National Center for Competency Testing

Messenger RNA (mRNA) Vaccines

COURSE DESCRIPTION

A new vaccine technology has emerged that uses messenger RNA (mRNA) to elicit an immune system response against an undesired pathogen. This helps to prevent disease with that pathogen later. What is messenger RNA (mRNA)? How do mRNA vaccines differ from traditional vaccine technologies, such as protein subunit, inactivated, and live attenuated virus vaccines? This CE course answers these questions and also describes, in non-technical language, DNA's transcription into mRNA and translation into the proteins from which our bodies are built.

Valid for P.A.C.E.® credit through 12/31/2022

* ASCLS P.A.C.E.® is an approved continuing education agency by the California Department of Health Laboratory Field Services, Accrediting Agency #0001.

*NCCT is approved as a provider of continuing education programs in the clinical laboratory sciences by the ASCLS P.A.C.E.® Program, provider #122.

Ver 1

December 2020

COURSE TITLE: Messenger RNA (mRNA) Vaccines

Author: Tami J. Maffitt, MLS(ASCP)^{CM}
Director, Recertification
National Center for Competency Testing

Number of Clock Hours Credit: **1.0** (determined by P.A.C.E.®)
Course # 1220121
Level of Instruction: Advanced
P.A.C.E. ® Approved: X Yes __ No

OBJECTIVES

Upon completion of this continuing education course, the professional should be able to:

1. Name where DNA is found within the body.
2. Describe the components of DNA and its structure.
3. List the types of nucleotides found in DNA and identify complementary base pairs.
4. Define “gene” and discuss what a gene sequence is.
5. List the steps required for a gene to become a protein.
6. Describe the goal of DNA transcription and identify the enzyme primarily involved in this process.
7. Explain where transcription occurs in the cell.
8. Define mRNA and its purpose.
9. Compare the similarities and differences between DNA and mRNA.
10. Describe the goal of mRNA translation and identify the cellular structure that performs this action.
11. Define codon, amino acid, and polypeptide.
12. Explain how a codon is interpreted by a ribosome.
13. Interpret a codon and assign its corresponding amino acid.
14. Discuss how a virus normally affects the cells it infects and how a virus causes disease.
15. Describe the methodology behind mRNA vaccines and explain how the steps needed for protein translation are fewer than in a real viral infection.
16. List at least three types of immune responses that are expected to be triggered by an mRNA vaccine.
17. Describe the specific methodology behind the mRNA vaccines against the SARS-CoV-2 virus and why they don’t cause an infection with the virus.
18. Explain how an mRNA vaccine would protect against COVID-19.
19. Compare and contrast mRNA vaccines with traditional vaccine types.

INTRODUCTION

A vaccine technology has emerged that uses molecules called messenger RNA (mRNA) to elicit an immune system response against an undesired pathogen. Some of the vaccines currently becoming available to fight COVID-19 utilize this mRNA technology.

Since the technology is new, many individuals have questions about how these mRNA vaccines work. What is messenger RNA (mRNA)? How do mRNA vaccines differ from traditional vaccine technologies, such as protein subunit, inactivated/killed, and live attenuated virus vaccines? This CE course answers these questions and also describes, in non-technical language, DNA, DNA's transcription into mRNA, and mRNA's translation into the proteins that build our bodies. These concepts are vital to understanding the mRNA vaccine mechanism of action.

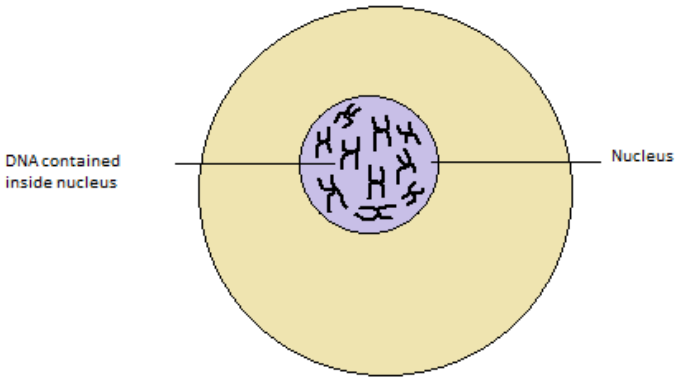
DNA

Deoxyribonucleic acid, or DNA, is a long, chain-like molecule that is comprised of substances called nucleotides. But more generally, and more importantly, **DNA is the genetic code that makes up all living things**. This DNA coding system is shared across all organisms on earth.

WHERE IS DNA FOUND?

DNA is found inside of the nucleus of all nucleated cells in every organism. In humans, nucleated cells include skin cells, tissue cells, muscle cells, white blood cells, gametes (sperm and egg cells), and many others; in fact, almost all cells of the body are nucleated. This means that almost every cell that makes up an individual's body carries their entire personal genetic code within it. In humans, mature red blood cells are not nucleated and therefore contain no personal genetic material (however immature red blood cells do). The red blood cells of some animals, such as lizards and birds, do contain a nucleus and therefore do carry the animal's genetic material within them. When organisms reproduce, it's this genetic code that is passed to the offspring through the parent's gamete cells (sperm cells from the father; egg cell from the mother). In the body, cells are constantly dividing to create new cells.

Every time a cell divides, the DNA **replicates** into another copy and the nucleus divides. Therefore, when one cell divides to become two, both cells have the body's entire genetic code within them.



