COVID-19 mRNA Vaccines

Mechanism of Action for:

- Moderna COVID-19 Vaccine (mRNA-1273)
- Pfizer BioNTech COVID-19 Vaccine (BNT-162b2)

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UNIVERSITY of WASHINGTON

IDEA INFECTIOUS DISEASES EDUCATION & ASSESSMENT

Acknowledgments and Permission

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  - David Spach, MD (University of Washington) and Cognition Studio, Inc.
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Slides WITH Text

DNA versus RNA

- To understand mRNA vaccines it is important to understand fundamental differences between DNA and RNA
- DNA has two backbone strands whereas RNA usually has only one strand
- DNA functions to encode, store, and replicate genetic information
- RNA coverts the genetic code information contained in the DNA to proteins
- RNA contains the uracil base pair in place of the thymidine base pair used in DNA

Deoxyribonucleic acid (DNA) **Ribonucleic acid (RNA)**

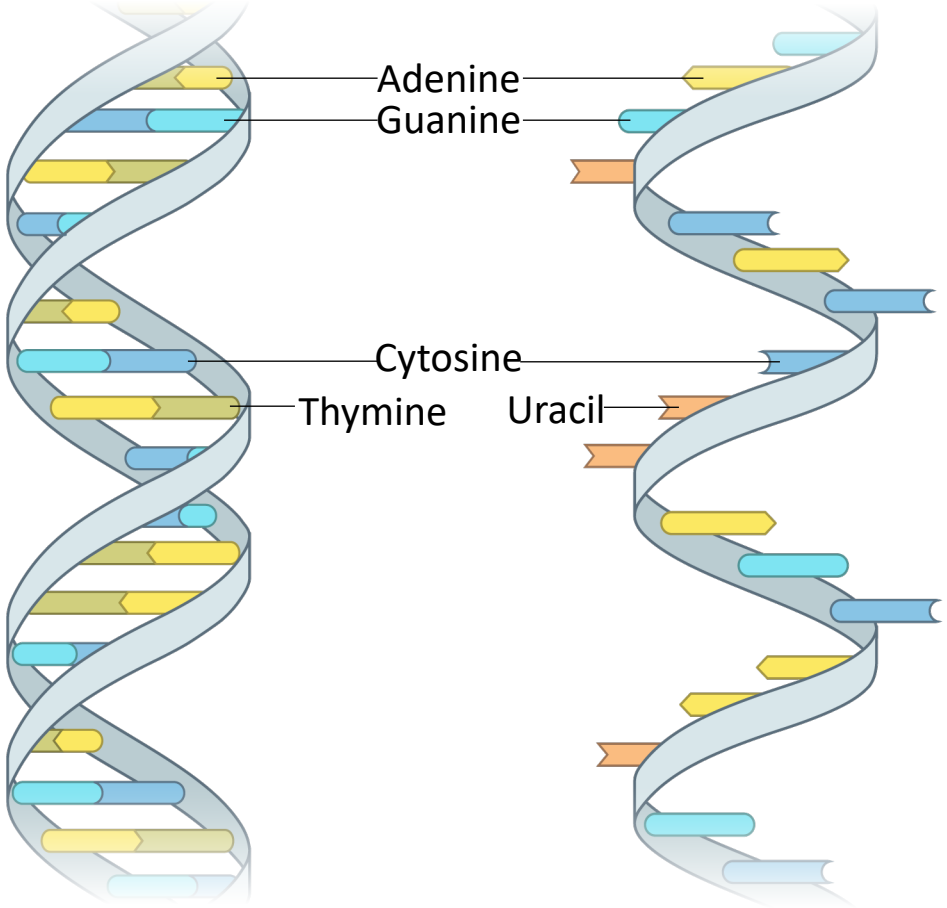


Image credit: Cognition Studio, Inc.

Basic Flow of Genetic Information for Protein Formation in Humans

- In human cells, the flow of genetic information to protein formation is DNA to RNA to protein
- DNA replication is the process whereby identical copies of the original DNA are made and this occurs in the nucleus of the cell
- Transcription occurs in the nucleus and it is the first step in protein synthesis: an RNA copy is made from DNA and the RNA then moves into the host cytoplasm
- Translation is the process by which mRNA is decoded in the process of protein synthesis and this occurs in the cell cytoplasm

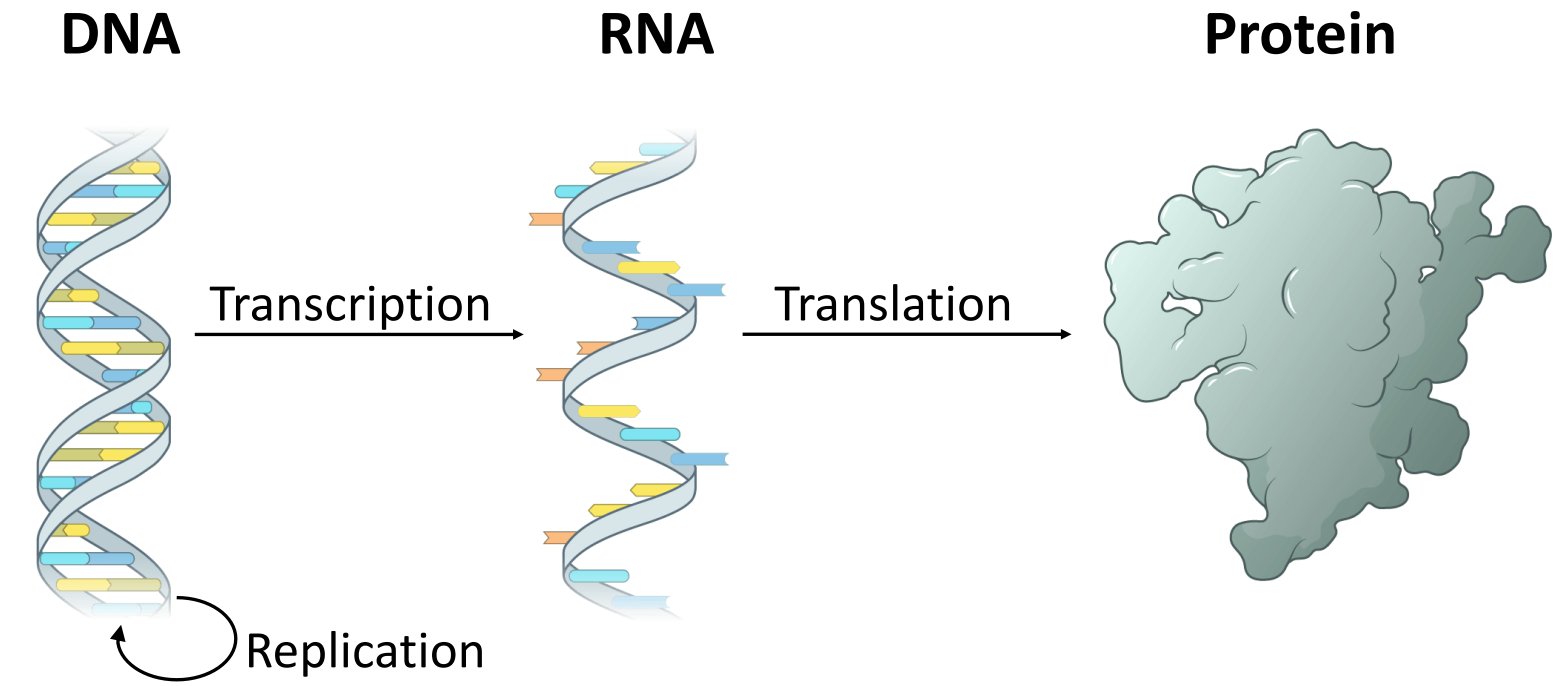
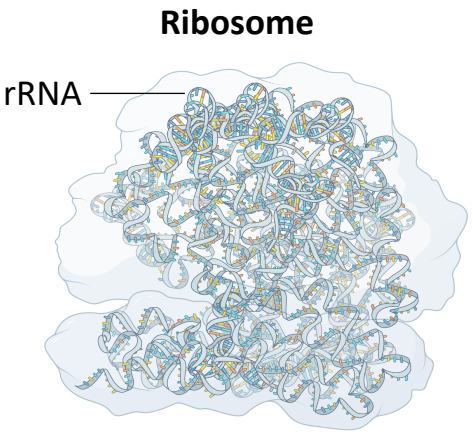


Image credit: Cognition Studio, Inc.

Ribosome Structure and Function

- The ribosome is made up of about 2/3 rRNA and 1/3 proteins
- Each ribosome has a large and small subunit
- The ribosome provides template slots for the sequential addition of the amino acids in the formation of the polypeptide protein precursor
- The ribosome also functions as an enzyme that catalyzes the reaction needed to link amino acids together



