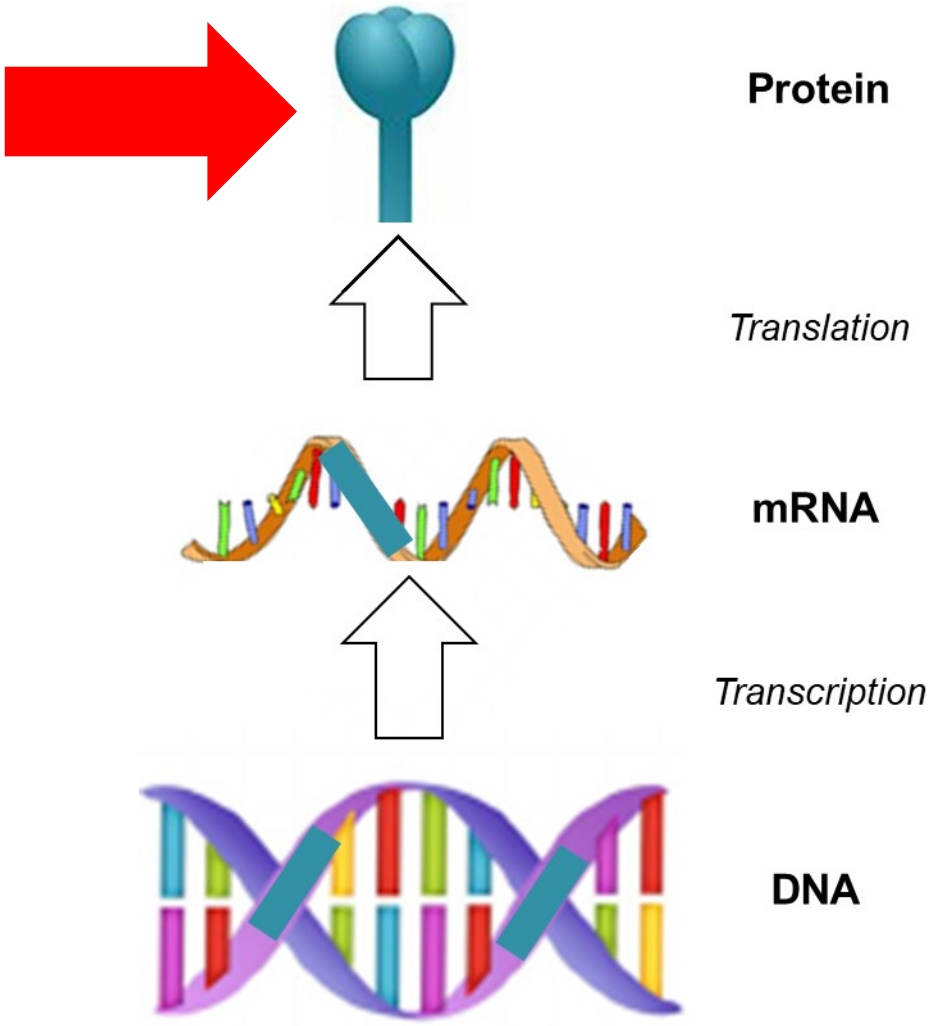
- Transcription (DNA->mRNA) happens inside the **nucleus** of the cell
- Translation (mRNA->protein) happens inside the **cytosol** of the cell

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

Protein Subunit Vaccines:



Subunit Protein Vaccines:

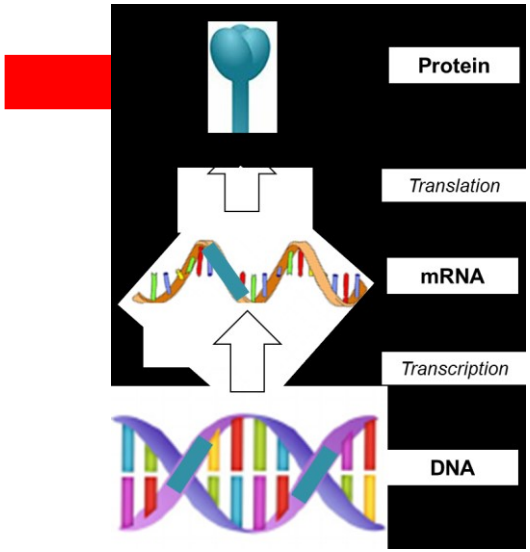
- Deliver vaccine antigens as proteins which directly elicit an immune response.
- An established technology
- Elicit a strong antibody response
- Commonly use adjuvants
- Generally slower manufacturing timelines