Nucleated cell

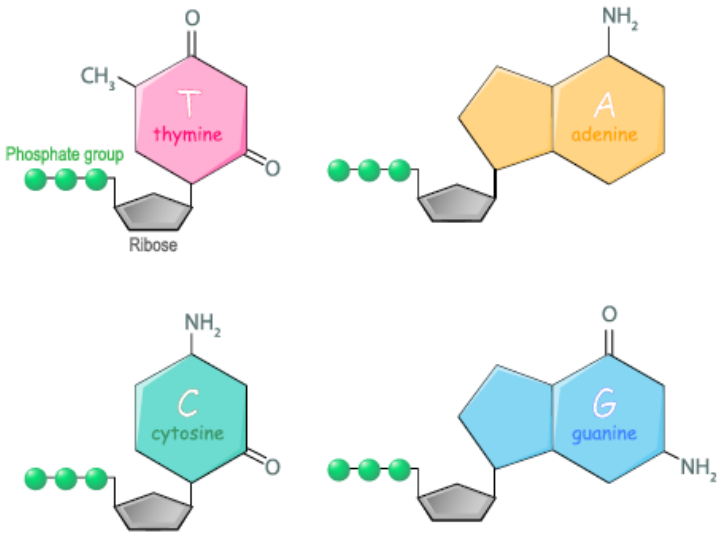
WHAT IS DNA MADE OF?

DNA is comprised of fairly simple chemical components:

- Phosphate,
- A sugar called deoxyribose,
- Four nitrogenous bases - adenine (A), cytosine (C), guanine (G), and thymine (T).

Together, a phosphate group + deoxyribose sugar molecule + one of the four nitrogenous bases = a single DNA **nucleotide**. The nucleotides with adenine or guanine bases are called *purine* nucleotides; those with cytosine or thymine are *pyrimidine* nucleotides. Nucleotides are the building blocks of DNA and therefore are the building blocks of all organisms. There are only four types of nucleotides that make up the entire genetic code of all organisms on earth. It's truly incredible that all diversity of the planet is attributable to such a simple code.

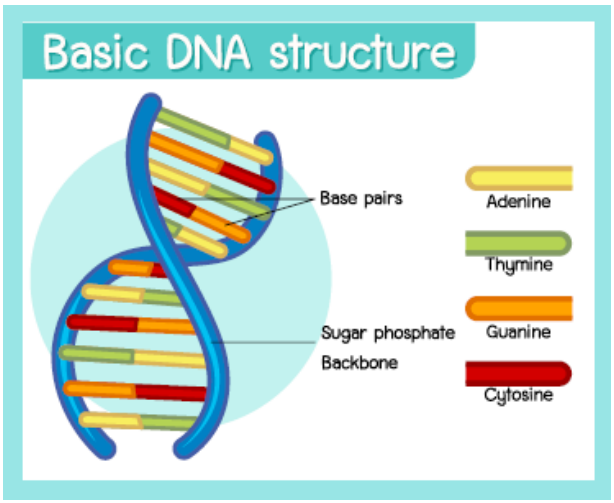
The chemical structure of a nucleotide



DNA STRUCTURE, CHROMOSOMES, AND GENES

To better visualize DNA's structure, think of a spiraling ladder where the phosphate + sugar group is the ladder's rails and the nitrogenous bases are the ladder's rungs. The phosphate group + deoxyribose sugar "rails" are called the **backbone** of the DNA strand. DNA is **double-stranded**, thus each DNA molecule has two backbones. The nitrogenous bases- A,C,G, and T- are positioned in pairs between the backbones, like rungs of a ladder. A DNA molecule is a very long chain and is wound into a helix (spiral) shape.

A DNA strand contains the four nucleotides in a variety of orders along its length. The order in which the nucleotides occur is called a **sequence**. These sequences of nucleotides are codes for our bodies to make specific proteins; these proteins make up different parts of our bodies. The entire nucleotide sequence along a DNA strand is not all used for coding proteins. Rather, there are specific sections of nucleotide sequences, called **genes**, that code for the proteins. Gene sequences on our DNA have a beginning and an end and are generally 10,000 to 50,000 nucleotides long. The proteins our genes code for become our cells, tissues, organs, and everything else that our bodies consist of.



DNA chain is double-stranded. The second DNA strand, called the **complementary** DNA strand, also contains its own set of nucleotides. Thus, sets of paired nucleotides occur along the entire length of a DNA chain. These pairs of nucleotides- called **base pairs**- are hydrogen-bonded together in the middle. What is most fascinating is the nucleotides can only base pair with one other type of nucleotide, as demonstrated below:

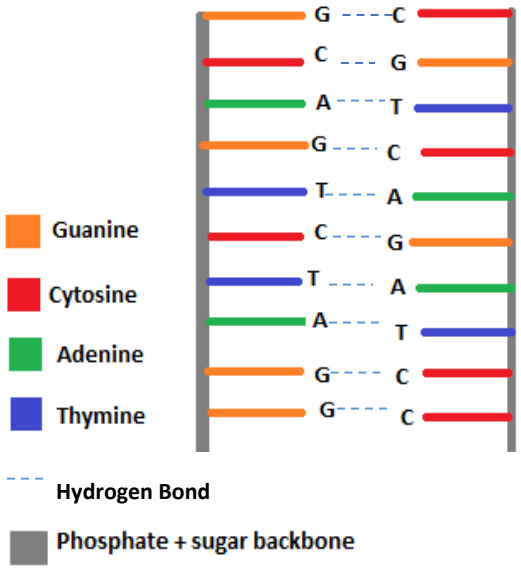
Purine nucleotides		Pyrimidine nucleotides
Adenine (A)	+	Thymine (T)
Guanine (G)	+	Cytosine (C)

