INTRODUCTION

SARS-CoV-2 is a virus that, starting in 2020, has caused the largest global pandemic in recent history. The disease caused by this virus, COVID-19, has affected millions of people worldwide. In this activity, you'll watch the animation series *Biology of SARS-CoV-2* and answer related questions to check your understanding. The concepts you'll learn will help you better understand COVID-19 and coronaviruses, as well as other viruses and outbreaks in the past, present, and future.

PROCEDURE

There are four animations in this series. Watch each animation, pausing between animations to answer the questions below in the spaces provided.

PART 1: Infection

Watch the first animation, *Infection*, which shows how SARS-CoV-2 infects and replicates inside human cells.

1. Describe the shape and location of SARS-CoV-2's protein spikes.

2. What is the function of the spike protein?

3. Predict how mutations in the gene that encodes the spike protein might affect the types of cells the virus infects.

4. Draw and label a model that shows how complementary base-pairing is used to create a new strand of DNA during cellular DNA replication. Your model should include the following labels: template strand, new strand, base pair, and DNA polymerase.

5. List the similarities and differences between cellular DNA replication and the RNA genome replication process used by coronaviruses.

Similarities	
Differences	
Cellular DNA replication	**RNA genome replication for coronaviruses**

Remdesivir is an antiviral drug with potential to treat SARS-CoV-2 infections. It is a broad-spectrum antiviral, meaning it has activity against many different viruses. Remdesivir can be incorporated into a new RNA chain as a virus replicates and can interfere with the viral replication machinery.

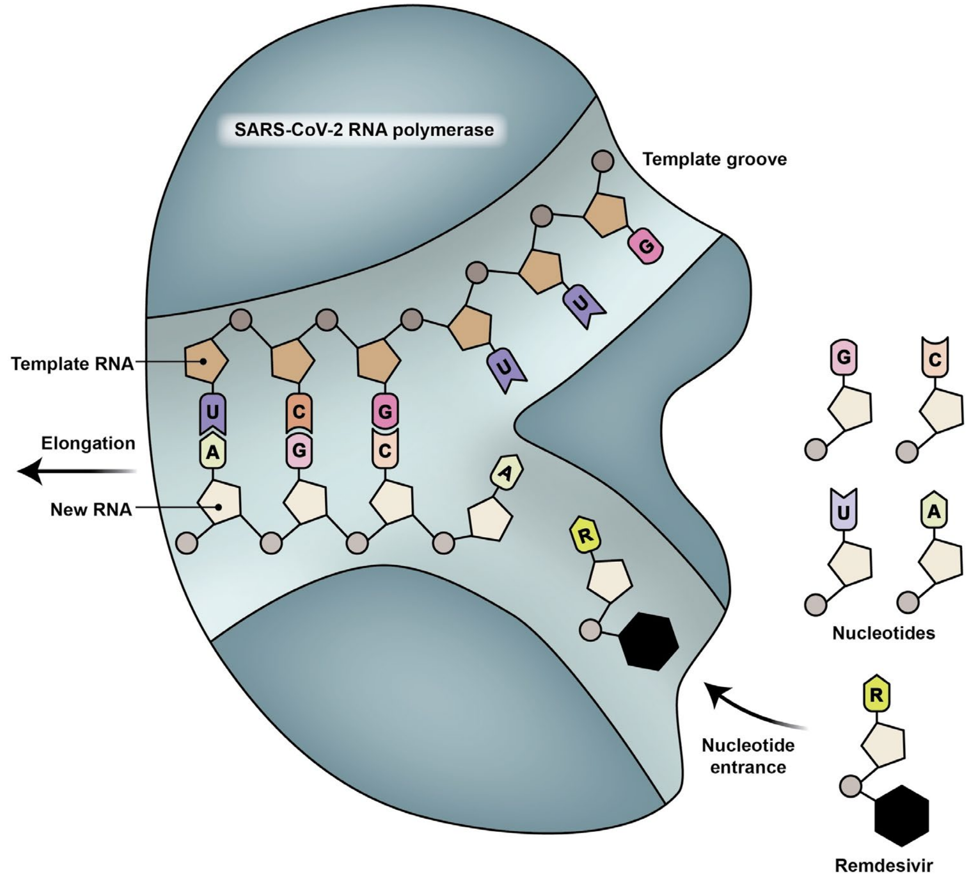

Figure 1. A representation of remdesivir and the viral replication machinery for SARS-CoV-2.