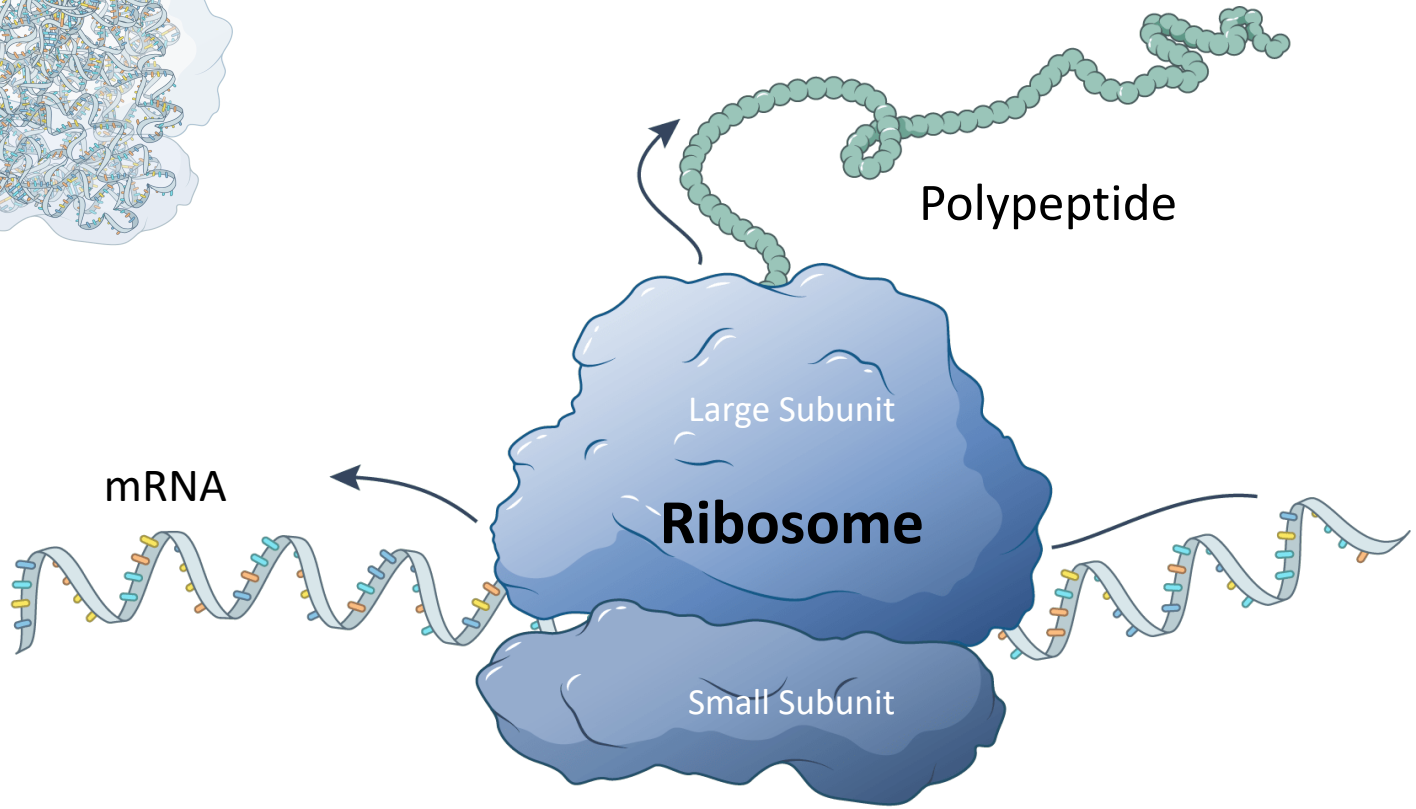
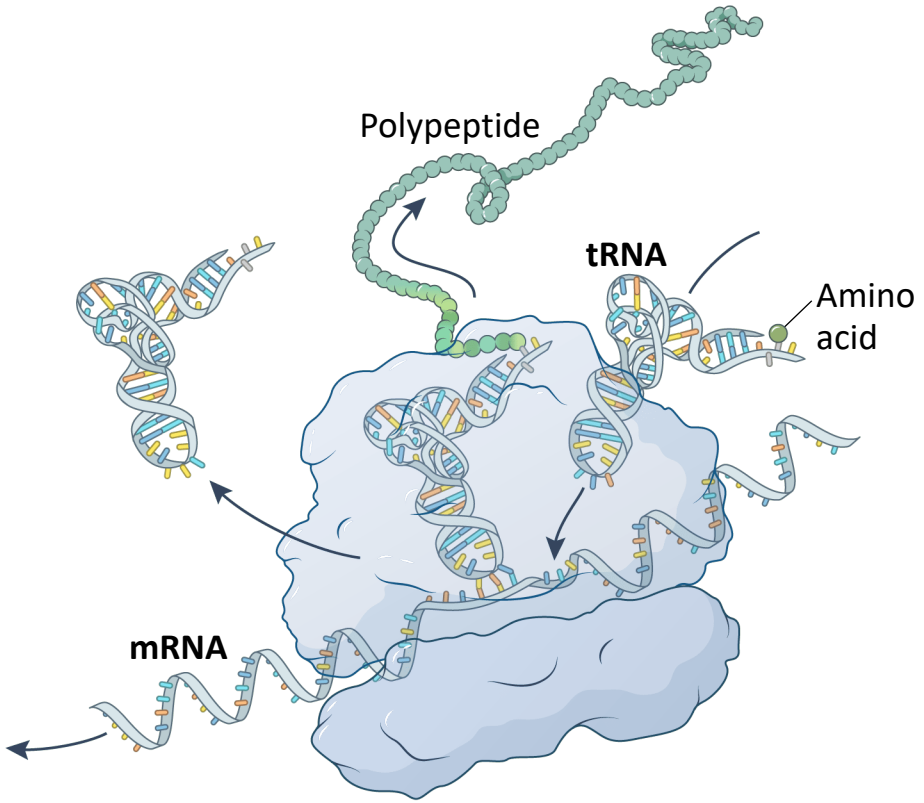


Image credit: Cognition Studio, Inc.

Types of RNA

- The three most common types of ribonucleic acid (RNA) are:
  - messenger RNA (mRNA)
  - transfer RNA (tRNA)
  - ribosomal RNA (rRNA)
- The RNAs play an essential role in protein production
- mRNA carries the genetic information from the nucleus to make proteins in the cytoplasm
- tRNA connects mRNA with the amino acids encoded by the mRNA codon
- rRNA is the main structural functional component of the ribosome and it serves to catalyze reactions



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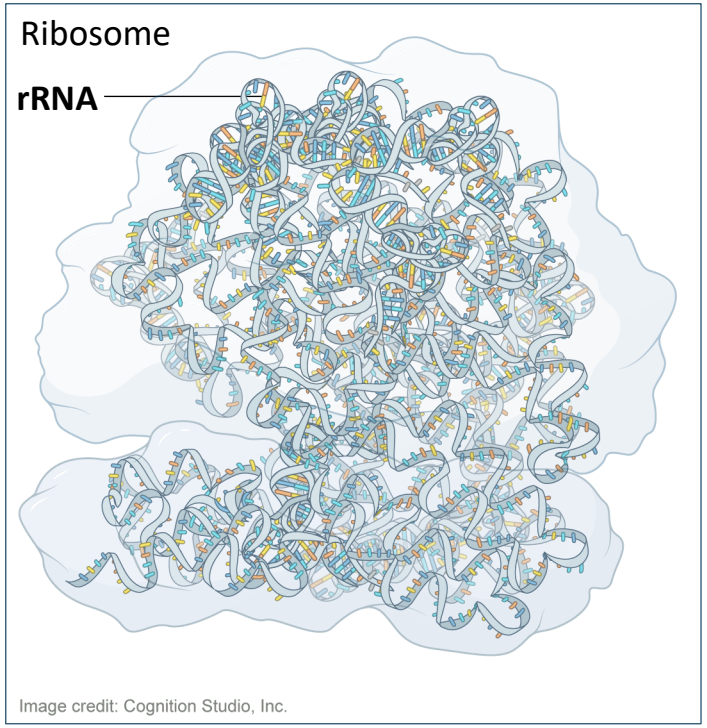
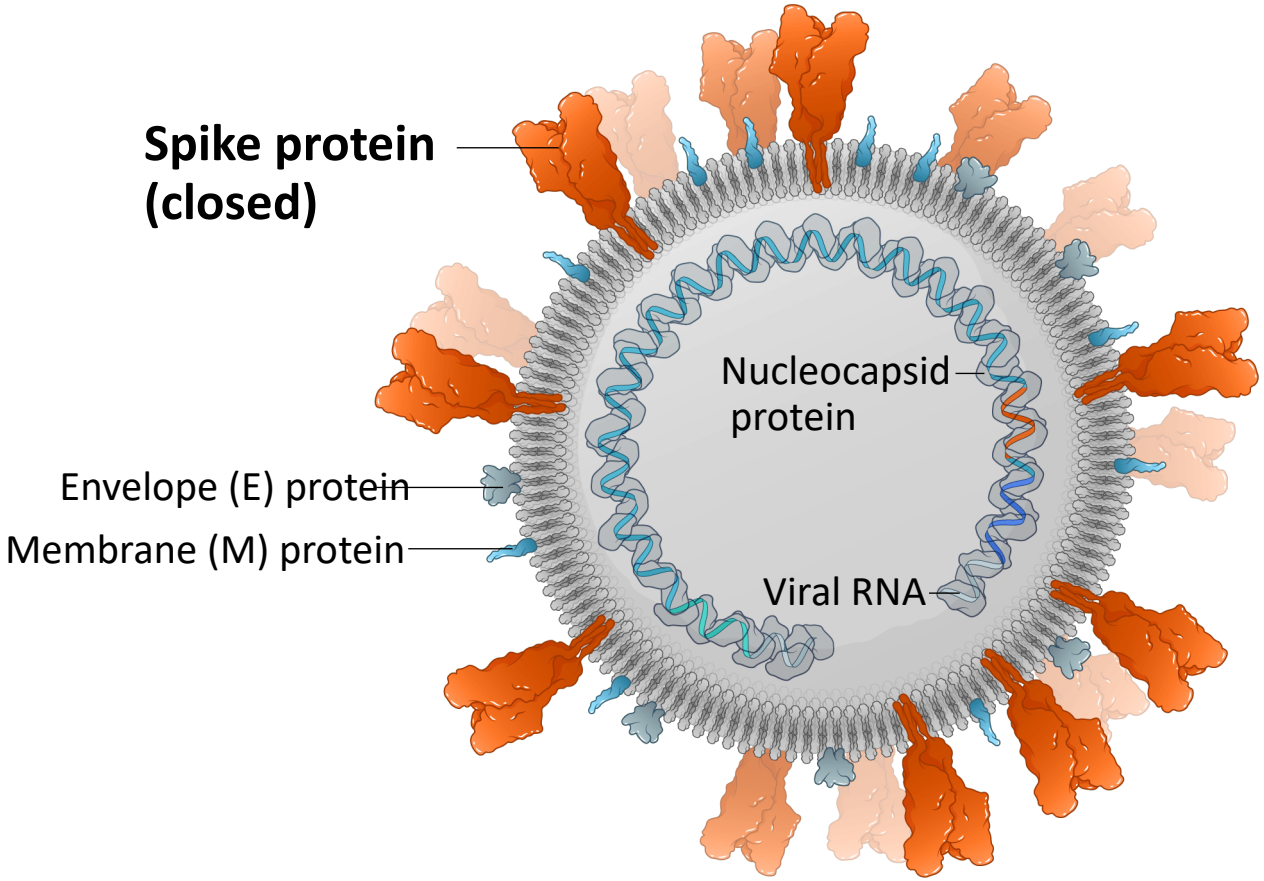


Image credit: Cognition Studio, Inc.

SARS-CoV-2 Virus Structure

- SARS-CoV-2 is a single-stranded RNA enveloped virus
- The spike protein is the major surface protein on SARS-CoV-2 and it plays a key role in binding to the host cell receptors
- The spike protein is the primary target of the host immune response to SARS-CoV-2 infection
- Spike protein is an optimal immunologic target to use for COVID-19 vaccines



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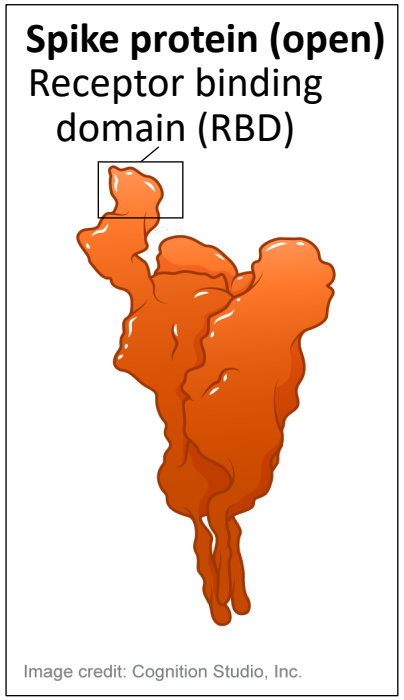

Image credit: Cognition Studio, Inc.