Put more simply:

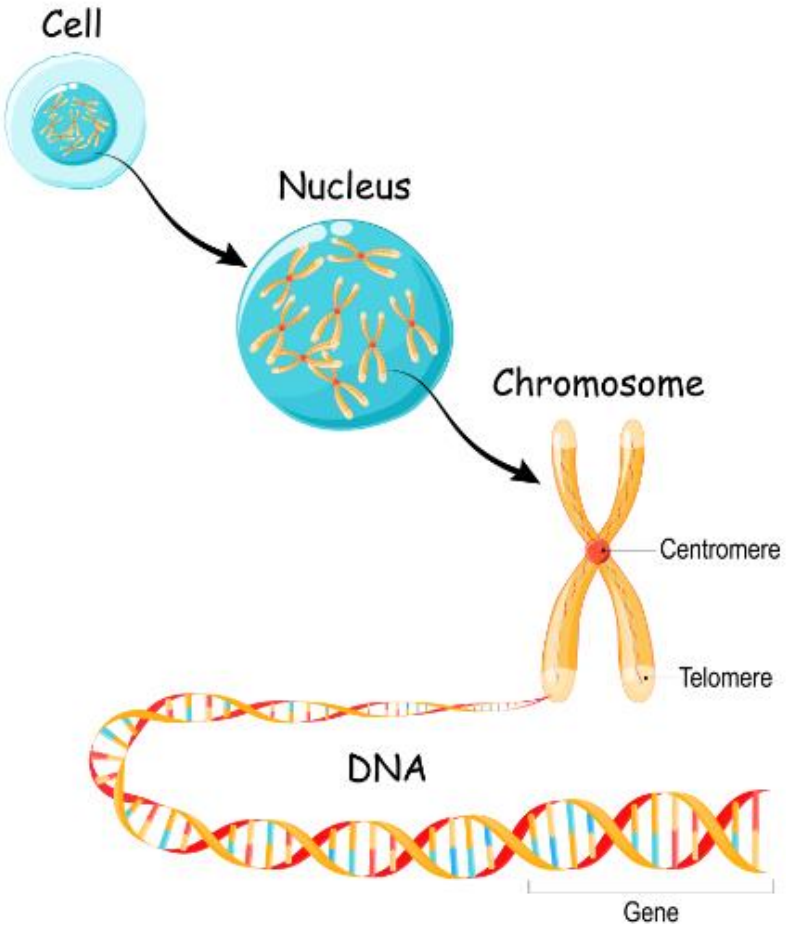
A pairs only with **T**

G pairs only with **C**

Thus, the nucleotide sequence of one DNA strand can always be predicted by knowing the sequence of the other strand. This is because adenine only bonds with thymine, and guanine only bonds with cytosine. Below is a simple diagram of an unwound portion of a double-stranded DNA chain. The sequence on the right is determined by the sequence on the left.



A DNA chain is millions of nucleotides long and contains hundreds of genes. Because of DNA's fragility, DNA winds into a helical (spiral) form which gives it more stability. Helical DNA chains further coil up with proteins called histones to form what's called a **chromosome**. Humans have 46 chromosomes total, but chromosomes are paired into sets of two. Therefore **humans have two sets of 23 chromosomes** (46 total). Individuals inherit 23 chromosomes maternally and inherit the other 23 paternally (in other words, one set comes from the mother and the other set comes from the father). All of the genes an individual inherits from their mother and father are contained within these two sets of 23 chromosomes. These genes code for the proteins that make up our entire bodies. In any one individual, some maternally-inherited genes are expressed and some paternally-inherited genes are expressed. This genetic diversity is what makes an individual unique.



An individual's entire genetic code is present inside each nucleated cell in the body. However, the entire genetic code is not *activated* within each cell type. For example, liver cells only use the liver-related genes (all non-liver related genes are inactivated within the liver cells), eye cells only use eye-related genes (all non-eye related genes are inactivated), etc.

HOW DO GENE SEQUENCES BECOME PROTEINS?

Genes consist of DNA sequence sections that are generally 10,000 to 50,000 nucleotides long. These gene sequences are a code for a specific protein or group of proteins that ultimately make up our entire bodies. How does this occur? The steps needed for a gene to be decoded into a protein are called **transcription** and **translation**.

Transcription - DNA is copied into a messenger RNA (mRNA) strand. This occurs in the cell's nucleus.

Translation- the mRNA strand is decoded into a protein. This occurs in the cell's cytoplasm (outside of the nucleus).

TRANSCRIPTION OF DNA INTO AN mRNA STRAND

Messenger RNA (mRNA) – a long, strand-like molecule that is similar to DNA but is single-stranded rather than double-stranded. RNA is a ribonucleic acid (DNA is a *deoxy*ribonucleic acid).

Transcription of DNA into an mRNA strand is performed inside a cell's nucleus by an **enzyme**. Enzymes are small substances produced in our bodies that catalyze the reactions needed for our bodies to function. For example, enzymes are responsible for the breaking down of dietary fat in our gut, changing starches we eat into sugars for fuel, and helping the liver break down toxins in the body. Enzymes also play a significant role with DNA activity.

The enzyme responsible for transcribing DNA into mRNA is called **RNA polymerase**. Using a DNA gene sequence as a **template,** RNA polymerase builds a new single strand of mRNA based on that sequence. The start of a gene sequence on DNA is marked with a substance called a **promotor.** RNA polymerase detects this promotor and binds itself to that site on the DNA strand. Once attached, RNA polymerase separates the two complementary DNA strands in that small section. Once the DNA is opened in that section, RNA polymerase reads the nucleotide sequence on one of the DNA strands and that sequence becomes the template for building an mRNA strand.