COVID-19 Protein Subunit vaccines:

Novavax

Sanofi

Virus-Like Particle Vaccines (VLP)



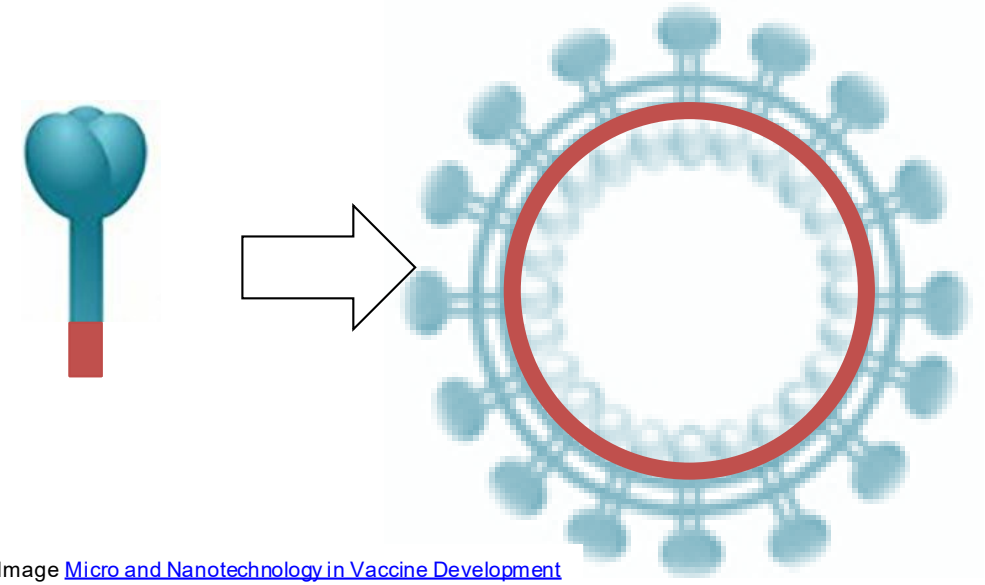


Image Micro and Nanotechnology in Vaccine Development

VLP Vaccines

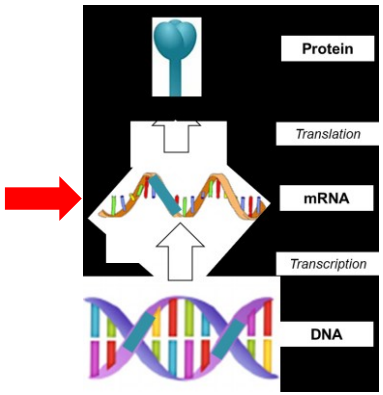
- Deliver vaccine antigens as proteins which directly elicit an immune response.
- An established technology
- Elicit a strong antibody response
- Commonly use adjuvants
- Generally slower manufacturing timelines

COVID-19 VLP vaccines:

Medicago

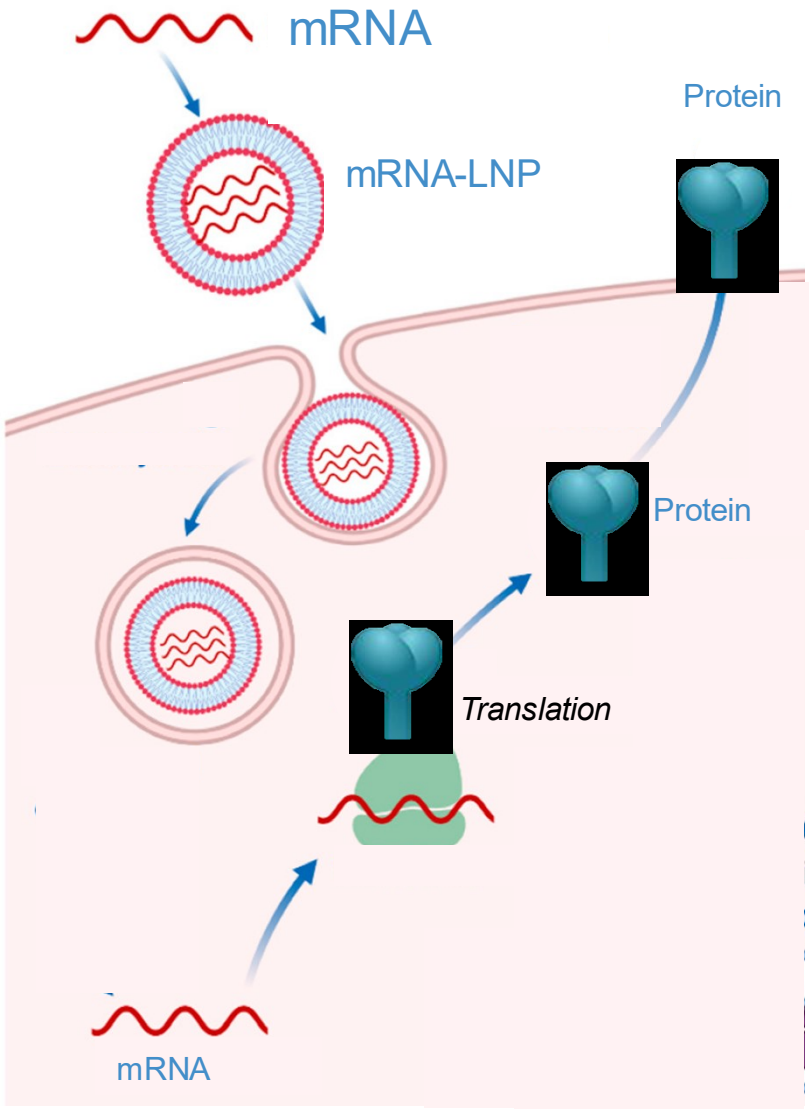
Messenger RNA (mRNA) Vaccines:

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



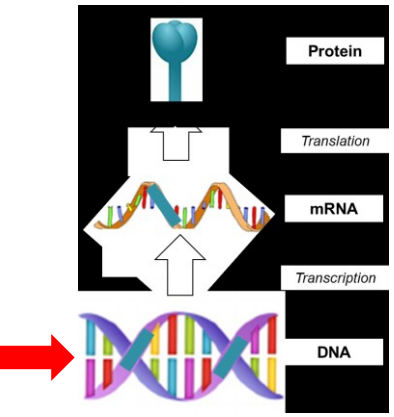
mRNA vaccines:

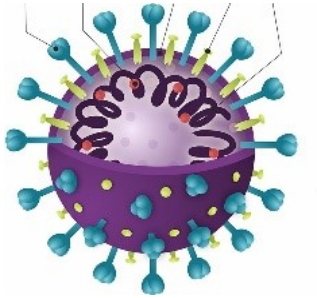
Moderna

Pfizer/BioNTech

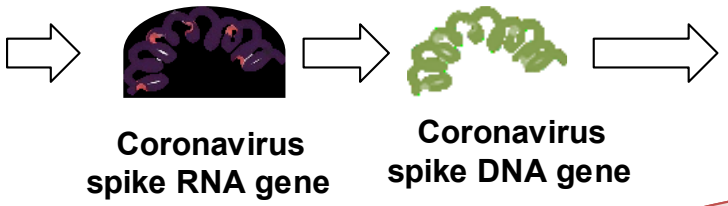
Image: Opportunities and Challenges in the Delivery of mRNA-Based Vaccines

