Case Study ch 14&15: Immune Systems

Immune responses to SARS-CoV-2 ___/15 pts

Team Role*	First and Last Name of group member
Coordinator	Avery McKoski
Facilitator	Olivia Ostrander
Recorder	Tanner Kaiser
Devil's Advocate	Chloe Mullis

*See role descriptions in syllabus and/or group assignment instructions document

Read the following items associated with the case study:

Watch this overview video: https://youtu.be/pf1dBxYlxPo **Immune Response to Viruses: How the Body Reacts**

Read the following article:
https://www.the-scientist.com/news-opinion/when-the-immune-response-makes-covid-19-worse-69239

Watch this SARS-CoV-2 evolution video
https://media.hhmi.org/biointeractive/click/covid/evolution.html

Review Ch 14 and 15 textbook chapters and lecture slides

Questions:

Part I: Innate response – starts immediately upon infection

1. Once the SARS-CoV2 virus *enters* the body, list three (3) innate effector defenses that will be utilized? (1.5 pt)

After SARS-CoV2 virus enters the body, cells will begin to produce interferons to act as a warning signal to neighboring cells, infected cells will be removed by natural killer lymphocytes, and macrophages will ingest and break down free viruses via phagocytosis.

2. When a cell is infected with SARS-CoV-2, which Pattern Recognition Receptors will detect the viral RNA genome? (1 pt)

- RIG-like receptors will detect the uncapped single stranded viral RNA.

B. When this PRR comes in contact with the SARS-CoV-2 RNA, what cytokine will the cell be triggered to produce? (1 pt)

- The cell will be triggered to produce interferons

3. The article "When the Immune Response Makes COVID-19 Worse" describes that inability to produce effective interferons can lead to increased vulnerability.
   A) Define what interferons are and describe the functional outcomes of effective interferons (1 pt)

"Interferons are proteins that bind to specific surface receptors on cells in danger, warning them about the viral invaders and orchestrating a signaling pathway that will keep the viruses from multiplying." When effective, interferons attach to specific surface receptors on cells in danger warning about the invading virus and/or preventing the virus from multiplying. They stimulate cytokine production, antigen presentation, and natural killer cell function.

   B) Describe what will happen if a virus continues replicating *without* an effective interferon response. (1 pt)

The disease will move to another stage if the interferons are ineffective- the virus will successfully replicate and get more severe. "Then you get the secondary hyperinflammation that goes systemic, and that's where comorbidities come into play."

4. One major systemic effect of COVID-19 infections is organ inflammation (i.e. myocarditis).

   A) Name the purpose of inflammation (1 pt)

Inflammation is an innate immune response that recruits phagocytes to the site of infection. Inflammation occurs to contain the site of damage, localize the area, eliminate the virus, and restore tissue function.

   B) Describe 2 innate immune processes that activate inflammation. (1 pt)

Inflammation is activated by complement proteins as well as when microbe associated molecular patterns (MAMPS) and damage associated molecular patterns (DAMPS) are detected by pattern recognition receptors.

Part II: Activating the adaptive response – starts day 6-8

Describe what adaptive immune responses (specific cells and proteins/cytokines) that could possibly be employed by the body:

1. What innate immune specific cell would be used by the body to identify the presence of SARS-CoV-2 and relay information to adaptive cells?: (1 pt)

Dendritic cells would be used by the body to identify the presence of SARS-CoV-2 and present the antigen to the adaptive cells.

2. Highlight which adaptive immunity cells from this list are directly activated by the cell identified in part II #1. Select all that apply. (0.5 pt)

   - ☐ Naïve B cells
   - ☐ Naïve helper T cells
   - ☐ Naïve cytotoxic T cells
   - ☐ Dendritic cells
   - ☐ Macrophage cells

3. Describe in detail the mechanism for activation of the cells selected in part II #2. This is a good time to refresh what surface proteins, signals and receptors are used in the process. (1 pt)

   - Regarding naïve cytotoxic T cells, the dendritic cell will present the antigen to the T cell as well as secrete Co-stimulatory molecules. The antigen will then bind to the TCR with the CD8 cluster of differentiation present, confirm the co-stimulatory molecules, and become activated.
   - Regarding naïve helper T cells, the dendritic cell will present the antigen to the T cell as well as secrete Co-stimulatory molecules. The antigen will then bind to the TCR with the CD4 cluster of differentiation present, confirm the co-stimulatory molecules, and become activated.

4. Circle/highlight which adaptive immunity cells are activated by the cells identified in part II #2 to create an effective response to neutralize the infectious agent or component. Select all that apply. (0.5 pt)

   - ☐ Naïve B cells
   - ☐ Naïve helper T cells
   - ☐ Naïve cytotoxic T cells
   - ☐ Dendritic cells
   - ☐ Macrophage cells

Part III: The activated functions of the adaptive immune response

1. Once activated, Plasma cells will begin to secrete antibodies that bind specific molecules on SARS-CoV-2. List at least 3 functional outcomes of antibodies coating SARS-CoV-2. (1.5 pt)

   - Neutralization
   - Opsonization
   - Complement System Activation

2. Once activated, T_C cells will destroy human cells that have been infected by SARS-CoV-2. Describe in detail the mechanism by which T_C cell detect infected cells in order to accomplish targeted apoptosis. (1 pt)
   The virally infected self-cells present viral peptides on MHC class I molecules → Tc cells recognize viral peptides presented by an infected self-cell and initiate apoptosis in that target. It also releases cytokines that alert neighboring cells → target cell then undergoes apoptosis.

Part IV: A moving target - SARS-CoV-2 evolution

1. Watch this video before beginning this section. 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.

   A mutation in one of the virus's genes might cause a silent mutation in the gene encoding for the protein, not affecting the protein's function at all. It could also cause a missense mutation in which one of the nucleotide base pairs of the gene encoding for the protein is changed thereby altering its function. Finally, it could cause a nonsense mutation in which a nucleotide base pair is changed in the gene encoding for the protein causing an early stop codon, a shorter protein, an alteration in its function, or leaving it non-functional all together.

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

   Once a mutation in the viral genome has occurred, the virus that begins to replicate in other host cells will pass on that mutated genome. Some mutations may provide a selective advantage in new viruses that the non-mutated viruses do not have. These versions of the virus become more abundant in a population overtime. Some mutations provide a disadvantage, and these versions become less popular. Other times, a neutral mutation could occur which would cause the virus to spread no more or no less.

3. Fill in the last column of the table below to indicate the number of nucleotide differences between the virus from Washington and the viruses from other states.

	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	6
Colorado	C	C	C	C	A	G	T	2
Kansas	C	T	T	C	G	G	T	5
California	T	T	T	C	G	T	T	7

4. 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. Why did you choose this order?

   Washington, Colorado, Kansas, Utah, California

   The longer it took for the virus to arrive in the state, the longer it was infecting people and acquiring genetic mutations.

5. Why is tracking evolutionary changes of a virus important for our society?

It is essential because, within evolutionary changes, the virus could be spread easier over time. It could also become less effective or powerful. Or, it could become resilient, fast, and effective. It is vital to gauge these viruses' age, power, and resilience so we can be educated on the threat they hold (or lack thereof). It can also help scientists develop treatments and vaccines. Mutations may change the characteristics of the virus forcing us to need to change previous vaccines that may be ineffective against new mutations. In this way, the medical field can stay ahead of new variations of the virus and keep humans healthy.