COVID-19 mRNA Vaccines

- COVID-19 mRNA vaccines consist of mRNA surrounded by a lipid nanoparticle (LNP)
- The LNP has two main functions:
  1. Protect the mRNA from being degraded and destroyed
  2. Facilitate cellular uptake of the mRNA
- The coding region (orange) is a genetically engineered sequence of nucleoside modified mRNA that encodes for the prefusion-stabilized SARS-CoV-2 spike protein
- The Cap 5′ and 3′ UTR elements enhance the stability and translation of the mRNA

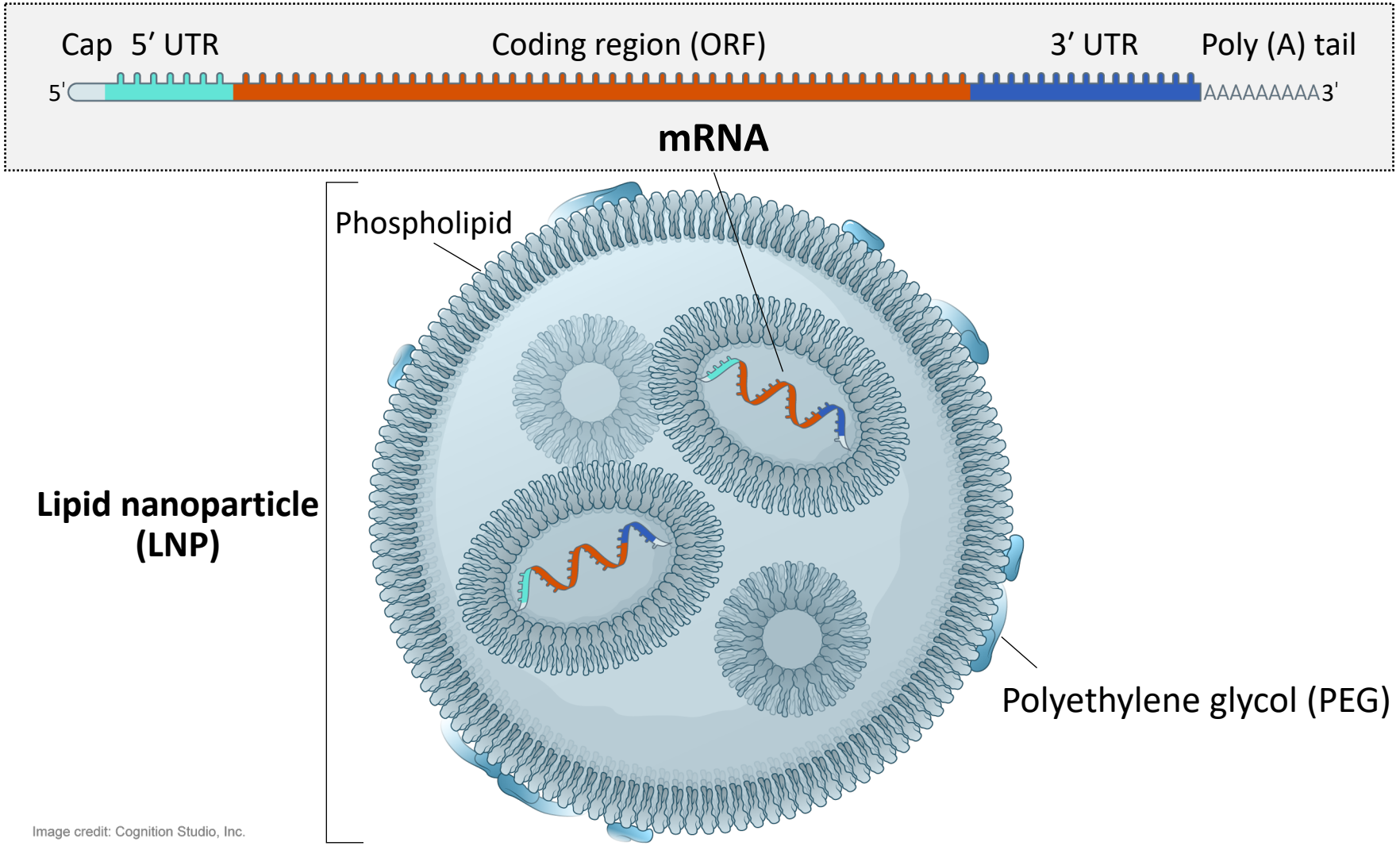

Image credit: Cognition Studio, Inc.

COVID-19 mRNA Vaccines

- This is a simplified view of the lipid nanoparticle (LNP) that surrounds the mRNA
- The LNP has two main functions:
  1. Protect the mRNA from being degraded and destroyed
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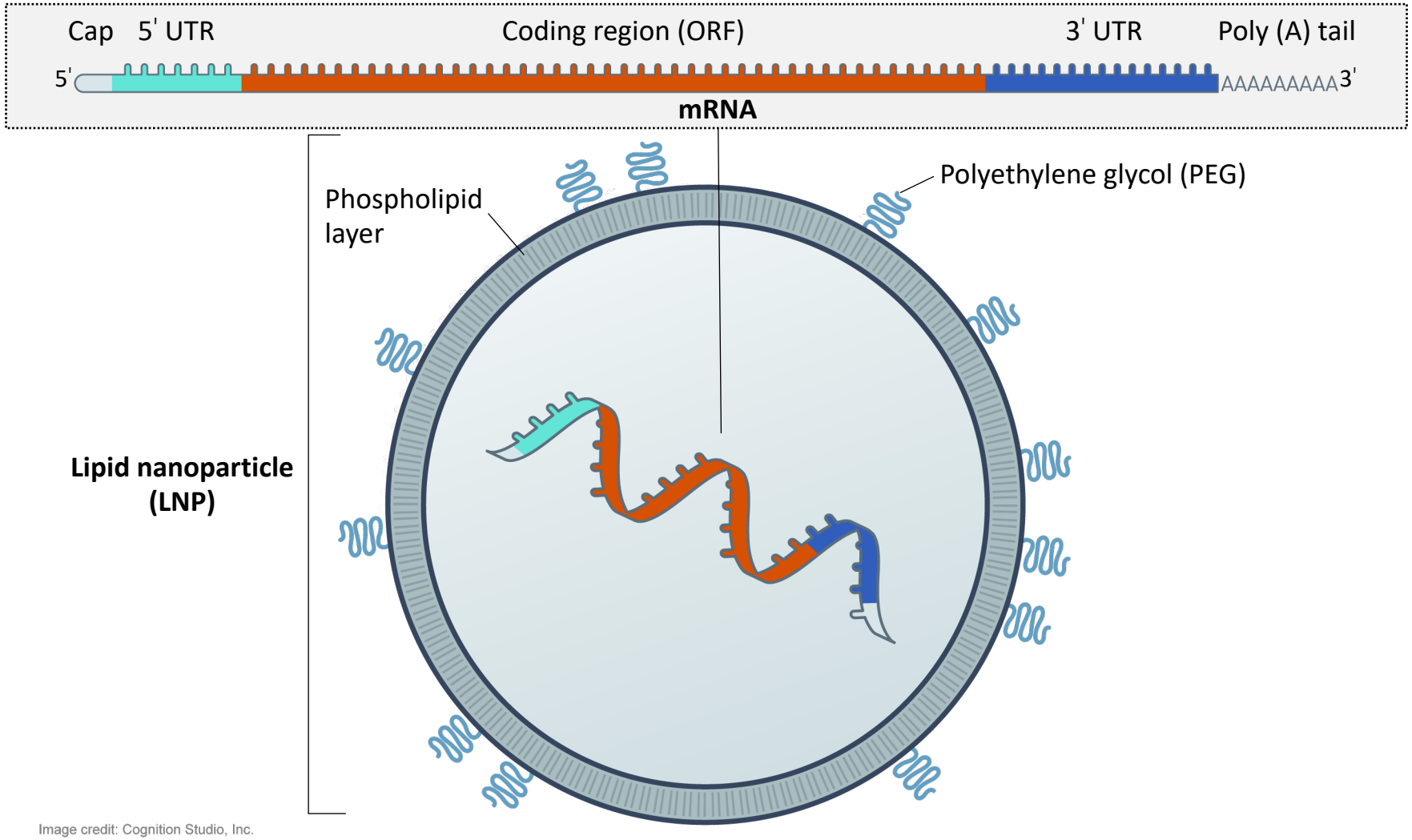
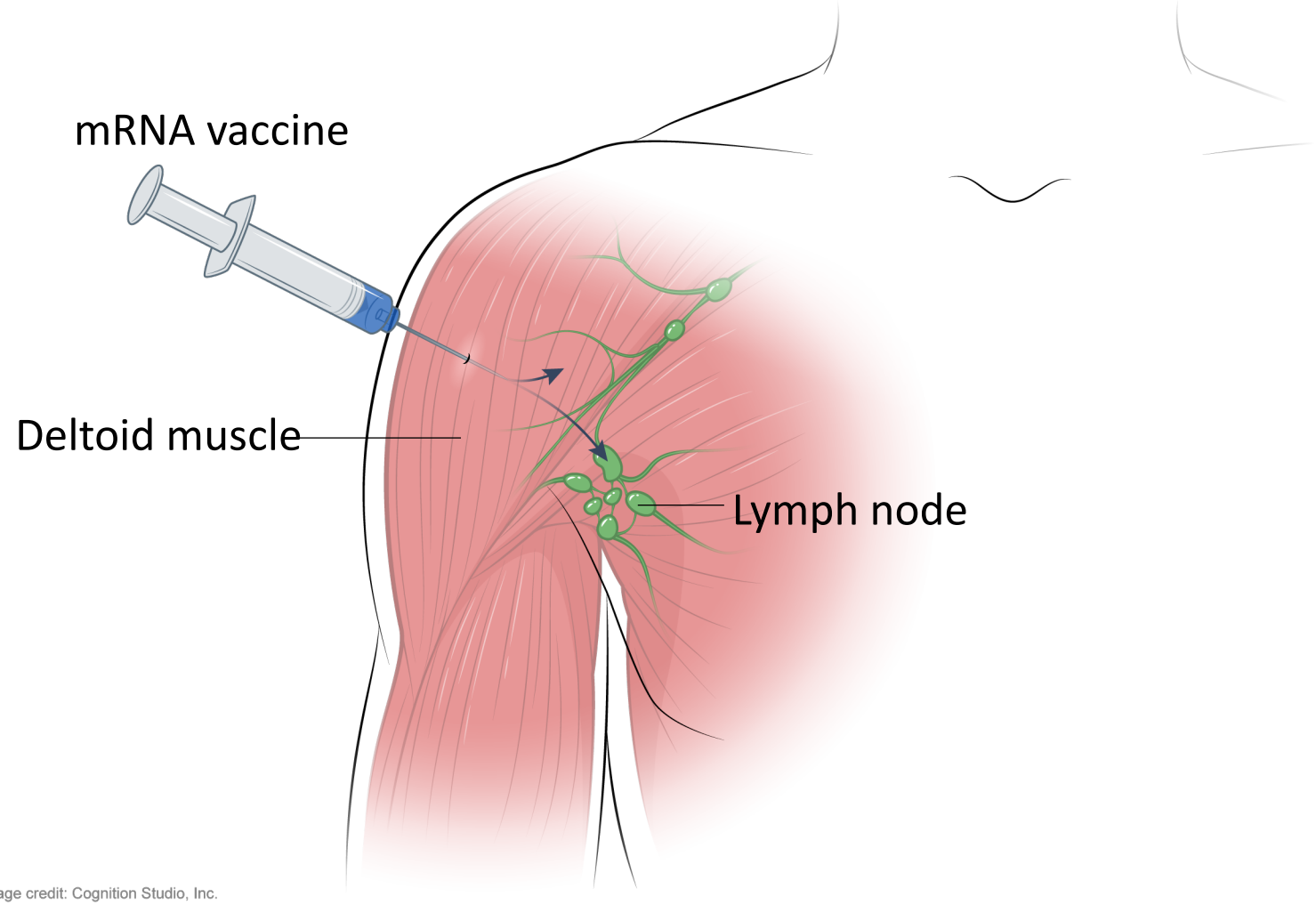


Image credit: Cognition Studio, Inc.