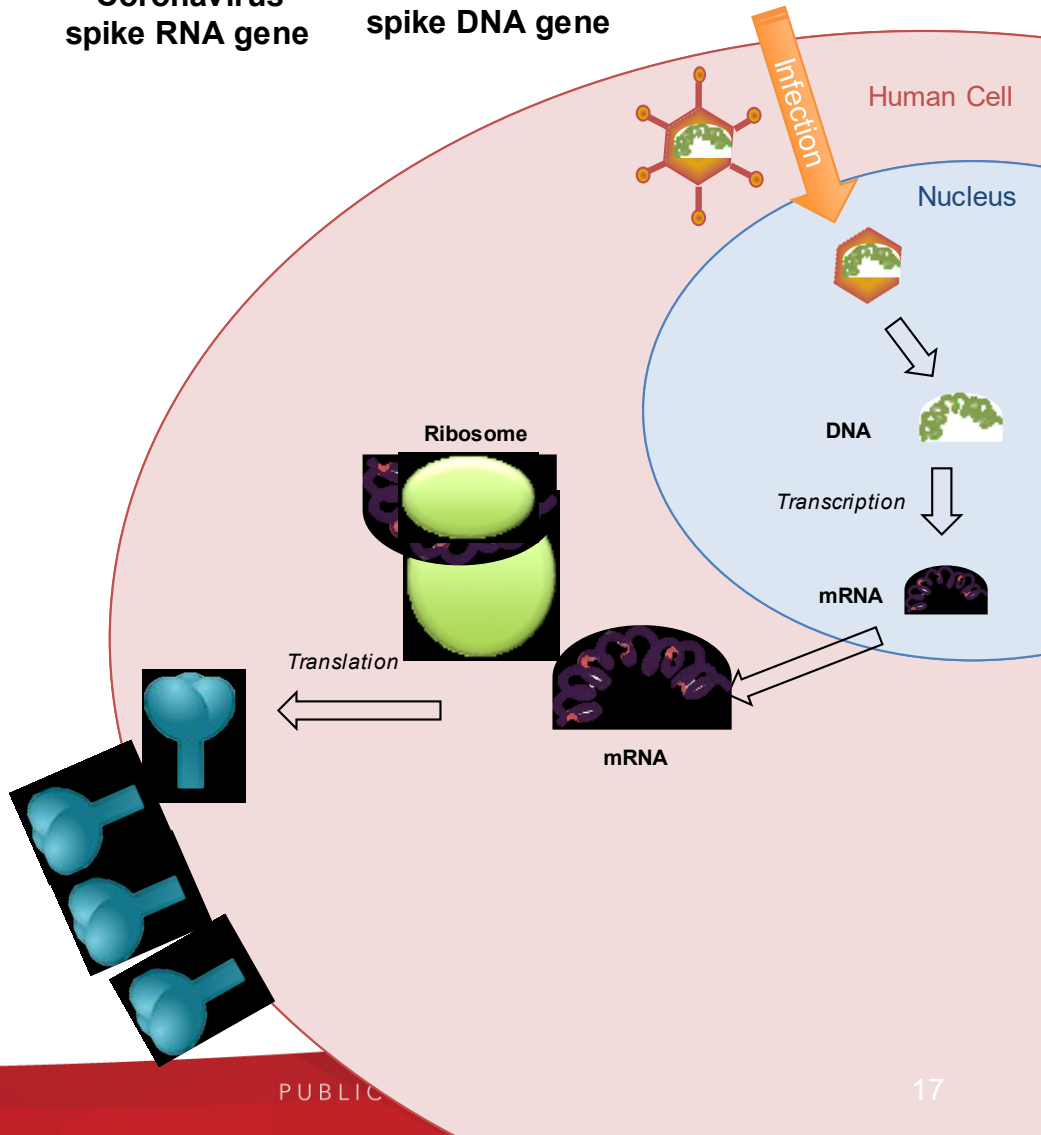
COVID-19 Viral Vector Vaccines





SARS-CoV-2





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

