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Biology 067: Emerging Diseases Midterm
Tuesday, October 16, 2007

Instructions:

1. For each question, numbers in brackets indicate the number of points. The **relative number of points** (80 pts total) should give you a rough idea of **how much time to spend** per question.

2. Read through the **entire** question **carefully before starting to write** your answer. The **space** that has been left between questions **roughly approximates** how long your answers will be, depending on the size of your handwriting (you can use extra space on the last page if needed). You should also **feel free** to use **PICTURES** to **help explain ideas** when **appropriate**.

3. Aim for **CLEAR**, **CONCISE, COMPLETE** answers.

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1. (16 pts total) You are studying an interesting **new variant** of the SARS coronavirus that can **infect mouse cells but not human cells** in the lab. You notice that if you take a plate of **human cells**, layer the virus on top of the cells, then wash the cells, that **all of the virus remains in the wash liquid**, rather than sticking to the cells. If you do the same experiment with **mouse cells**, the **virus stays stuck to the mouse cells**. When you determine the nucleotide sequence of the genome of this new SARS virus and compare it to an **old SARS-CoV** that **infects both mouse and human cells**, you find **differences in one gene**. The part of the gene that shows differences is depicted below:

SARS-CoV-old	mRNA	CCU-GCU-UGG-AAC
Infects mouse and human cells	protein	Leu-Ala-Trp-Asn
SARS-CoV-new	mRNA	CCU-GCU-UGU-AAU
Infects mouse but not human cells	protein	Leu-Ala-Cys-Asn

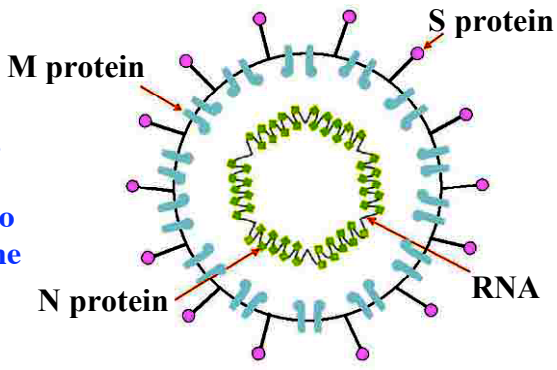
a) (2 pts) What are the subunits that are attached to each other to form proteins called?

amino acid

b) (4 pts) Circle the difference in the new SARS-CoV gene that you think is likely to prevent infection of human cells.

(note: the gene—the unit that is passed from parents to offspring—is the RNA, not the protein, although the protein is directly responsible for the difference in cell entry)

c) (10 pts) After consulting the picture of the SARS virus particle below, predict which protein(s) might differ between new and old forms of SARS-CoV. Explain your answer (2-3 sentences).



Either the S or the M protein might differ between the two viruses. These proteins are found on the surface of the virus and therefore may be important for binding to a cellular receptor for infection. The new virus cannot infect or bind to mouse cells but not human cells and therefore a change in one of these proteins could prevent binding to the cell.

2. (28 pts total) In a 2006 episode of his (comic) TV show "The Colbert Report," Stephen Colbert went on the following rant:

> "Besides I'm against vaccines, I think we should get rid of them ... No one gets rubella or polio anymore. Why are we wasting our time and money vaccinating our kids against them? **But the main reason I don't like vaccines is that most of them work by injecting you with antibodies someone or something else produced. Oh, I'll just let rat # 253 develop polio and then I'll take a hit off that serum when he's through. Anyone with any guts would face those viruses one on one**."

Colbert's "main reason" he doesn't like vaccines (in bold above) shows that he doesn't understand how vaccines work. Concerned that your rebellious teenage brother might take Colbert seriously, you decide to explain a few points to your brother (briefly—his attention span is short).

a) (16 pts) Explain why injection of the Salk poliovirus vaccine (which is composed of inactivated poliovirus that cannot infect cells) should help protect someone from polio later in life, including at least two cells or molecules involved in protection. Highlight how this action is similar to and different from Colbert's description. (~4 sentences)

Injection of an inactivated poliovirus exposes one's B cells to the surface proteins of the virus. A B cell with a receptor that binds to poliovirus can then start making antibodies (with signals from a helper T cell) that will bind to poliovirus surface proteins. Later in life, if one is exposed to poliovirus, memory B cells can start making antibodies that will bind to the virus and prevent it from entering cells (or cause it to be eaten by a macrophage), preventing infection and subsequent disease. Thus, although antibodies are involved (as Colbert mentioned), the vaccine contains virus to induce an antibody response in the human (who really is facing the virus one-on-one!), not rat antibodies.