COVID-19 mRNA Vaccine Delivery

- The mRNA vaccines—Moderna COVID-19 Vaccine (mRNA-1273) and Pfizer-BioNTech COVID-19 (BNT-162b2)—are administered as intramuscular injections
- Both of the mRNA vaccines require 2 doses
- Moderna COVID-19 Vaccine
  - Give 2 doses (each 0.5 mL)
  - Give 1 month (28 days) apart
  - Each dose contains 100 µg mRNA
- Pfizer-BioNTech COVID-19 Vaccine
  - Give 2 doses (each dose 0.3 mL)
  - Give 3 weeks (21 days) apart
  - Each dose contains 30 µg mRNA
- The vaccines should not be interchanged



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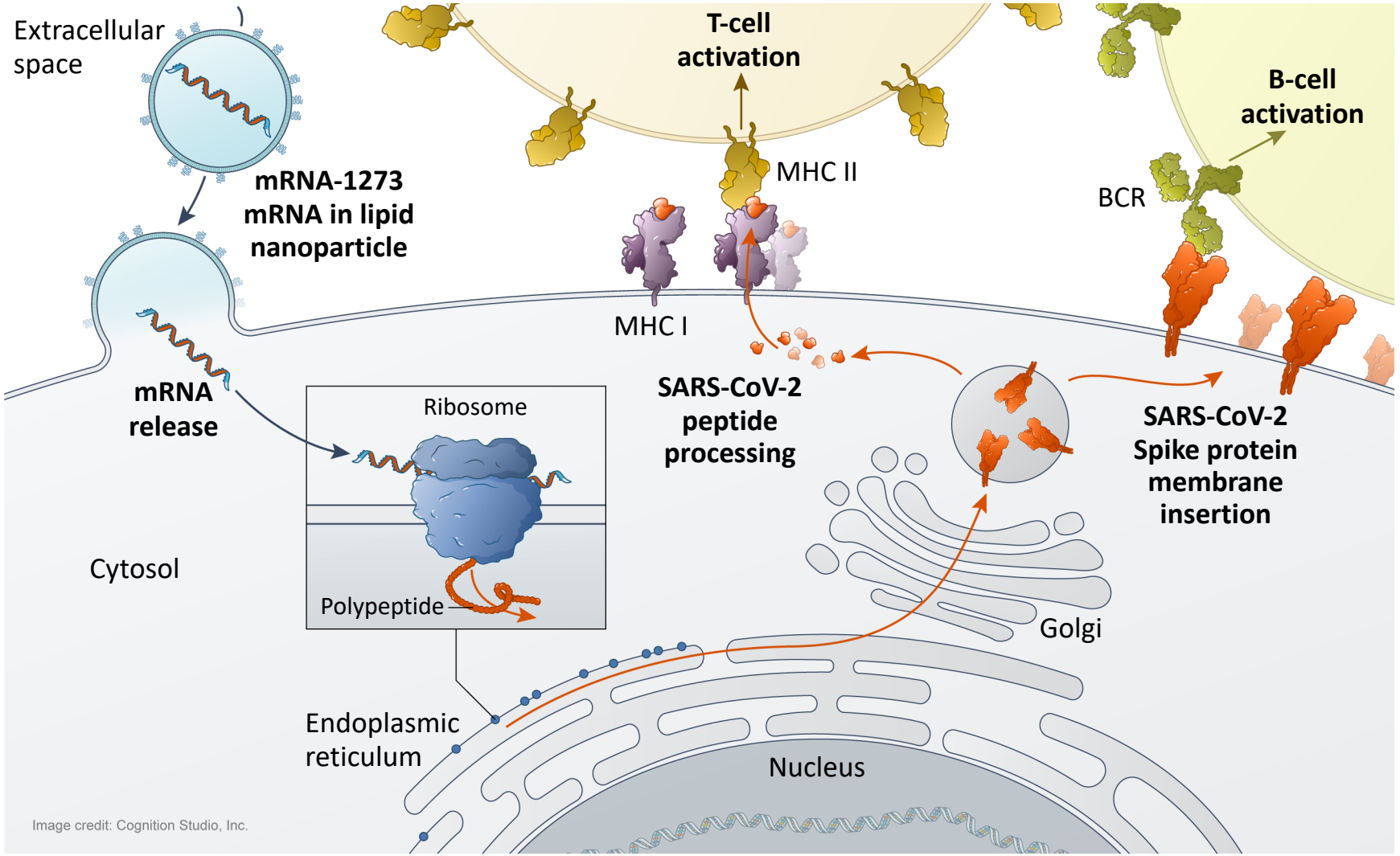
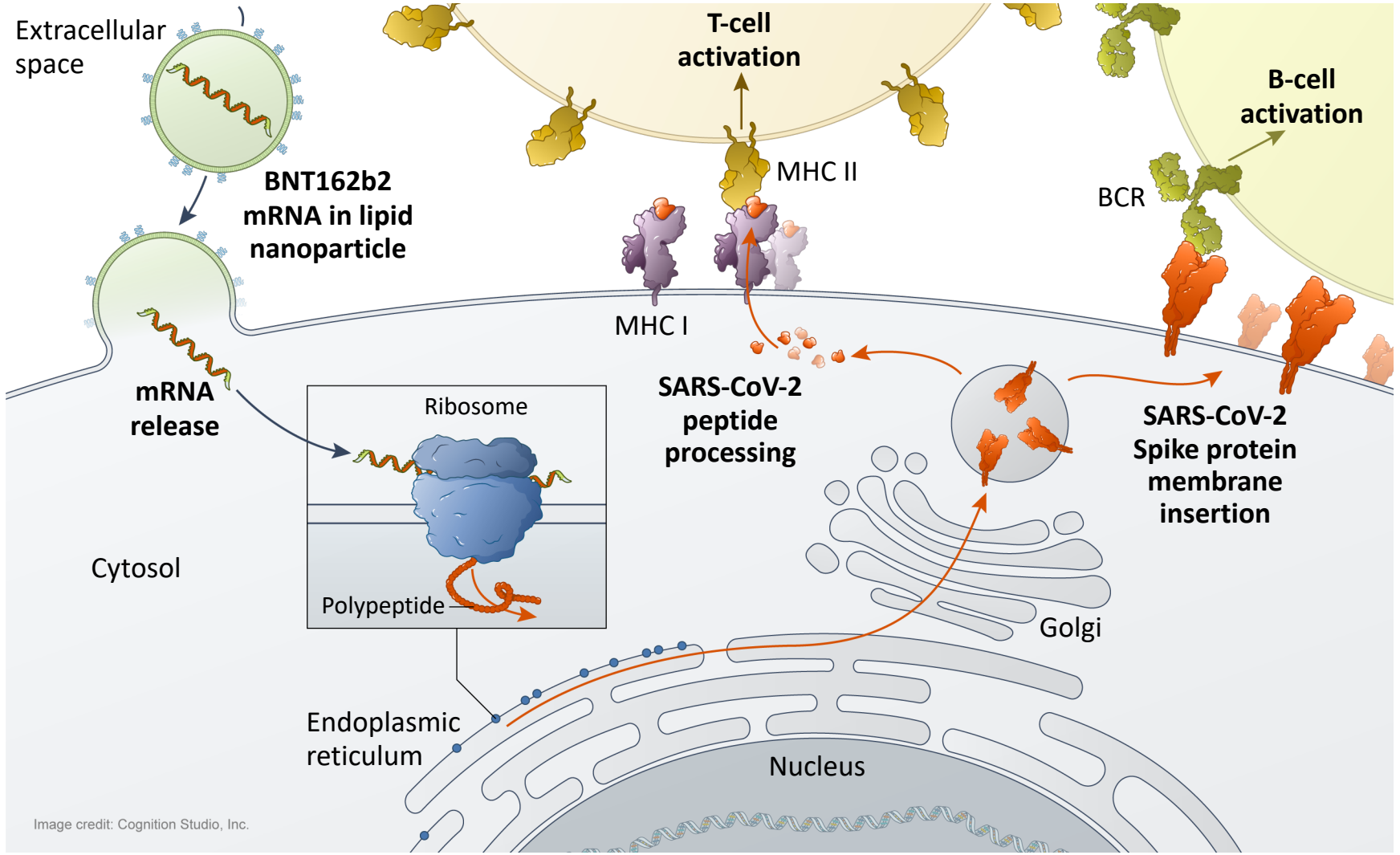
Moderna COVID-19 Vaccine (mRNA-1273): Mechanism of Action

- The mRNA-1273 enters the cell cytoplasm and does not enter the nucleus
- The mRNA is non-replicating and is present transiently within the cell
- The mRNA is translated by the ribosomes to form prefusion-stabilized SARS-CoV-2 spike proteins
- The spike proteins are shuttled to the surface of the cell and are presented to the immune system
- The spike proteins are also processed into small peptides that also are presented to the immune system



Pfizer-BioNTech COVID-19 Vaccine (BNT-162b2): Mechanism of Action

- The BNT-162b2 mRNA enters the cell cytoplasm and does not enter the nucleus
- The mRNA is non-replicating and is present transiently within the cell
- The mRNA is translated by the ribosomes to form prefusion-stabilized SARS-CoV-2 spike proteins
- The spike proteins are shuttled to the surface of the cell and are presented to the immune system
- The spike proteins are also processed into small peptides that also are presented to the immune system



Immune Response to COVID-19 mRNA Vaccines

- The immune system responds to the antigens on the surface of the cell produced by the COVID-19 mRNA vaccines
- The vaccines generate cellular immune responses (T-cell) and and humoral responses (B-cell)
- The immune response includes:
  1. Activation of cytotoxic $CD8^+$ T cells that can destroy cells infected with SARS-CoV-2
  2. Activation of $CD4^+$ T cells that augment both $CD8^+$ T-cell and B-cell responses
  3. Generation of memory T and B cells that can quickly respond to future SARS-CoV-2 infection
  4. Activation of B cells to produce antibodies against SARS-CoV-2

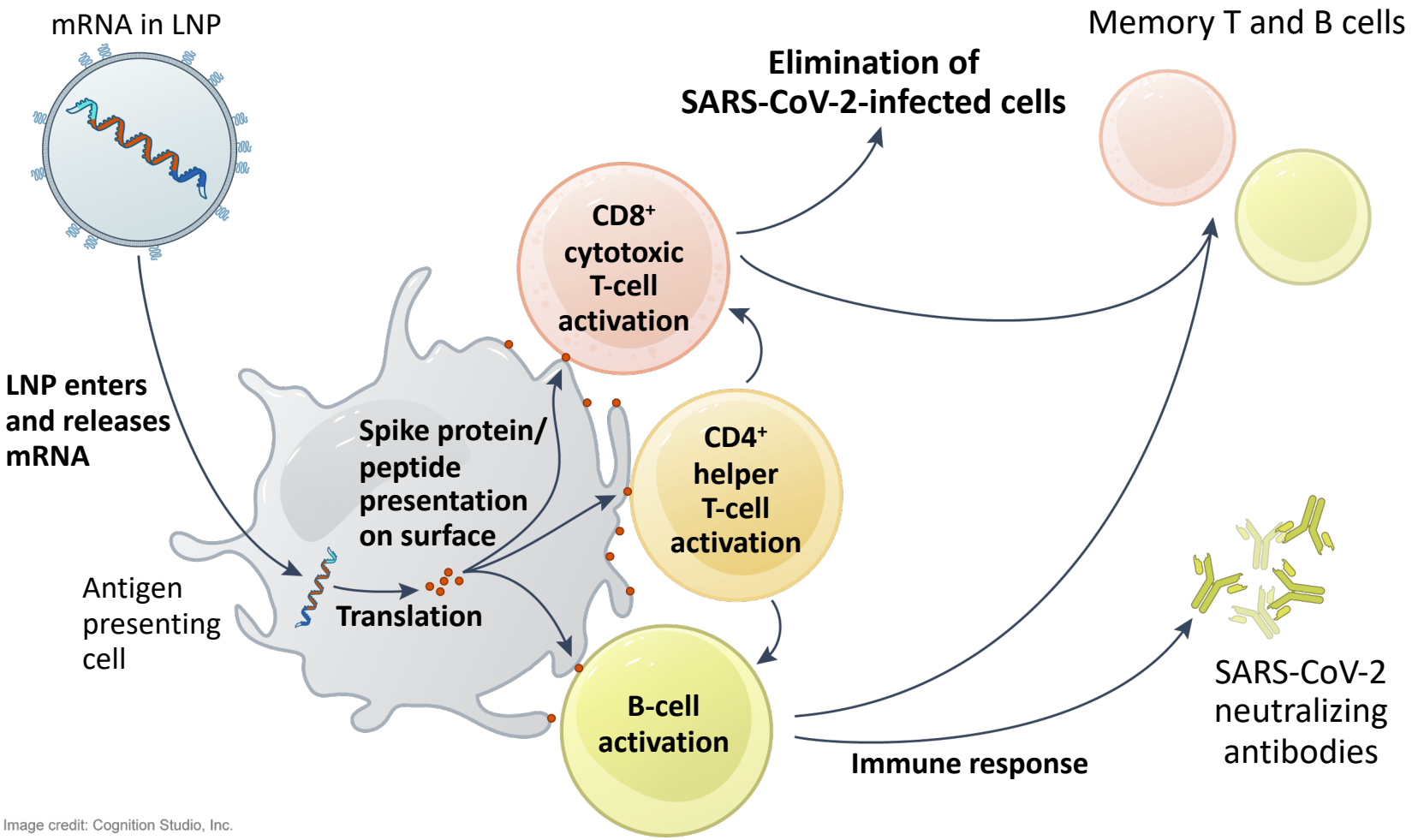


Image credit: Cognition Studio, Inc.