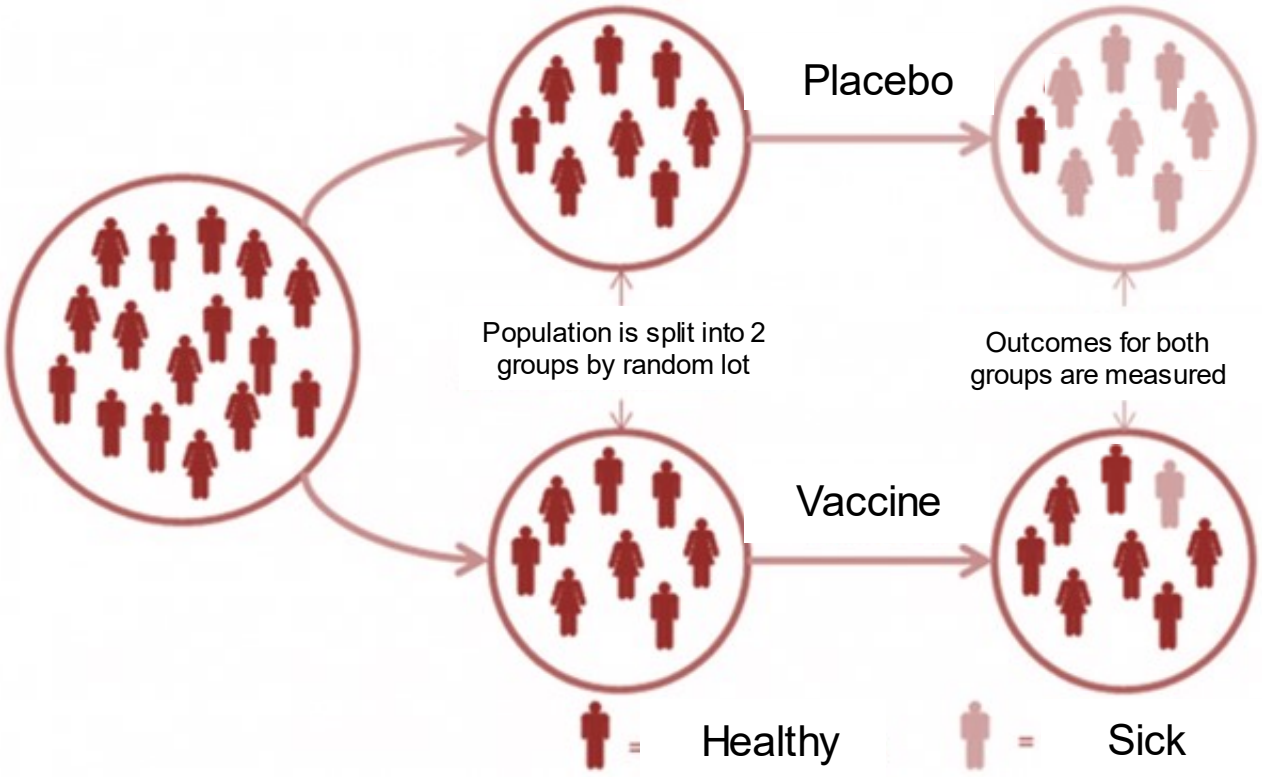
COVID-19 VLP vaccines:

Janssen and 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)

