Questions Allocation:

- Tanatswa: #13,14,15,16, & 17- Finished
- Savannah: #8,9,10,11, & 12 - Finished
- Danielle Wolcott: #4,5,6,7, & 18 -Finished
- Teresa Hooker: #1,2,3, & 19- Finished

Questions to be answered are in red.
If you use a reference other than the one I have provided, please cite it according to the *Nature* citation method.

Virology Introduction
Viruses have *either* a double stranded (DS) DNA, single stranded (SS) DNA, DS RNA, or SS RNA genome. SS RNA viruses can be (+) with a 5' to 3' RNA genome, or (-) with a 3' to 5' genome.
The following diagram outlines how RNA viruses replicate their nucleic acid and express their genes (make proteins). Coronaviruses are a Class IV virus.

1. Give an example of each type of RNA virus according to the genome in the following diagram (Class III-VI). For example, you can give coronavirus for Class IV. **(4 points)**

III. Birnaviridae
IV. Coronavirus
V. Orthomyxoviridae
VI. HIV

2. What other viruses are Class IV viruses? Name at least two. (1 point)

Flaviviridae
Astroviridae

Coronaviruses
There were coronaviruses before SARS appeared on the scene in 2003! Refer to the following article:
https://www.the-scientist.com/news-opinion/a-brief-history-of-human-coronaviruses-67600

3. Write a short paragraph about the history of coronaviruses from its discovery until 2021. (1 point)

Coronavirus was first discovered in humans during the mid-1960's. Coronaviruses received that name because of their spike-like exterior, reminding scientists of the Sun's Corona (Atmosphere). COVID-19/SARS-CoV-2, the most recent outbreaks of coronavirus, is only one among many of this type of virus. Others include NL63, 229E, OC43, and more. All of these viruses seem to come with the same type of symptoms, but SARS-CoV-2 had

been deemed the most lethal. The origin of coronaviruses, what species it began with, and the length of time humans have hosted them are currently unknown, and because they are always mutating the question may remain unanswered.

SARS-CoV-2 Genome and Structure

Go to the attached PDF entitled "A Structural View of SARS-CoV-2 RNA Replication Machinery" and refer to Section 2 and 3.1 and Figure 1.

4. What could be an advantage of being a virus with a genome that acts like mRNA? (1 point)

An advantage of a virus with a genome that acts like mRNA, is that the genome could be translated directly into a viral protein.

5. The virus does not have ribosomes. How is the viral RNA going to be translated? (1 point)

The genomic RNA (gRNA) has a 5' cap and a 3' poly(A) tail and can act as mRNA for immediate translation of the viral polyproteins.

6. What features on the genome are similar to eukaryotic mRNA? (1 point)

The 5' cap and the 3' poly(A) tail are similar to eukaryotic mRNA.

7. The genome also contains 5' and 3' untranslated regions. What does that mean? (1 point) (This is not a trick question and should be straight forward. Look at the terminology.)

The highly structured untranslated region plays an important role in the regulation of RNA replication and transcription.

8. The term polycistronic was introduced in genetics when comparing the gene expression of prokaryotes and eukaryotes. **The SARS-CoV-2 genome is described as polycistronic. Define the term polycistronic. (1 point)**

The term polycistronic refers to a single mRNA that can encode for multiple proteins. Either the mRNA is split to make different proteins or a long polypeptide chain is made and then separated after translation (polycistronic mRNA).

9. What is an open reading frame? (1 point)

An open reading frame refers to which nucleotides are paired together to form a codon which is then read during translation. Based on start or stop codons, the mRNA will continue to be read in sets of three (a codon) until it reaches a stopping point. There are no stop codons within the reading frame (Austin).

10. What is a nonstructural protein? (1 point)

Nonstructural proteins are proteins that are made by the organism but are not used inside that organism. Instead they are inserted into the host and are used in some way to help that organism flourish within that host. Some can be used to help the organism replicate within the host or to make the host a more hospitable environment for that organism's survival (Rohaim, 2020)

11. How many nonstructural proteins does SARS-CoV-2 make? (1 point)

The SARS-CoV-2 virus contains 16 nonstructural proteins (Laguipo, 2021).