Moderna COVID-19 Vaccine (mRNA-1273)

- **Indication**
  - Investigational (Not approved by U.S. FDA)
  - Authorized for use under an Emergency Use Authorization (EUA) for active immunization to prevent coronavirus disease 2019 (COVID-19) in individuals 18 years of age and older
- **Dosing and Schedule**
  - Administer intramuscularly as a series of two doses (0.5 mL each) 1 month apart
- **Vaccine Storage (See EAU Fact Sheet* for Details)**
  - Multiple-dose vials are stored frozen between -25° to -15°C (-13° to 5°F)
  - Do not store on dry ice or at temperatures below -40°C (-40°F)
  - Vials can be stored refrigerated between 2° to 8°C (36° to 46°F) for up to 30 days prior to first use
  - Store in original carton to protect from light
  - Unpunctured vials may be stored between 8° to 25°C (46° to 77°F) for up to 12 hours
  - After first dose withdrawn, keep vial between 2° to 25°C (36° to 77°F) and discard vial after 6 hours and do not refreeze

*Moderna COVID-19 Vaccine Fact Sheet (https://www.fda.gov/media/144637/download)

Pfizer-BioNTech COVID-19 Vaccine (BNT-162b2)

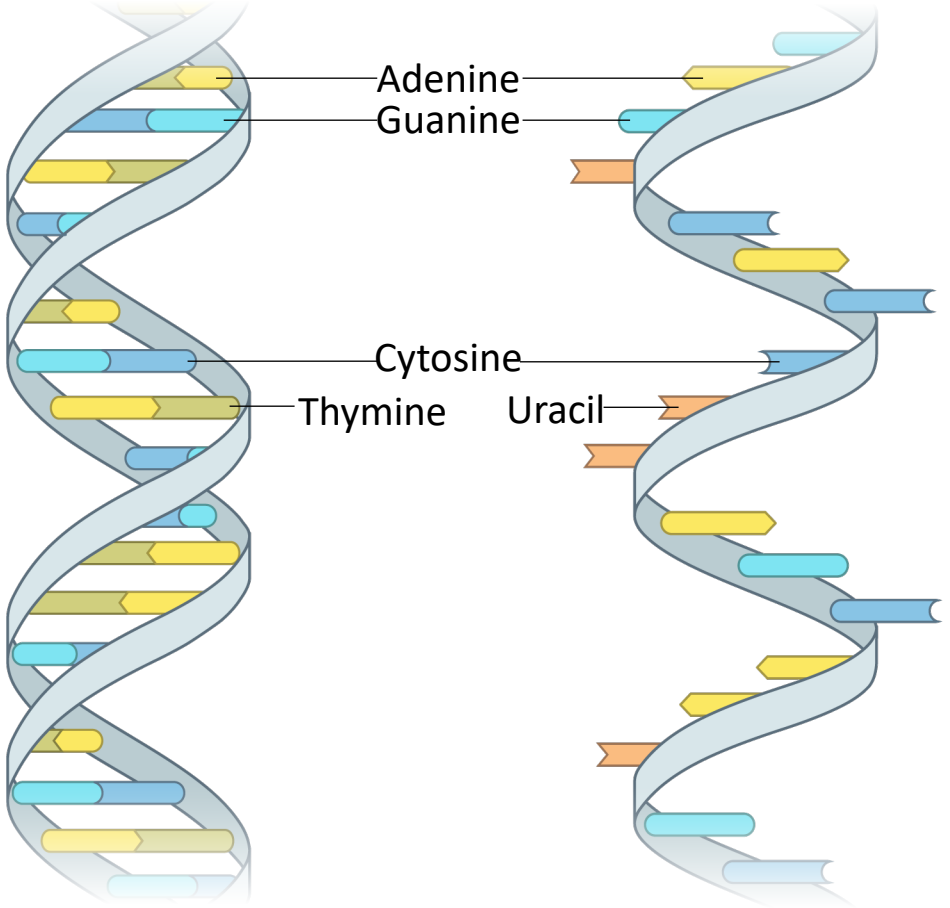
- **Indication**
  - Investigational (Not approved by U.S. FDA)
  - Authorized for use under an Emergency Use Authorization (EUA) for active immunization to prevent coronavirus disease 2019 (COVID-19) in individuals 16 years of age and older.
- **Dosing and Schedule**
  - Administer intramuscularly as a series of two doses (0.3 mL each) 3 weeks apart
- **Vaccine Storage (See EAU Fact Sheet* for Details)**
  - Cartons arrive in thermal containers on dry ice
  - Thermal container maintains a temperature range of -90°C to -60°C (-130°F to -76°F)
  - Vials require storage in ultra-low temperature freezer at -80°C to -60°C (-112°F to -76°F)
  - Vials require protection from light until ready to use
  - Thaw and store undiluted vials in refrigerator at 2°C to 8°C (35°F to 46°F)] for up to 5 days (120 hours)
  - For immediate use, thaw undiluted vials at room temperature [up to 25°C (77°F)] for 30 minutes
  - After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use ≤6 hours from time of dilution; do not refreeze

*Pfizer-BioNTech COVID-19 Vaccine Fact Sheet (https://www.fda.gov/media/144413/download)

Slides WITHOUT Text

DNA versus RNA

Deoxyribonucleic acid (DNA) **Ribonucleic acid (RNA)**



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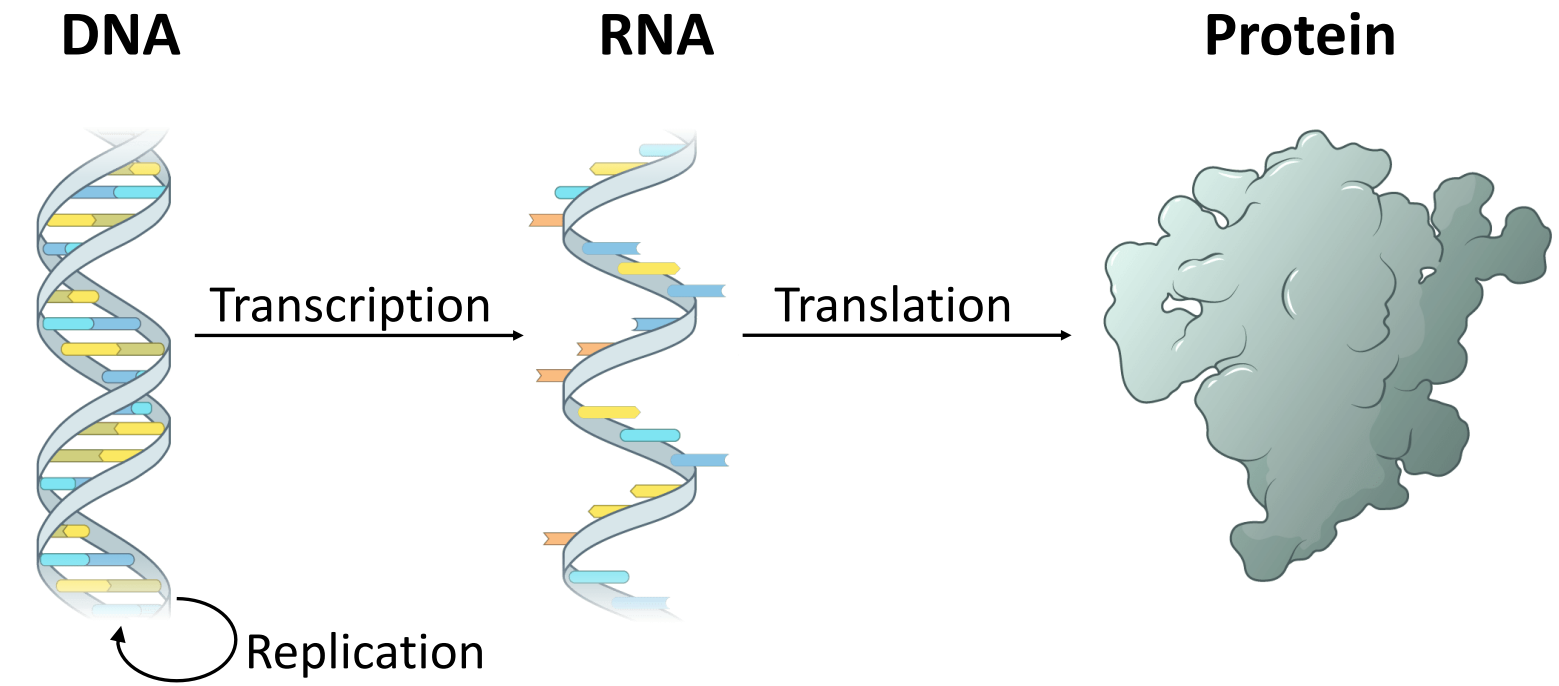

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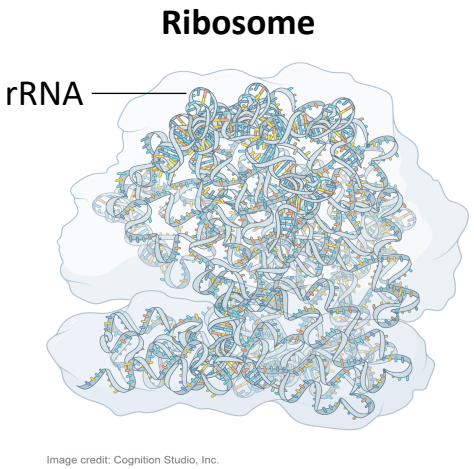
Ribosome Structure and Function