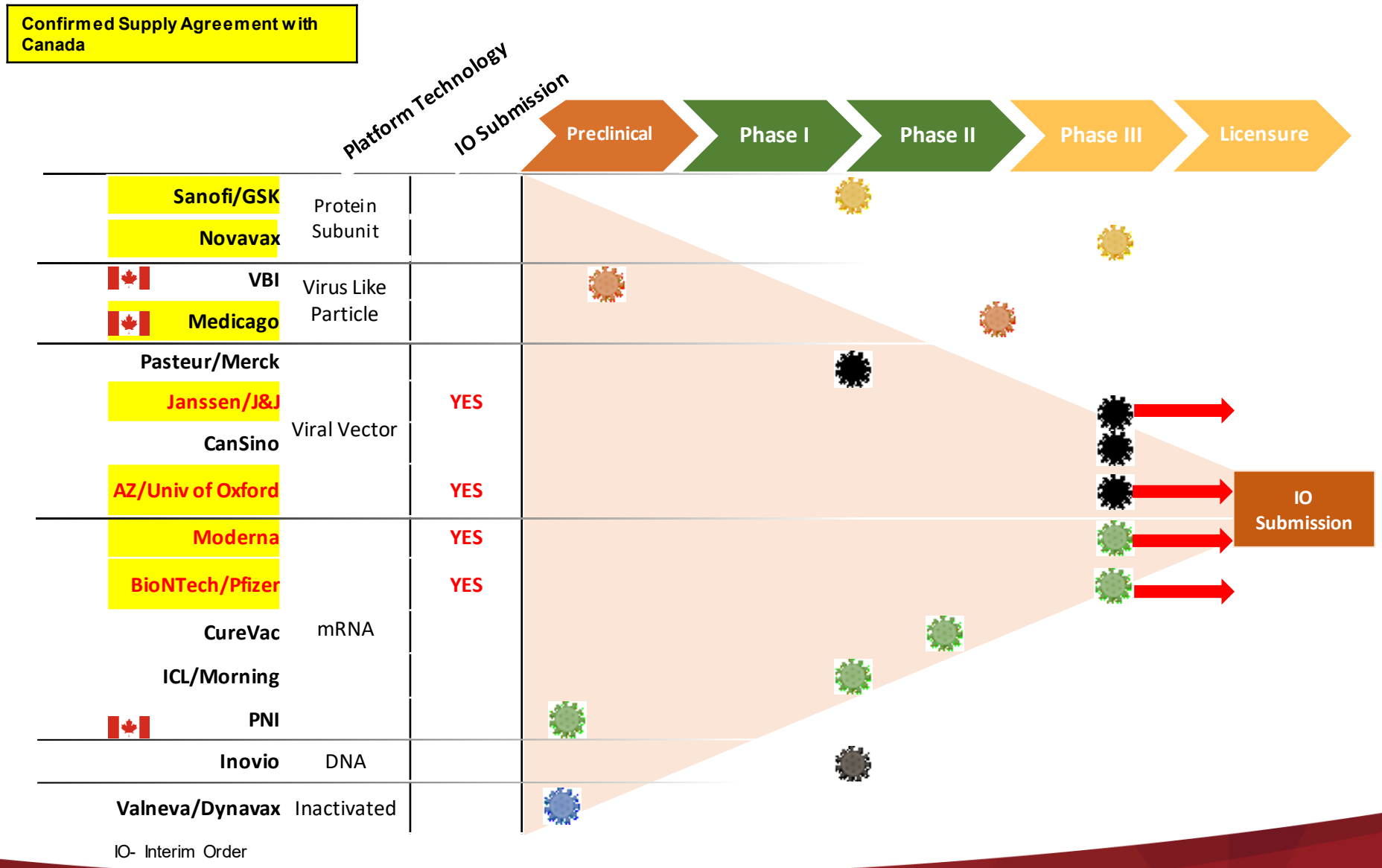
Vaccine Efficacy:

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 2020-12-03

COVID-19 Vaccine Development Landscape:

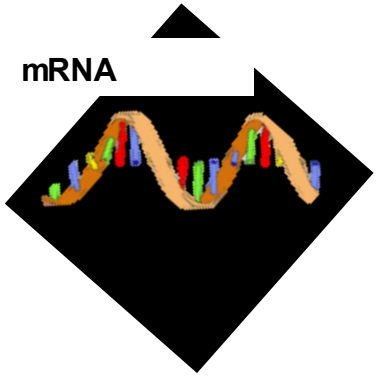


IO- Interim Order

mRNA VACCINES EXPECTED IN EARLY 2021

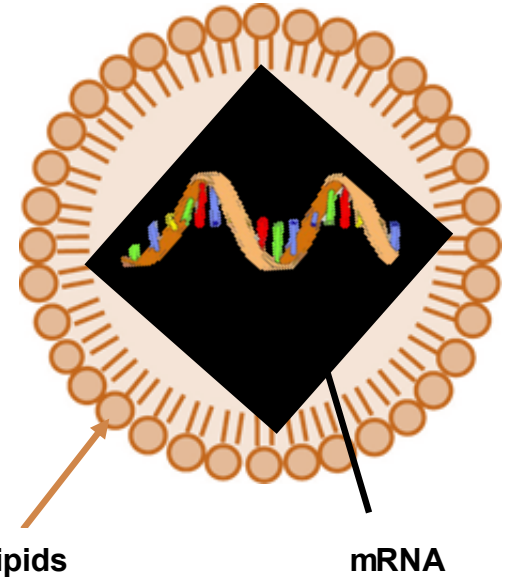
Pfizer and Moderna

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

mRNA Vaccines: Moderna and Pfizer/BioNTech

	Moderna (mRNA-1273)	Pfizer/BioNTech (BNT162b2)
Vaccine components:	mRNA formulated into a lipid nanoparticle (LNP)	mRNA formulated into a lipid nanoparticle (LNP)
Vial Size:	10 doses multi-dose	5 doses multi-dose
Reconstitution:	None needed.	Needs to be reconstituted with normal saline, not bacteriostatic 0.9% sodium chloride injection or any other diluent.
Administration and Dosing:	2 x 0.5 mL doses given IM 28 days apart	2 x 0.3 mL doses given IM 21 day apart
Handling:	Swirl the vial gently between doses, do not shake	Invert gently 10 times to mix. Do not shake.
Freezer Storage:	-20 C (freezer)	-75 C (ultrafreezer)
Transport:	Frozen only: -20 C	Ultrafrozen only: -75 C
Fridge Storage:	30 days at 2-8 C	5 days at 2-8 C

See Module 3 for more details

mRNA Vaccines: Moderna and Pfizer

Updated as of Dec 11 2020

	Moderna	Pfizer
Population of Phase 3 Trials:	Age: 18y+ Size: >30 000 in US, including: • >7 000 65y+ • >8 000 high risk* • >11 000 people of colour*	Age: 12-15y, 16-55y, 56+y Size: 43 000 Globally • 18 000 56-85y • 12 000 racially and ethnically diverse backgrounds
Efficacy Data	*Final Analysis at 196 cases* (185 placebo, 11 vaccine) Data starting from 2 weeks after Dose 2 Primary endpoint: **94.1% vaccine efficacy.** Efficacy in older adults not reported Secondary endpoint: 30 severe cases in study, all in placebo group. One COVID-19 death in study, in the placebo group.	*Final Analysis at 170 cases* (162 placebo, 8 vaccine) Data starting from 1 week after Dose 2 Primary endpoint: **95% vaccine efficacy.** Efficacy in 65y+: >94% Secondary endpoint: 10 severe cases in study, 9 in placebo group.
Safety Data	Median follow-up, ~2 months No serious safety concerns observed	Median follow-up, ~2 months (for 38,000 trial participants). No serious safety concerns observed.

Polack *et al*

*High risk including diabetes, severe obesity and cardiac disease; People of Colour including Hispanic, LatinX, Black or African American

Key Messages for COVID-19 Vaccine Candidates:

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

- *Canada has negotiated agreements in principle to supply vaccine to Canadians with 7 companies using 3 methods of delivering spike protein:*
  - *Protein subunit (including virus-like particle)*
  - *mRNA*
  - *Viral vector*

- *mRNA vaccine technology will be the first to market in Canada.*
  - *These vaccines are given as two doses, spaced 21 or 28 days apart*
  - *Reports have indicated >90% efficacy in preventing COVID-19 disease weeks after second dose (not all data publically available)*
  - *mRNA vaccines require lipid nanoparticle formulation, which means they have special storage temperatures and handling requirements.*

Additional Resources

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

Public Health Agency of Canada

https://www.canada.ca/en/public-health.html