The mRNA strand is built using nucleotides that are complementary to the DNA's gene sequence (recall that G and C pair together and A and T pair together). For example, if the DNA gene sequence contains a G, RNA polymerase will insert a C into the mRNA strand; if the DNA contains a T, RNA polymerase inserts an A, and so on. The new mRNA strand continues to be built until the entire gene sequence is transcribed using complementary nucleotides.

Recall the following nucleic acid arrangements for complementary base pairs:

A only pairs with **T**

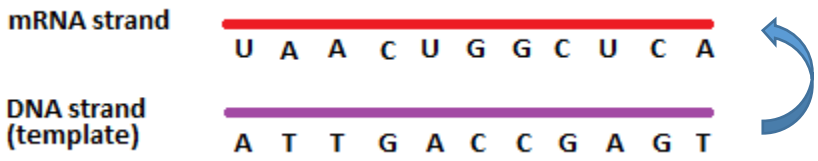
G only pairs with **C**

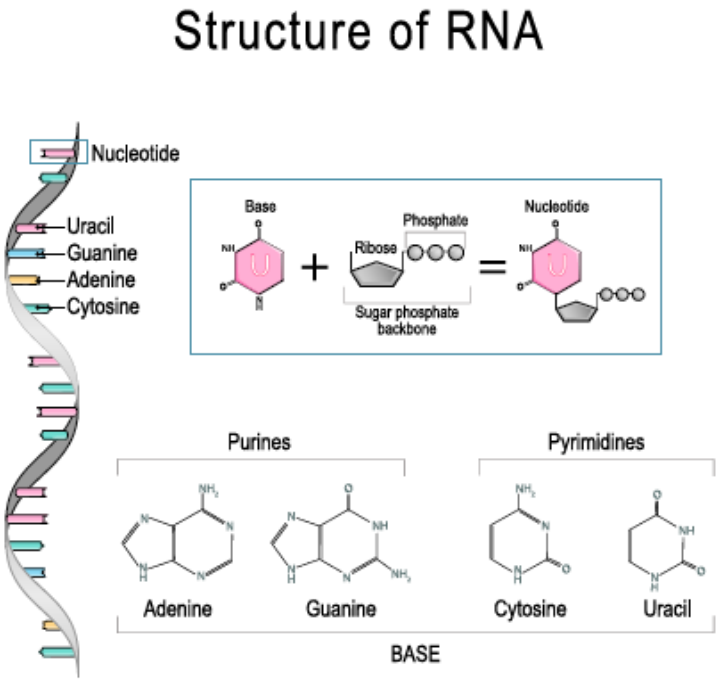
However, RNA does not contain thymine (T). In its place instead is **uracil (U)**. So, for every A in the DNA gene sequence, RNA polymerase inserts a U (rather than a T) as the complementary nucleic acid in the mRNA strand. So, for RNA:

A only pairs with **U** 

G only pairs with **C**

As the simple diagram below depicts, the mRNA strand contains a U in place of where a T would go. Uracil is chemically similar to thymine and acts in its place on an mRNA strand.





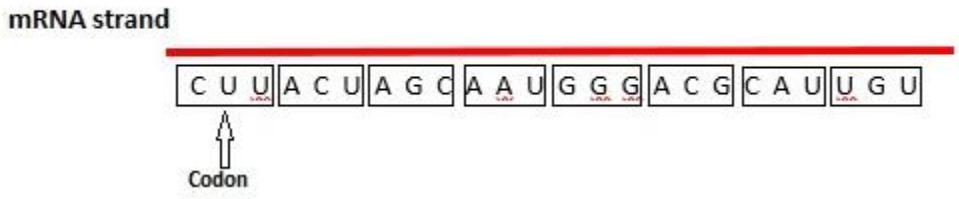
TRANSLATION OF mRNA INTO A PROTEIN

Once transcription is complete, the new mRNA molecule leaves the cell's nucleus and enters the cell's cytoplasm. By leaving the nucleus, the mRNA strand can find the location it needs to be decoded into a protein. In this context, the mRNA strand acts as a *messenger* to deliver the gene sequence to the protein-building structure in another part of the cell. This protein-building structure is called a **ribosome** and the decoding of the mRNA nucleotide sequence into a protein is called **translation**.

The production of a protein is referred to as protein *synthesis*. Proteins are synthesized from molecules in our body called **amino acids**. As a ribosome translates an mRNA, it reads the nucleotide sequence *three nucleotides at a time*. A set of three nucleotides is called a **codon**, and a specific codon corresponds to one specific type of amino acid. Many amino acids in a row create a **polypeptide,** which is a protein strand. Amino acids arranged in a certain order become a specific type of protein.

Recall the four types of nucleotides in mRNA (A,C,G,U). When the nucleotide sequence of mRNA is read as a codon (a set of three nucleotides), there is a limited number of possible combinations of the four types of nucleotides. With four possibilities in groupings of three, there are 4^3 (4 x 4 x 4) = 64 possible nucleotide combinations in a codon. In other words, there are 64 possible codons, and each codon corresponds to a specific amino acid.

Below is a simple diagram to demonstrate a series of codons (sets of three nucleotides) as they are read by a ribosome and translated into the corresponding amino acid. Recall that a chain of amino acids is called a polypeptide, which is a protein strand.



According to the genetic code tables below, the above mRNA strand portion translates into the following chain of amino acids:

Leucine, Threonine, Serine, Asparagine, Glycine, Threonine, Histodine, Cysteine.