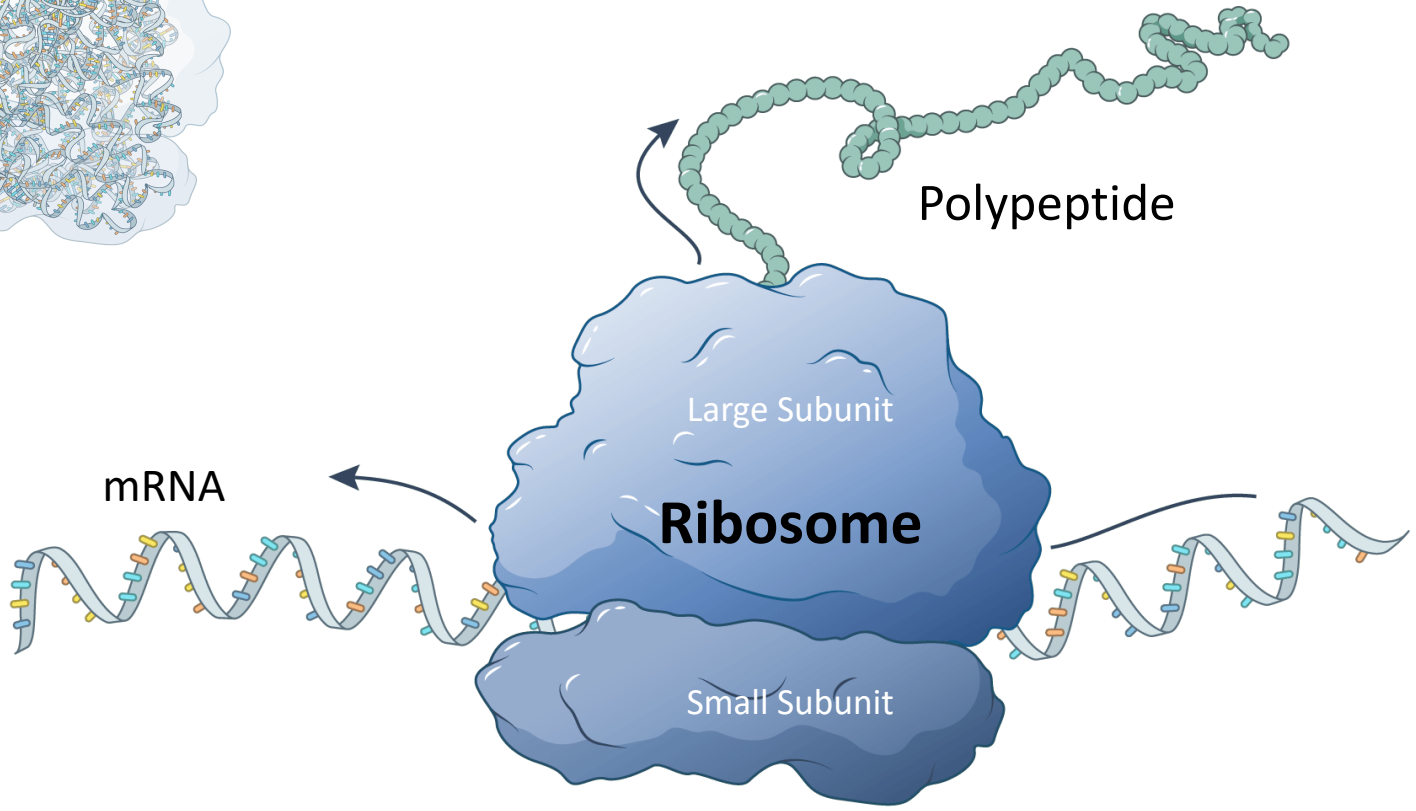
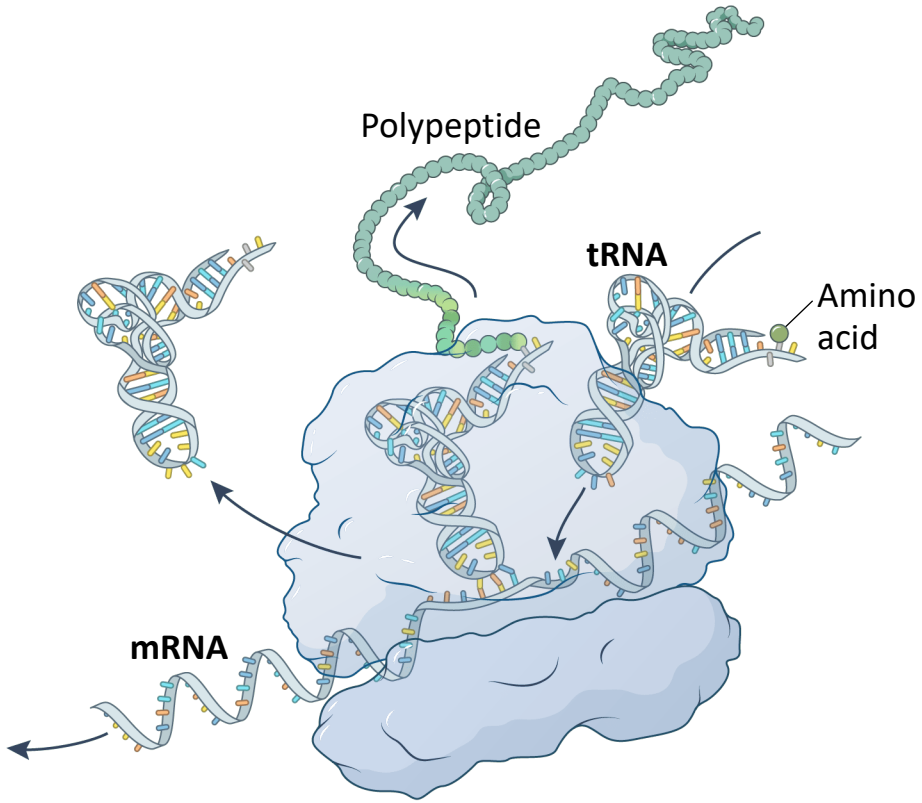


Image credit: Cognition Studio, Inc.

Types of RNA



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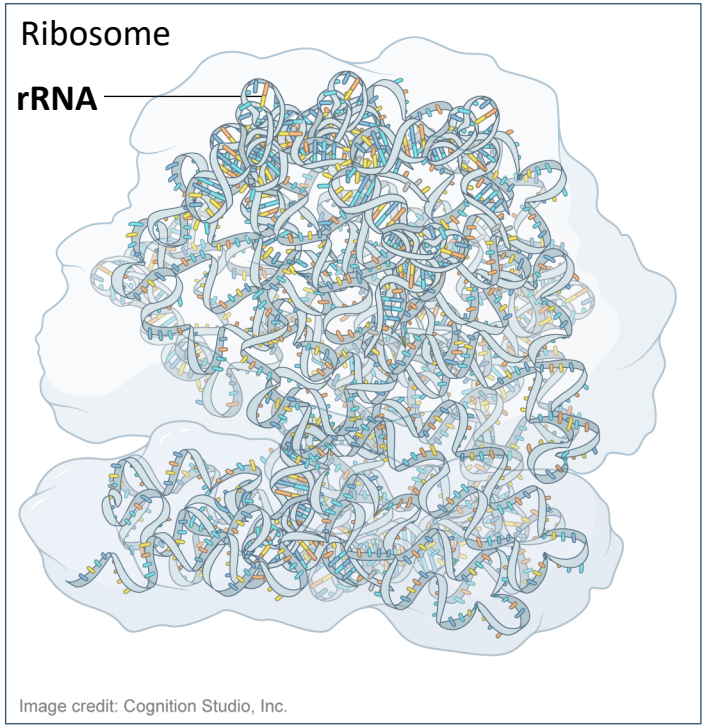

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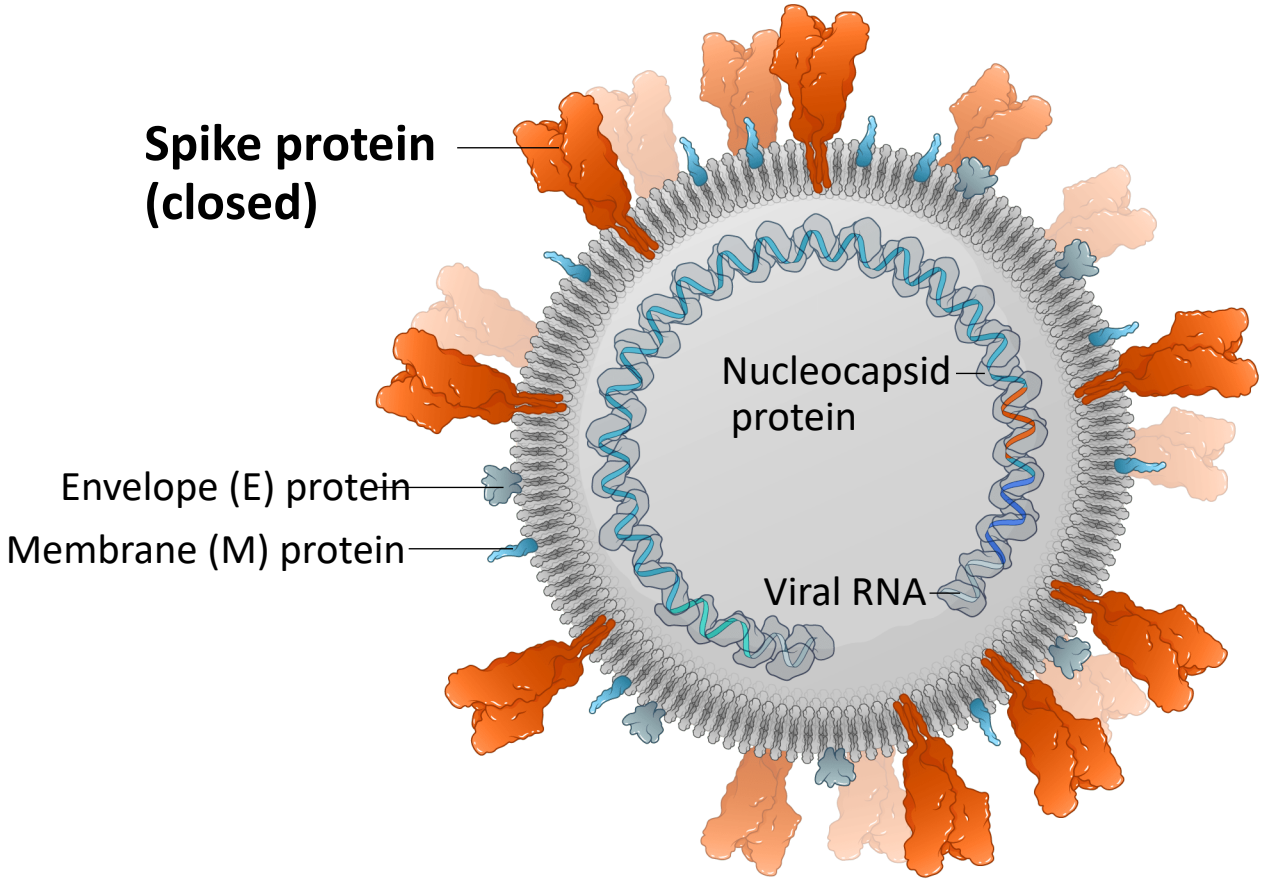
SARS-CoV-2 Virus Structure



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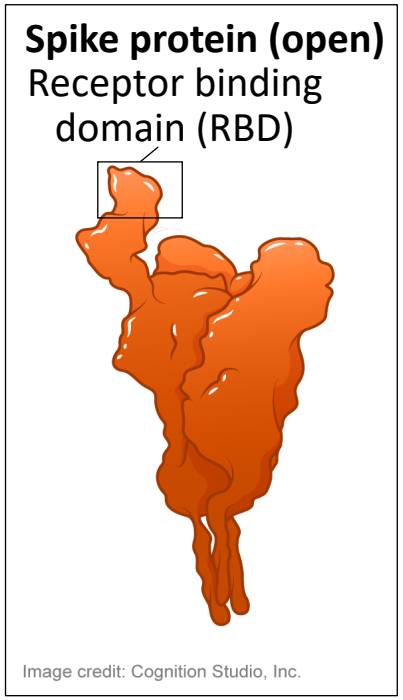