12. How does the polyprotein 1ab become separate proteins? (1 point)

Enzymes are used to break the poly protein 1ab at distinct sites to separate it into different proteins. This cleavage allows them to separate and perform their separate functions within the viral organism (Sheith, 2021).

13. What are some of the roles for the nonstructural proteins? (1 point)

The role that the nonstructural proteins play is an important role. It is important for complex replicase machinery. The complex replicase machinery has enzyme activities that are rare or absent in positive stranded RNA viruses.

14. When we recently discussed transduction in class, we talked about the ability of a bacteriophage stopping its host cell from gene expression. **What SARS-CoV-2 nonstructural protein stops host gene expression? (1 point)**

The SARS-CoV-2 nonstructural protein that stops the host gene from expression is the Nsp1 protein.

15. What is a structural protein? How many structural proteins does SARS-CoV-2 have? (1 point)

A structural protein is a protein that maintains the structure and shape of a cell. SARS-CoV-2 has four structural proteins.

16. Refer to Figure 4 in the following article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7194867/#:~:text=Coronaviruses%20(CoVs)%20 are%20a%20group,as%20they%20harbor%20the%20viruses. **Name the structural proteins and describe where they are located in the virus. (4 points)**

The first structural protein is the S-spike protein that is located in the outer spiky glycoprotein. The second structural protein is the M-membrane protein that is located in

the type 3 transmembrane glycoprotein. The third structural protein is the N-nucleocapsid protein that is located in the phospholipid bilayer.

17. Referring back to the PDF entitled "A Structural View of SARS-CoV-2 Replication Machinery" (Figure 1), we see 9 accessory factor coding regions at the 3' end of the genome. Refer to https://virologyj.biomedcentral.com/articles/10.1186/s12985-020-01402-1, Background (Information), paragraph 5. **What is the role of accessory factors or accessory proteins? In your answer, address how necessary they are for the virus. (1 point)**

The role of the accessory factors or accessory proteins is they play an important part in pathogenicity, or spread by modulating the host interferon signaling pathways. The accessory factors or accessory proteins are necessary for increasing stability and forming higher ordered structures.

SARS-CoV-2 Variants of Concern

Refer to:
https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/scientific-brief-emerging-variants.html; scroll down to "Emerging Variants"

Three variants of concern are UK B.1.1.7, South Africa B.1.351, and Brazil P.1

18. **What area of the genome has mutated for all three of these variants? Is this part of a nonstructural or a structural protein? (1 point)**

UK B.1.1.7, South Africa B.1351, and Brazil P.1 all have the genome mutated at N501Y. This genome, N501Y, is part of a nonstructural protein.

19. **Why is a mutation in the above area so important? (1 point)**

Mutations like these are important because, as the virus adapts, it can become more contagious, easier to spread, and harder to treat.

The following information is not necessary for this assignment, but might be of interest to you.
SARS-COV-2 "life" cycle:
https://www.nature.com/articles/s41579-020-00468-6#:~:text=1)%2C%20coronaviruses%20express%20and%20replicate,structures%20essential%20for%20RNA%20synthesis.

Citations (numbers need to be deleted but they need to be in the order used in the document)

8- polycistronic mRNA. *Oxford Reference*
https://www.oxfordreference.com/view/10.1093/oi/authority.20110803100335437

9- Austin, C. Open Reading Frame. *Genome.gov;*
https://www.genome.gov/genetics-glossary/Open-Reading-Frame

10- Rohaim, M. Naggar, R. Clayton, E. Munir, M. Structural and functional insights into non-structural proteins of coronaviruses. *US National Library of Medicine;* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7682334/#:~:text=Table%201%20%20%20%20Nonstructural%20Protein%20%28nsp%29,scaffold%20protein%20...%20%2011%20more%20rows%20 (2020).

11- Laguipo, A. SARS-CoV-2's nonstructural proteins dysregulate immune responses, study finds. News Medical Life Sciences. https://www.news-medical.net/news/20210122/SARS-CoV-2e28099s-nonstructural-proteins-dysregulate-immune-responses-study-finds.aspx (2021).

12- Sheith, R. The Role of Replicase Polyprotein 1ab in SARS-CoV-2 and the Analysis of its Cleavage Sites. *Ysjournal*. https://ysjournal.com/the-role-of-replicase-polyprotein-1ab-in-sars-cov-2-and-the-analysis-of-its-cleavage-sites/ (2021).