There are only 20 different common amino acids, so each amino acid has more than one codon that corresponds to it. A table containing codons and their corresponding amino acids is provided below. Read the table starting with the first letter of the codon (left side of table), then the second letter (top of table), then the third letter (right side of table).

Ala	Alanine
Arg	Arginine
Asn	Asparagine
Asp	Aspartic acid
Cys	Cysteine
Gln	Glutamine
Glu	Glutamic acid
Gly	Glycine
His	Histidine
Ile	Isoleucine
Leu	Leucine
Lys	Lysine
Met	Methionine. (start codon)
Phe	Phenylalanine
Pro	Proline
Ser	Serine
Stop	Stop Codon. Polypeptide is complete.
Thr	Threonine
Trp	Tryptophan
Tyr	Tyrosine
Val	Valine

Second Letter

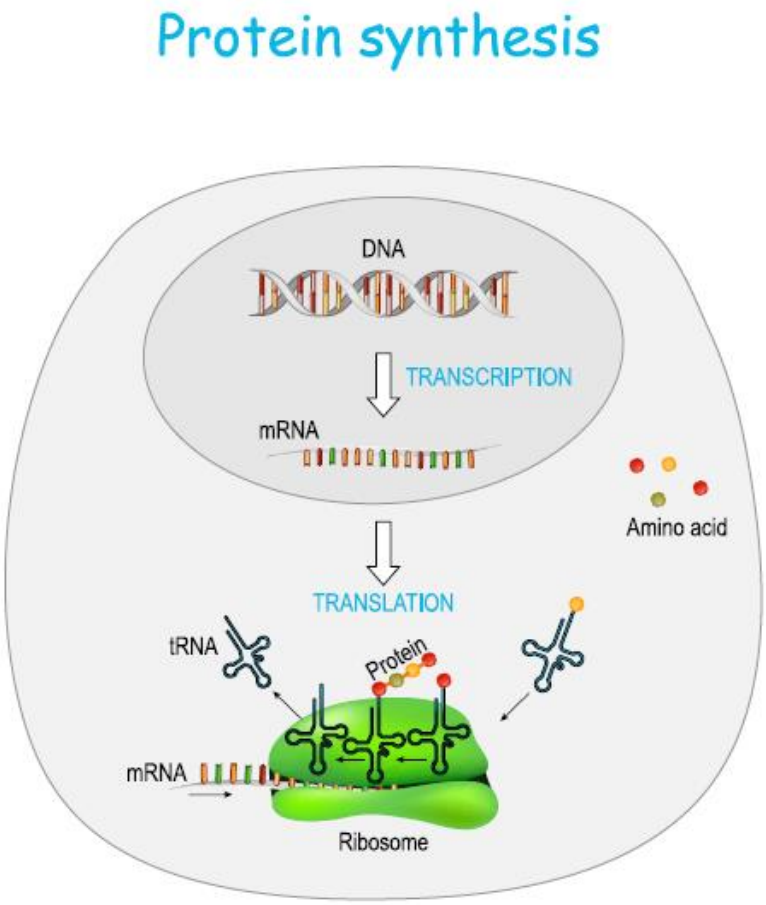
First Letter	U		C		A		G		Third Letter
U	UUU UUC	Phe	UCU UCC UCA UCG	Ser	UAU UAC	Tyr	UGU UGC	Cys	**U** **C**
	UUA UUG	Leu			**UAA** **UAG**	**Stop** **Stop**	**UGA** UGG	**Stop** Trp	**A** **G**
C	CUU CUC CUA CUG	Leu	CCU CCC CCA CCG	Pro	CAU CAC	His	CGU CGC CGA CGG	Arg	**U** **C** **A** **G**
					CAA CAG	Gln			
A	AUU AUC AUA	Ile	ACU ACC ACA ACG	Thr	AAU AAC	Asn	AGU AGC	Ser	**U** **C**
	AUG	**Met**			AAA AAG	Lys	AGA AGG	Arg	**A** **G**
G	GUU GUC GUA GUG	Val	GCU GCC GCA GCG	Ala	GAU GAC	Asp	GGU GGC GGA GGG	Gly	**U** **C** **A** **G**
					GAA GAG	Glu			

An actual polypeptide will begin with the start codon AUG (the amino acid methionine) and will end with one of the "stop" codons (UAA, UAG, or UGA). The ribosome knows where to start

translation because the codon AUG signals the amino acid methionine, and methionine is the start of every polypeptide. The three *stop* codons do not code for an amino acid but they tell the ribosome to stop translating and complete the polypeptide.

Translation of codons into a polypeptide chain involves many additional steps. However, these details are beyond the scope of this course. The following link is a free educational video that explains the mRNA translation steps in more detail.

Translation (mRNA to Protein) (click link to view educational video)



POLYPEPTIDE TO PROTEIN

A chain of amino acids is a polypeptide. The amino acids within a polypeptide are chemically bound together. Once a polypeptide is synthesized, it will fold into a three-dimensional protein. A protein must take on the correct three-dimensional shape in order to function correctly. The amino acid sequence of a polypeptide determines what its three-dimensional shape will become. The chemical bonds between each adjacent amino acid interact to cause the polypeptide to fold into its proper three-dimensional shape and become a functional protein. Some proteins then bind with other proteins to become more complex protein structures.

It's important to note that transcription, translation, and protein synthesis is always occurring inside the cells of a living organism.