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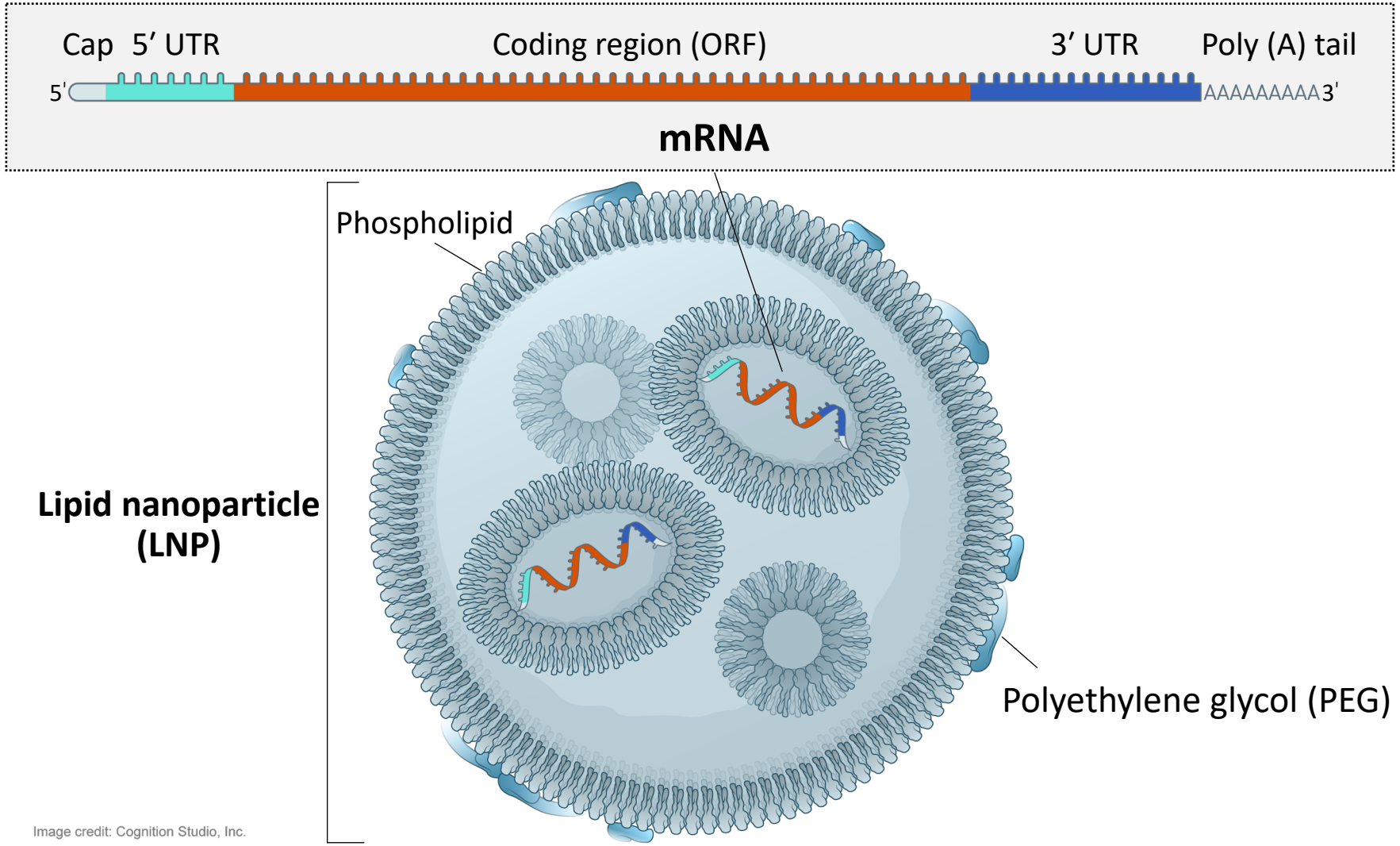
COVID-19 mRNA Vaccines



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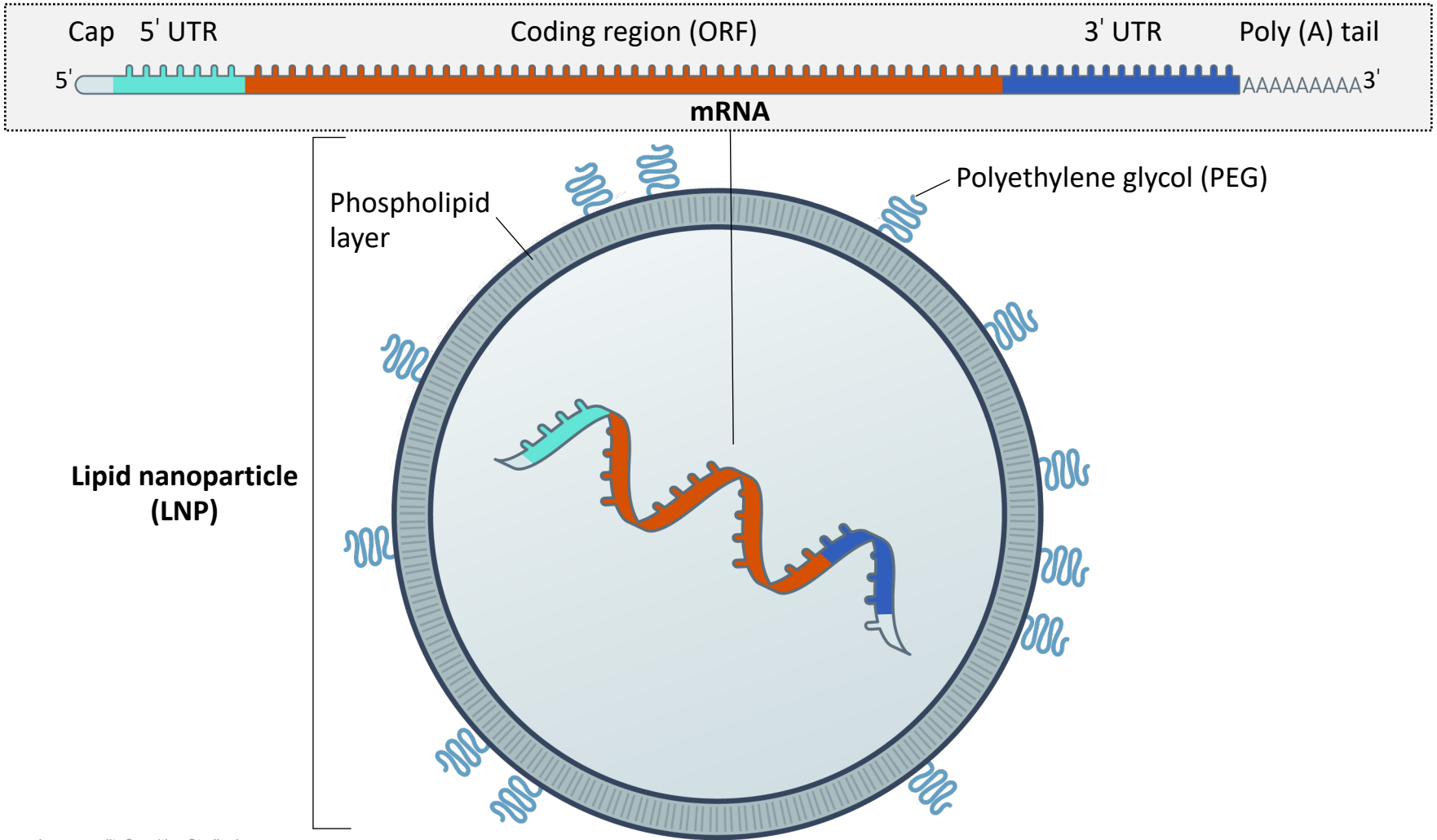

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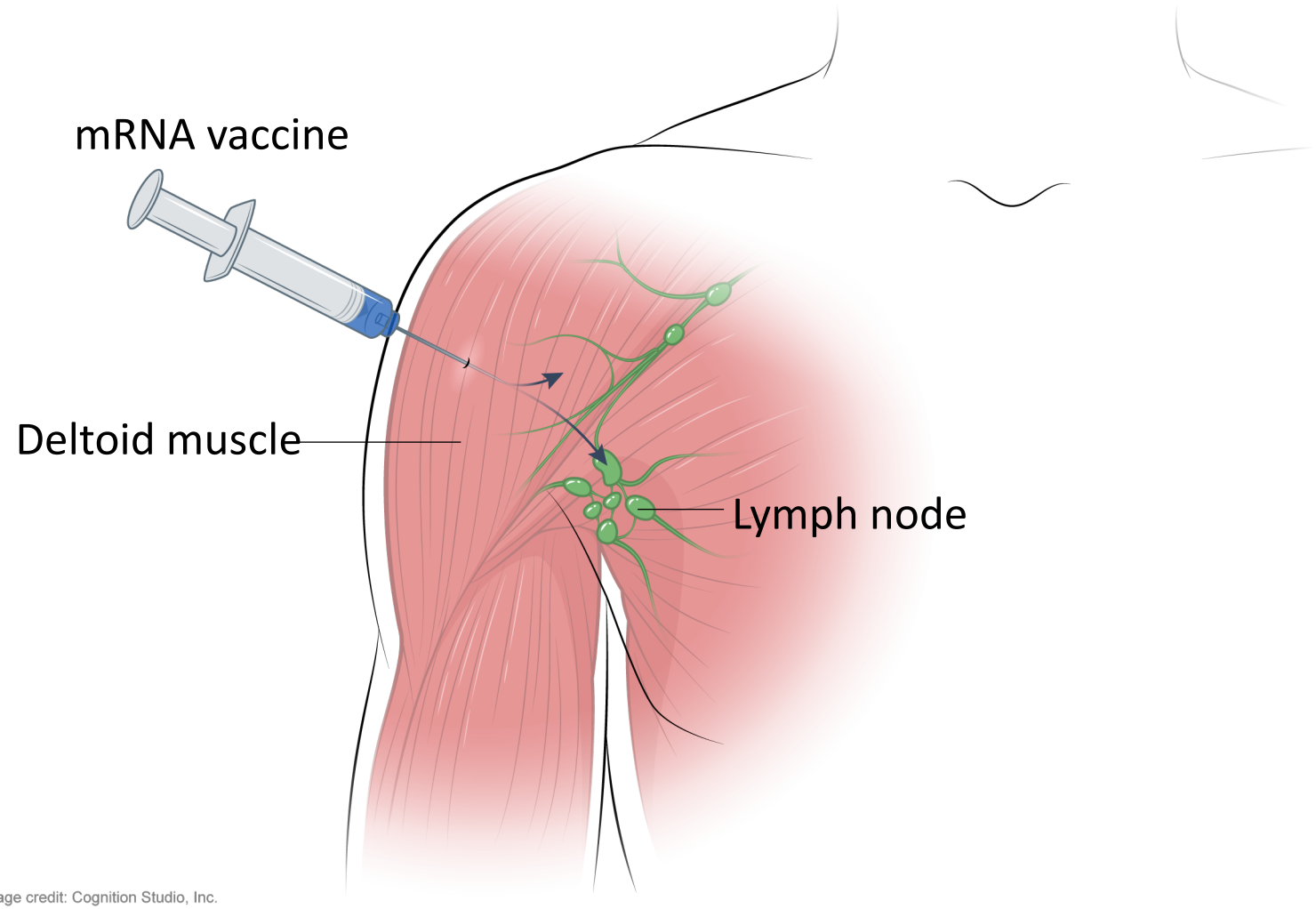
COVID-19 mRNA Vaccine Delivery