6. Figure 1 shows that remdesivir "mimics" an important component of RNA replication. Which component of RNA replication has a structure similar to that of remdesivir?

7. Propose a hypothesis about how remdesivir might inhibit the virus's replication process.

PART 2: Evolution

Watch the second animation, *Evolution*, which shows how SARS-CoV-2 and other viruses may change over time due to mutations.

8. When SARS-CoV-2 replicates in cells, mutations can occur in the virus's genome. Explain how a mutation (insertion, deletion, or substitution) in one of the virus's genes might affect a protein it encodes.

9. What impacts might mutations have on the transmission of the virus?

The earliest SARS-CoV-2 infections in the United States were detected in the state of Washington in January 2020. Scientists have since sequenced SARS-CoV-2 genomes from infected individuals throughout the country.

Table 1 shows some sequence data for the gene that encodes the spike protein, which was sequenced from SARS-CoV-2 viruses collected in different states. (The last column of the table is left blank for you to fill in later.) The gene's sequence in the virus collected from Washington early in the pandemic is between 99% and 100% identical to that of viruses collected from Utah, Colorado, Kansas, and California later on. However, some mutations have occurred at specific locations in the gene over time.

Table 1. Data on the sequences of spike proteins from SARS-CoV-2 viruses collected in different states from January to May 2020. Note that during the process of amplifying and sequencing the viral RNA genomes, the RNA is converted to DNA. Data from GenBank.

	Position in the sequence alignment							**Number of differences**
State	1059	3037	14408	18060	23403	25563	28144	
Washington	C	C	C	T	A	G	C	–
Utah	C	T	T	C	G	T	T	
Colorado	C	C	C	C	A	G	T	
Kansas	C	T	T	C	G	G	T	
California	T	T	T	C	G	T	T	

10. Which of the following types of mutations is represented in Table 1? ________
    a. substitutions
    b. insertions
    c. deletions

11. At which stage of viral infection did these mutations most likely occur?

12. Fill in the last column of Table 1 to indicate the number of nucleotide differences between the virus from Washington and the viruses from other states.

13. Knowing that the virus from Washington probably arose first, make a list below predicting the order, from first to last, in which the viruses from these states arose.
    a. Washington
    b. ___________
    c. ___________
    d. ___________
    e. ___________

14. Why did you select this order?

PART 3: Detection

Watch the third animation, *Detection*, which shows several ways to test whether someone has been infected by the SARS-CoV-2 virus.

15. List the three types of molecules detected by the tests in the animation.

16. Imagine that three individuals get all three tests. Propose a possible explanation for each individual's test results, as shown in the following table.

Individual	**RT-PCR test**	**Antigen test**	**Antibody test**	**Explanation**
1	Positive	Positive	Negative	
2	Positive	Negative	Negative	
3	Negative	Negative	Positive	

PART 4: Vaccination

Watch the fourth and final animation, *Vaccination*, which shows how different types of vaccinations for SARS-CoV-2 prevent disease.

17. Antigen protein vaccines deliver the spike protein directly into the body. The DNA and mRNA vaccines, however, make the cells of the body generate the spike protein. Briefly describe how the body generates spike proteins for each vaccine type.

    a. DNA vaccines

    b. mRNA vaccines

18. Do the genetic instructions (DNA and mRNA) vaccines contain the virus's full genome? If not, what region(s) of the genome do they contain?

19. Do the antigen protein vaccines contain all the proteins in the virus? If not, which protein(s) do they contain?

20. For each vaccine type in the animation, propose a test that could detect an active viral infection *without* false positives from that vaccine. (*Hint*: It may help to review the tests for active infections in the *Detection* animation. Note that there may not be a good test in every case.)

Vaccine type	**Proposed test without false positives**
Inactive whole virus	
Antigen proteins	
Genetic instructions (DNA or mRNA)	