VIRUSES

The previous sections of this course described DNA, mRNA, and protein synthesis. Viruses also require proteins to be translated from their genetic material in order to multiply and spread, but they cannot perform this action on their own. They require a host's cellular functions to perform these tasks.

A virus is a very small infectious particle; so small they cannot be seen under an ordinary light microscope. Viruses consist of genetic material (either DNA or RNA, but not both) and a protein coat and **are incapable of multiplying on their own**. Their genetic material can only be translated into proteins by something else - or someone else - as viruses lacks the "cellular machinery" needed to synthesize their own proteins from their DNA/RNA.

This is where host organisms come in, and this is why viruses infect us. A virus needs to enter (infect) a host's cells in order to multiply and spread. The host's cells provide the enzymes, amino acids, and other components required to synthesize viral proteins. In other words, viruses generally work by entering a host's cells and "hijacking" their cellular machinery to create new copies of itself. This is possible because the genetic code is shared among all organisms. A viral infection tricks the host's body into making viral proteins.

HOW DOES A VIRUS CAUSE DISEASE?

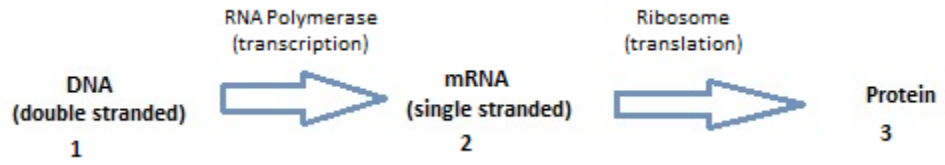
When a host is exposed to a virus, the virus enters the host's cells using one of several possible types of mechanisms, depending on the type of virus. Once a virus successfully enters a host cell, the virus sheds its protein coat and releases its genetic material inside of the cell. The viral genetic material then directs the host's cells to synthesize viral proteins and replicate the entire viral genome. This hijacking of the host's cells limits or even stops the synthesis of the host's own proteins.

In the next step of viral infection, the newly synthesized viral proteins and genome are assembled to create a new virus. The new virus then exits the cell and goes on to infect a new cell. There it also replicates itself, which impacts the host cell's ability to create proteins as normal. While the virus is multiplying and moving into new cells, the immune system recognizes the foreign viral proteins and begins destroying the infected cells.

Different viruses target different types of cells in the host's body. For instance, an upper respiratory virus targets the cells of the upper respiratory tract, an intestinal virus infects the cells of the gastrointestinal tract, etc. The associated cell destruction and subsequent tissue damage, which are largely due to the host's own immune response, cause the symptoms associated with viral infections.

RECAP

This course has covered a lot of information pertaining to DNA, RNA, and protein synthesis. The below diagram recaps the main steps that lead to protein synthesis in the body. It's important to learn these basic steps in order to understand the concept behind mRNA vaccines.



HOW mRNA VACCINES WORK

Messenger RNA (mRNA) vaccines are different from the traditional vaccines used in the past, such as live attenuated vaccines, killed/inactivated vaccines, and protein subunit vaccines. An mRNA vaccine works by injecting pre-made mRNA strands that are translated into viral proteins. The mRNA strands are designed to contain a specific nucleotide gene sequence that codes for a portion of a known viral protein. Just as with a natural infection, the viral protein will then trigger an immune system reaction.

In relation to the above diagram, an mRNA vaccine's actions begin at step 2.

An mRNA vaccine contains synthetic mRNA strands which are created from nucleotides of a known viral gene sequence. In order to inject the synthetic mRNA into the body, the mRNA molecules are encapsulated inside lipid nanoparticles (LNPs). LNPs are similar to the liposomes that have been used for many years for the delivery of certain injected prescription drugs. The synthetic mRNA strands need to be encapsulated in order to protect them from RNA digesting enzymes that naturally occur in the body. These RNA digesting enzymes will break down the mRNA strands before they have the chance to complete their task. Furthermore, mRNA does not usually occur outside of cells, therefore an immune response may be triggered against any directly injected mRNA strands before they have a chance to enter the individual's cells. LNP encapsulation also allows the mRNA to readily cross the cell membranes and enter our cells. The mRNA strands by themselves have no ability to cross a cell membrane due to their chemical makeup. Thus, the LNPs are used as a delivery vehicle to bring the injected mRNA strands into the cytoplasm of our cells where the next action can be taken. **The injected mRNA molecules do not enter the nucleus of the cells**, but they stay in the cytoplasm where the ribosomes are located. The injected mRNA only need to be translated into a protein; they have no other purpose in our cells.

COVID-19 mRNA VACCINES

The mRNA vaccines developed for prevention of COVID-19 code for a portion of the "S" spike protein that is found on the surface of the SARS-CoV-2 virus. The spike protein on the virus's surface allows it to enter a host's cells. Immune systems identify the spike protein as a foreign substance and mount an immune reaction against it.

In a *real* infection with SARS-CoV-2 virus, the virus enters a host's cells and the host's cellular machinery transcribes the virus's gene sequences into viral mRNA. However, the vaccine mimics the virus without any actual virus being present. Because the injected viral mRNA codes only for a portion of the spike protein and no other component of the virus's structure, this

injected mRNA cannot result in a fully built virus and, thus, *cannot cause COVID-19.* What the vaccine can do, however, is trigger an immune response from our bodies. This is the basis of all vaccines, and this is a desirable outcome.

Translation of Injected mRNA to Viral Spike Protein

Once inside the cell's cytoplasm, the lipid nanoparticle portion is digested and the mRNA strands are released. The ribosomes within our cells then begin translating the viral mRNA into the viral spike protein. The end result is a portion of the spike protein is present inside of the cells, but a full virus cannot be assembled so no viral infection occurs. However, the immune system still has what it needs to mount a response.