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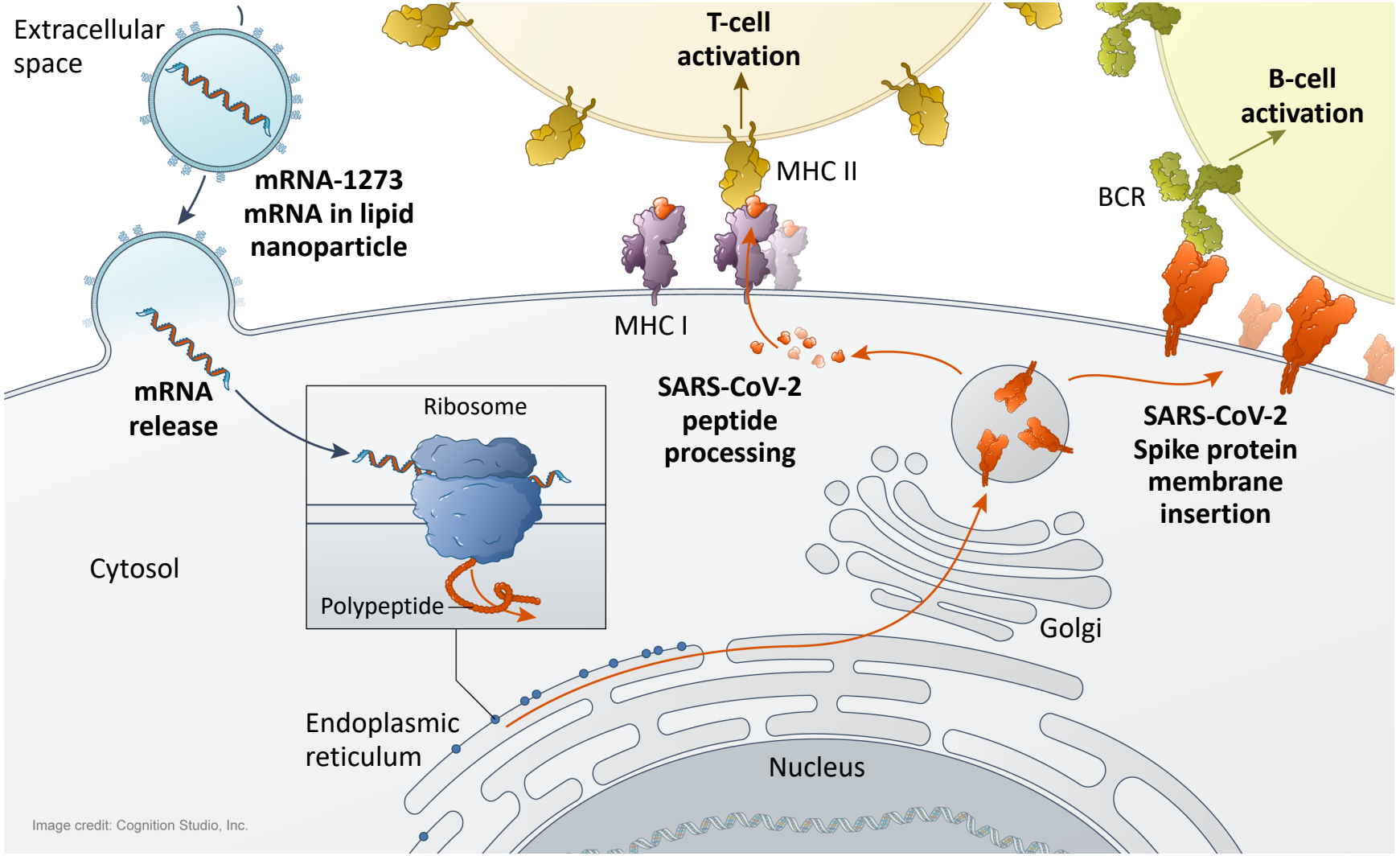
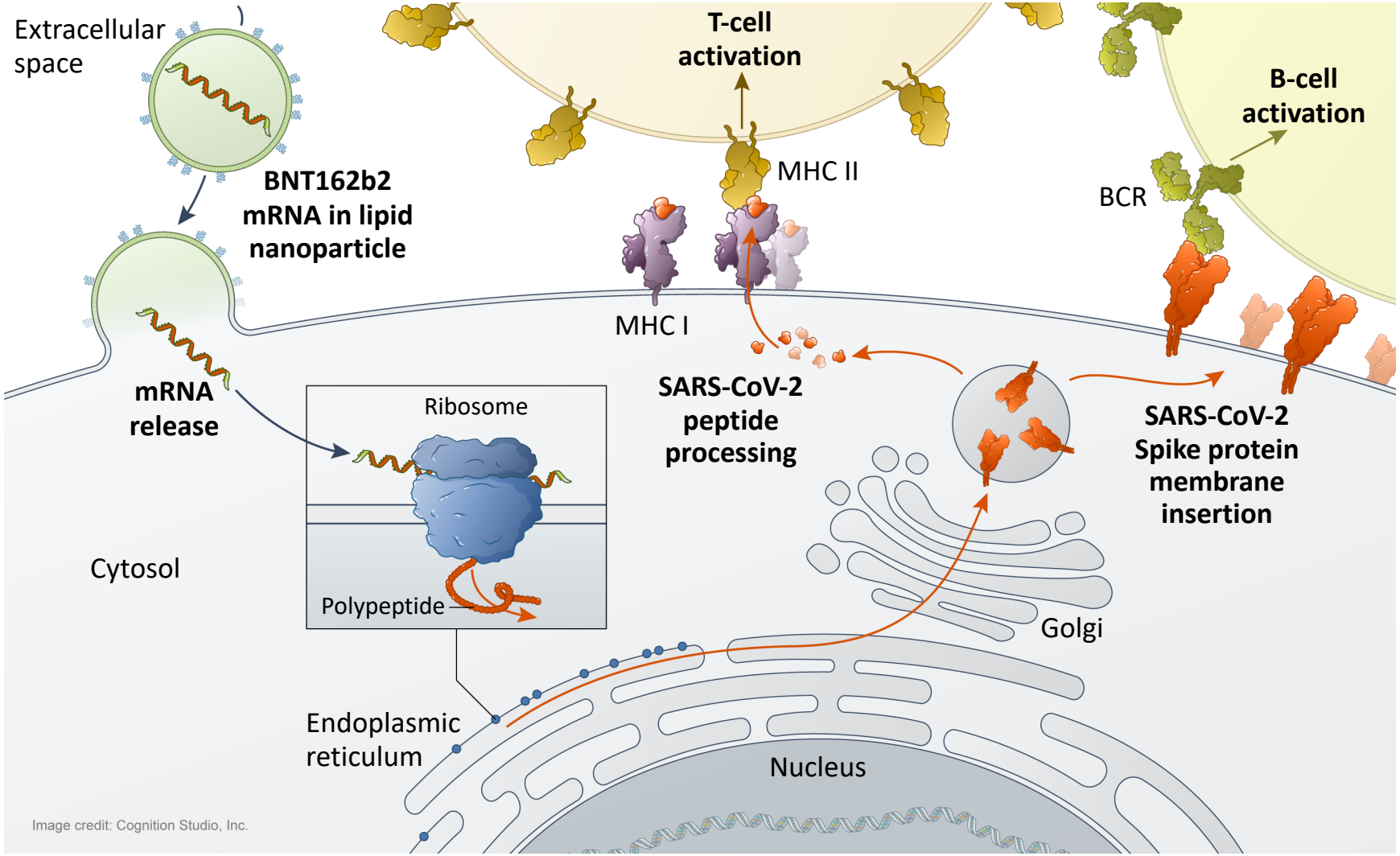
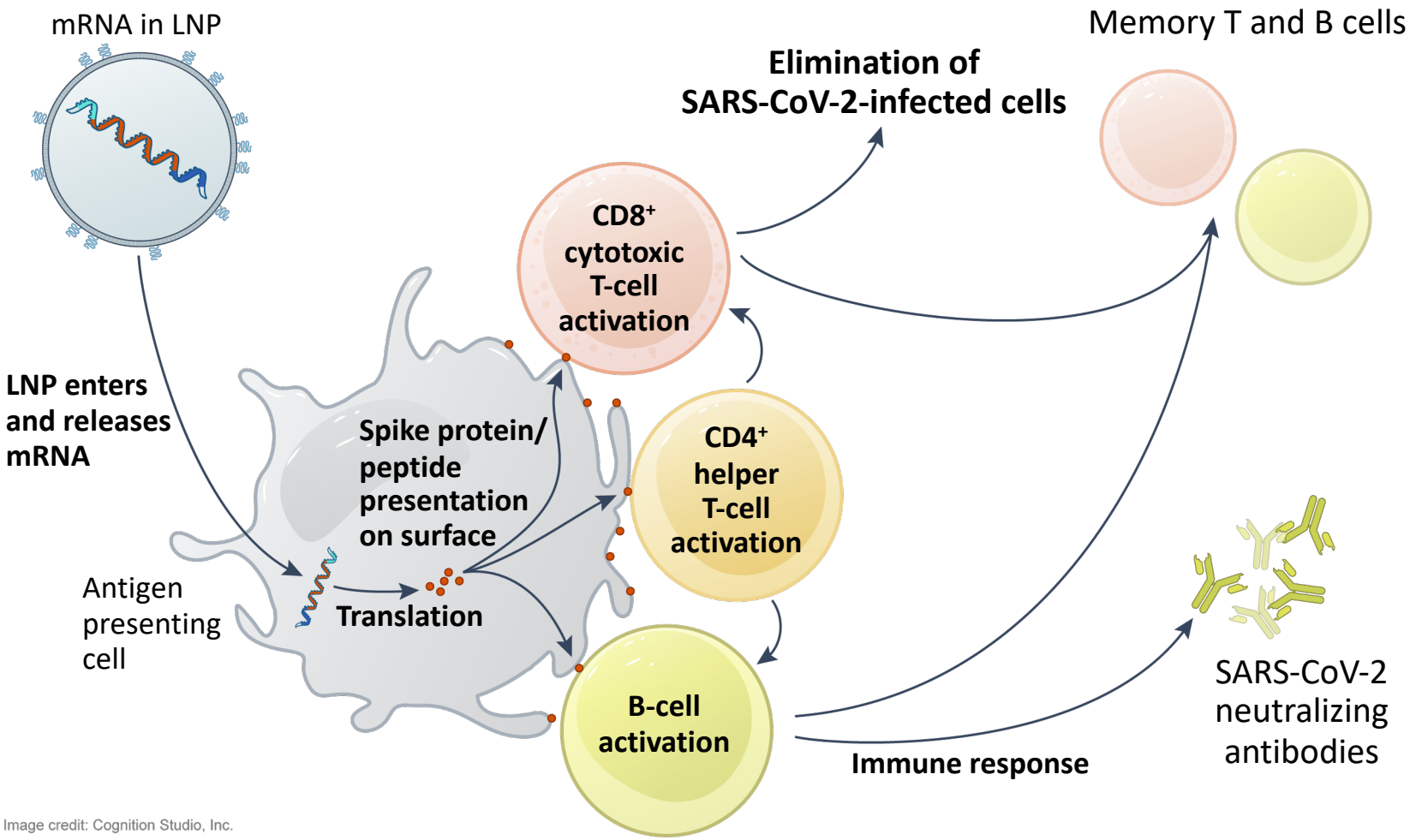
Moderna COVID-19 Vaccine (mRNA-1273): Mechanism of Action



Pfizer-BioNTech COVID-19 Vaccine (BNT162b2): Mechanism of Action



Immune Response to COVID-19 mRNA Vaccines



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*Source: Moderna COVID-19 Vaccine Fact Sheet for Health Care Providers (https://www.fda.gov/media/144637/download)

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*Source: Pfizer-BioNTech COVID-19 Vaccine Fact Sheet (https://www.fda.gov/media/144413/download)