Contrary to Colbert's statement, some people do get rubella and polio. Last week, Donald McNeil of the New York Times reported a recent outbreak of polio in Nigeria. This outbreak has been linked to mutation of the **attenuated poliovirus** found in the **oral vaccine** frequently used in developing countries. **Attenuated poliovirus can still infect cells and replicate, but does not normally cause disease.** In his article McNeil wrote:

> **"This vaccine, invented by Albert Sabin, is easier to give, offers much stronger protection and can beneficially "infect" other family members or neighbors, protecting them too."**

b) (12 pts) Explain one reason why this Sabin vaccine might offer "much stronger protection" than the Salk vaccine. (1-2 sentences)

Since the virus in the Sabin vaccinecan infect cells, you can get a stronger response because a) there's more virus for B cells to recognize following replication in host cells (and therefore more B-cell activation), b) since the virus infects cells, you might be able to activate cytotoxic T cells that will be able to kill virus-infected cells later, rather than just B cells, which only deal with virus outside of host cells.

3. (30 pts total) You and your colleagues are studying a **possible tuberculosis outbreak** in Brunswick. You take **tissue samples** and **blood samples** from **patients** whose **symptoms** include **weight loss and coughing**. You look at the **tissue samples** under a **microscope**. Your colleague tests **blood samples** for the presence of **antibodies that bind to *M. tuberculosis***.

a) (3 pts) What type of tissue samples will you take and why?

I would take lung samples, since *M. tuberculosis* (hereafter referred to as *Mt*) infects the lungs and the patients are coughing, suggesting a lung infection.

b) (3 pts) What type of a microscope will you use and why?

I would use a light microscope since tuberculosis is caused by a bacterium, which is large enough to be seen with a light microscope.

Experimental results

Patient	microscopy	antibodies
1	-	-
2	+	+
3	+	-
4	-	+

+ = evidence for tuberculosis
- = no evidence for tuberculosis

c) (12 pts) Based on the results shown in the table, what predictions would you make about the agent causing each of the patients' symptoms? Explain each prediction in one sentence.

Patient 1 has no sign of *Mt* infection and therefore her symptoms may be caused by another agent that affects the respiratory tract.

In patient 2, we see both mycobacteria and antibodies to *Mt*, suggesting that *Mt* is causing disease.
The presence of bacteria in the lungs of patient 3 suggests that this patient is infected with *Mt*, which is causing symptoms.
The presence of *Mt* antibodies in patient 4 suggests that she was at least exposed to Mt and therefore her disease may have been caused by *Mt*.

d) (4 pts) What stage of disease do you think patient 4 might be in? Explain your answer in one sentence.

Patient 4 may be in recovery stage--when the immune system has rid the body of detectable bacteria (as detected by microscopy), but still has antibodies for Mt.

e) (8 pts) What treatment would you recommend for patient 2? Would you recommend the same treatment for patients 1? Why or why not? For patient 4? Why or why not?

I recommend antibiotic treatment for patient 2, since he clearly has tuberculosis by both tests. Patient 4 may or may not need antibiotic treatment, since there may still be bacteria left in the body in small numbers (for safety, given the severity and transmissibility of tuberculosis, I would probably put this patient on antibiotics for awhile). I would not recommend antibiotic treatment for patient 1, since there is no evidence so far that the disease is of bacterial origin (and superfluous treatment could therefore increase resistance among other bacteria).

4. (6 pts) Explain one causal factor for Ebola Hemorrhagic Fever (EHF). Include whether it is an agent, host or environmental factor and how it leads to disease.

One of many possible answers: One environmental factor that leads to EHF is the reuse of syringes and/or needles. Since Ebola virus is a blood-borne pathogen, it can be passed from one patient to another through the re-use of syringes.