The Immune Response

Normally, all cellular proteins that are synthesized inside a cell must be "evaluated" by the immune system (including our own proteins). For our own proteins, the immune system recognizes them as "self" and does not respond with an immune reaction. However, viral proteins will elicit an immune response. The immune response that is triggered by these synthesized viral proteins is multifaceted.

- Inside the cell, the viral protein will trigger activation of **cytotoxic T cell lymphocytes** (called a cell-mediated immune response). This will lead to the cytotoxic T cells destroying the entire cell that is harboring the viral protein.
- The destroyed cell will release the viral protein into the body's tissues where it will be discovered by **B cell lymphocytes.** The B cells will begin to secrete specific antibodies against the viral protein (called a humoral immune response). These antibodies react to that particular viral protein and will neutralize/destroy it.
- Viral proteins released outside the cell can also be engulfed by white blood cells called **macrophages**. Once these macrophages engulf the viral proteins, they will process the components of the viral protein and present them to another kind of lymphocyte called a **T helper cell**. The T helper cells will recognize the viral protein as a foreign substance and a massive immune response cascade will be triggered.
- The massive immune response that is triggered by T helper cells includes the proliferation of reinforcement cytotoxic T cells and B cells that are specific to that viral protein. The T helper cell then also proliferates itself. The cytotoxic T cells will go on to destroy any cells that contain the viral proteins (vaccine infected cells). The B cells will go on to secrete many more antibodies that are specific to the viral protein.

Since a limited amount of mRNA is injected with the vaccine, a limited amount of cells will harbor the viral protein. This means that a limited number of cells will be destroyed by the cytotoxic T cells. However, some non-serious side effects from an mRNA vaccine would still be expected, as the cellular damage would result in some inflammation.

HOW DOES THIS PROTECT AGAINST COVID-19?

The immune responses do not occur immediately. For example, days to weeks are needed for the immune system to generate adequate numbers of virus-specific antibodies to effectively fight a virus. The lag time between infection with the virus and the full immune response is when the virus replicates and infects enough cells to cause disease. By having the initial immune response to the virus already completed (due to the vaccine), the immune system is armed against that virus and prepared to act immediately should it be encountered again. A vaccinated individual can still become infected with the SARS-CoV-2 virus but would be less likely to develop the COVID-19 disease because the immune system is already prepared to act.

HOW DO mRNA VACCINES DIFFER FROM OTHER TYPES OF VACCINES?

Messenger RNA (mRNA) vaccines are a new generation of vaccines that possess some benefits over the conventional types of vaccines available on the market. Two strong benefits of mRNA vaccines are:

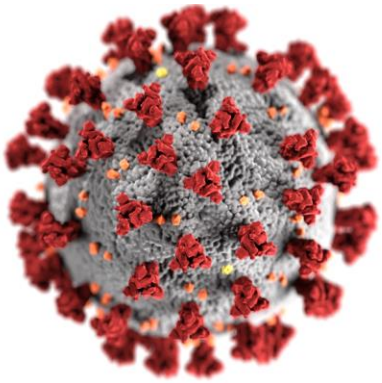
- Elicits both cell-mediated (cytotoxic) and humoral (antibody-mediated) immune responses
- No live virus infection required

Some common types of viral vaccines are listed below, along with descriptions of how the immune responses they elicit compare and contrast with those elicited from an mRNA vaccine.

Protein subunit vaccine – in a protein subunit vaccine, the viral protein itself would be injected rather than mRNA that codes for the protein. This means that the viral protein would never be inside of the cells and, thus, a cell-mediated (cytotoxic T cell) immune response would not be initiated. An antibody-mediated (humoral) immune response would still be successful. However, a cell-mediated (cytotoxic T cell) immune response is a vital component of the immune system's fight against most viruses.

Live attenuated virus vaccine- in a live attenuated virus vaccine, such as the MMR and varicella vaccines, the virus is living but has been modified and weakened by a chemical process to the point where it does not cause disease. However, the altered virus is still capable of infecting cells and multiplying itself (in a non-disease causing form). Because the live virus can infect cells, these vaccines elicit both cell-mediated (cytotoxic) and humoral (antibody-mediated) immune responses, as mRNA vaccines do. However, a drawback to live attenuated virus vaccines is that, in some people with weakened immune systems, the virus can return to a pathogenic form and cause disease. This is very rare and unlikely to occur, but this phenomenon has been observed with the polio vaccine.

Inactivated/killed virus vaccine - in an inactivated/killed virus vaccine, such as the influenza vaccine, the virus is not capable of infecting cells and multiplying. This leads to a less robust immune response since the cell-mediated response by cytotoxic t-cells only occurs when the offending substance is inside of the cells. However, a humoral (antibody) response still occurs.



This illustration, created at the Centers for Disease Control and Prevention (CDC), demonstrates the outer "crown" of a coronavirus. The red projections are the "spike" protein. The SARS-CoV-2 virus has its own unique spike protein gene sequences that differs from other coronaviruses. Photo Credit: Alissa Eckert, MSMI, Dan Higgins, MAMS

REFERENCES

"DNA replication and RNA transcription and translation." YouTube, Khan Academy, 10 Dec. 2014, www.youtube.com/watch?v=6gUY5NoX1Lk . Accessed 7 Dec. 2020.

"DNA." YouTube, Khan Academy, 22 Sept. 2009, www.youtube.com/watch?v=_-vZ_g7K6P0 . Accessed 12 Dec. 2020.

Exelead. "Liposomes and Lipid Nanoparticles As Delivery Vehicles for Personalized Medicine." Exelead: Contract Manufacturing for Liquid Injectables, 16 Nov. 2018, www.exeleadbiopharma.com/news/liposomes-and-lipid-nanoparticles-as-delivery-vehicles-for-personalized-medicine . Accessed 5 Dec. 2020.

"How mRNA Vaccines works against COVID-19 - Moderna / Pfizer." YouTube, MedicoVisual - Visual Medical Lectures, 5 Mar. 2020, www.youtube.com/watch?v=NE_EbYfkDKM . Accessed 8 Dec. 2020.

Griffiths,A, et al. (2008).” Introduction to Genetic Analysis”. New York. W.H. Freeman and Company

"RNA Vaccines (mRNA Vaccine) - Basis of Pfizer and Moderna COVID-19 vaccines, Animation." YouTube, Alila Medical Media, 18 Nov. 2020, www.youtube.com/watch?v=oMXGGmBfkf8 . Accessed 2 Dec. 2020.

TEST QUESTIONS - Messenger RNA (mRNA) Vaccines #1220121

Directions:

- Answer sheets: Read the instructions to assure you correctly complete the answer sheets.
- Online: Log in to your User Account on the NCCT website www.ncctinc.com.
  - **NOTE:** If the online test questions differ from the course test that follows the reading material, the CE course you are using is outdated or the question has been revised since you downloaded it. The online question is the most current and it should be answered accordingly.
- Select the response that best completes each sentence or answers each question from *the information presented in the course*.
- If you are having difficulty answering a question, go to www.ncctinc.com and select *Forms/Documents*. Then select *CE Updates and Revisions* to see if course content and/or a test questions have been revised. If you do not have access to the internet, call Customer Service at 800-875-4404.

1. DNA consists of which substances?

   a. Enzymes
   b. Ribosomes
   c. Nucleotides
   d. Amino acids

2. Where is DNA found inside the body?

    a. Inside the nucleus of all nucleated cells.
    b. Inside mature red blood cells.
    c. Inside all nucleated and non-nucleated cells.
    d. All of the above.

3. Which of the following show(s) a correct pairing of types of complementary nucleotides ("base pairs") in DNA?

    a. A – T
    b. C – G
    c. A – U
    d. Both options **a** and **b** are correct.

4. What is the correct name for the <u>order</u> in which nucleotides occur on a strand of DNA?

    a. Gene
    b. Sequence
    c. Chromosome
    d. Codon

5. Which of the following describes a **gene** on a DNA strand?

    a. A section of DNA with a specific nucleotide sequence that codes for a protein.
    b. The nucleotide sequence that spans the entire length of a full DNA chain.
    c. The section of a DNA strand that is transcribed by RNA polymerase and becomes an mRNA strand.
    d. Both options **a** and **c** are correct.

6. The goal of transcribing DNA into an mRNA strand is to create a copy of a gene's nucleotide sequence so it can be decoded into a protein.

    a. True
    b. False

7. Which of the following are differences between DNA and mRNA?

    a. DNA is double stranded, mRNA is single stranded.
    b. In mRNA, the nucleotide U replaces T.
    c. DNA can be directly translated into a protein and mRNA cannot.
    d. Both **a** and **b** are correct.

8. What cellular structure translates an mRNA strand into a protein?

    a. RNA polymerase
    b. Amino acid
    c. Ribosome
    d. Nucleus

9. The types of amino acids that make up a viral protein are the same types of amino acids that make up our own proteins, just in a different order.

    a. True
    b. False

10. Using the table on page 9, identify the amino acid that corresponds to the codon **CCA**.

    a. Glycine
    b. Alanine
    c. Proline
    d. Histidine

11. In a viral infection, viruses need a host's cells to transcribe mRNA and translate them into proteins.

    a. True
    b. False

12. Why can't mRNA vaccines cause a viral infection?

    a. Only mRNA is injected, not a full virus.
    b. The injected mRNA only codes for a specific protein and does not code the full virus.
    c. A full virus cannot be assembled in the host cell therefore no viral multiplication is possible.
    d. All of the above.

13. The injected mRNA strands travel into the nucleus of the cell to be translated into a protein.

    a. True
    b. False

14. What advantage does an mRNA vaccine have over traditional vaccine technologies?

    a. Both cell-mediated t-cell immunity and antibody-mediated b-cell immunity are triggered.
    b. No live virus is injected.
    c. Both **a** and **b**.

P.A.C.E.® Program Evaluation

NCCT
7007 College Boulevard
Suite 385
Overland Park, KS 66211

Directions: Please let us know whether this CE course met your expectations by answering the following questions. Your feedback helps us to make our products better for you!

Course Title: Messenger RNA (mRNA) Vaccines Course #: 1220121

OBJECTIVES

____Yes ____No 1. Did you meet the objectives while reading this CE course?

____Yes ____No 2. Did the test measure what you learned?

COURSE CONTENT

____Yes ____No 3. Were you satisfied with this course?

____Yes ____No 4. Was the CE course organized and useful for learning?

____Yes ____No 5. Was this CE course written at the right level for the practicing professional?

VALUE

____Yes ____No 6. Did you learn anything new?

____Yes ____No ____Maybe 7. Did you learn anything you might use at work?

What can NCCT do to make the CE courses better for you?

What would you like to learn about in the future? Please list *specific* topics!

Please include this evaluation with your answer sheet.