BB101: 2023

Mid-sem exam (30 marks)

You have 2 hours to answer this exam.

You must answer only within the space provided.

The questions are connected to each other so read them carefully.

Your queries about the question paper will not be clarified during the exam.

You should think carefully and give brief, to-the-point answers.

This exam is to see how well you have understood biology, so try and enjoy yourselves for the next two hours!

Part A:

The global pandemic was a once-in-a-lifetime event that was very difficult for all of us. It was caused by the coronavirus, SARS CoV-2 that spreads by the respiratory route (coughing and sneezing by the infected person). The disease outcomes include mild Covid, severe Covid, long-Covid and fatality.

In the beginning of the pandemic, we did not understand the virus well and so there were many early treatments that turned out not be useful. Having taken BB101, you are now in a position to understand these early treatments and give your expert opinions on them.

1) After sequencing, it was shown that the SARS CoV-2 genome has an exact nucleotide composition as follows: U (32.2%), A (29.9%), G (19.6%) and C (18.3%). Circle which of the following could be the genome of this virus. (1 mark)

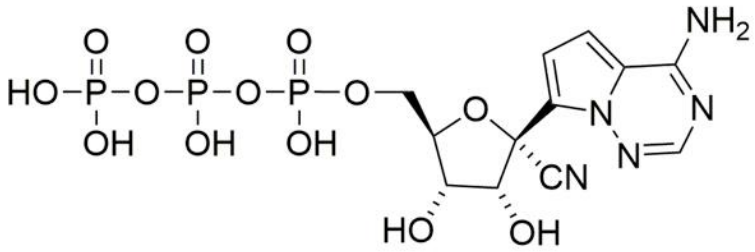
   A) Double stranded DNA
   B) Double stranded RNA
   C) Single stranded DNA
   D) Single stranded RNA

   The question mentioned that the "exact" nucleotide composition was given. This is different from Chargaff's experiments where he used chemistry to find out the nucleotide composition. The correct answer is (D). However, if anyone circled (B), in addition to (D), they can also get marks. Anyone who circled only (B) does not get any marks.

2) You want to distinguish between the different genomes shown in question (1), using an experiment. You realize that all these genomes would be different in their density. Which experiment/technique can separate nucleic acid molecules based on their density? (1 mark)

   Ultra-centrifugation, centrifugation, Meselson and Stahl experiment are all acceptable answers.

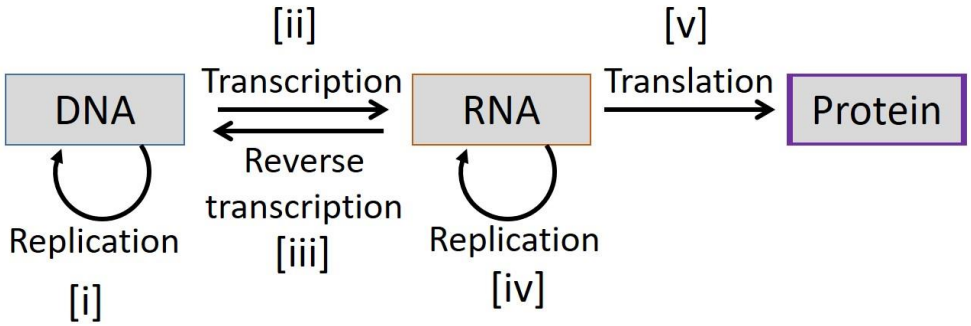
3) One of the treatments for Covid-19 was remdesivir, a chemical molecule that is metabolized by the human body into remdesivir triphosphate. Remdesivir triphosphate has the structure shown below.



Even though you are not supposed to mug up structures, you can surely answer which of the following biomolecules this drug resembles. Circle the correct answer. (1 mark)

A) Nucleotide
B) Lipid
C) Amino acid
D) Glucose

4) Remdesivir triphosphate is an inhibitor of RNA-dependent RNA polymerase (RdRP), an enzyme of coronaviruses. It works as a drug/medicine because it prevents coronavirus genome replication, but it does not affect human genome replication.
The "Central Dogma" is drawn below. Circle the correct answer that indicates the steps for the action of RdRP and human genome replication, respectively. (2 marks)



A) [iii] and [ii]
B) [iv] and [i]
C) [v] and [iii]
D) [i] and [iv]

The SARS CoV-2 genome is RNA (as you answered in question 1) and in this question you were told that the replication occurs due to an RNA-dependent RNA polymerase. This is the step shown in [iv]. The human genome is DNA so it will be replicated according to [i]. This explanation is not required for marks.

5) Chloroquine is another drug that was shown to be effective against SARS CoV-2 when tested in the lab against the virus growing in human cells. But when tested in clinical trials with human patients, it did not work. In the lab experiments, it was shown that chloroquine interferes with a step of the viral life cycle that takes place in the lysosomes resulting in accumulation of virus particles in this organelle. What instrument would you use to visualize this block of the life cycle? (2 marks)

Any kind of microscope.

6) At the beginning of the pandemic, there was an observation that countries having an active vaccination program for tuberculosis (TB) had lower cases of Covid-19. TB is caused by a bacterial pathogen, *Mycobacterium tuberculosis* (Mtb), that also infects respiratory cells. The vaccine for TB is called BCG and consists of killed Mtb bacteria. You decide to further study whether vaccination for TB does indeed result in protection against SARS CoV-2.
In general, which two types of immune cells are involved in protection after vaccination? (1 mark each for a correct immune cell)

B cells and T cells

7) You decide to study one of these types of cells, particularly the cells that produce antibodies. You have a theory that the killed Mtb bacteria in the BCG vaccine contain epitopes identical to SARS CoV-2 epitopes. What is an epitope? (2 marks)

An epitope is a part of a protein that is recognized by a specific antibody.

8) You do some clever analysis of the genome sequences of Mtb and SARS CoV-2, and find a short sequence of amino acids that is identical in the two organisms. When shown as the one letter amino acid nomenclature, this identical protein sequence is: ANTIGEN.
The genome sequences from the two organisms that encode the ANTIGEN protein sequence are given below.

Mtb: 5' GCU GAU ACU AUU GGG GAA GAU 3'
SARS CoV-2: 5' GCC GAC ACU AUC GGA GAG GAC 3'

Give an explanation as to how these sequences can code for the same protein. (2 marks)

The genetic code has many codons for a single amino acid. So, the same amino acid can be encoded by different codons, explaining this observation.

9) Next, you collect blood from many Covid patients who have mild symptoms. Half of these patients have been previously vaccinated with BCG and the other half of the patients have not been previously vaccinated with BCG.
You have a theory that "ANTIGEN" is the common epitope (between Mtb and SARS CoV-2) being recognized by the immune cells that will make antibodies. You set up an indirect ELISA with the patients' blood, to assay concentrations of antibodies that recognize this epitope.

If the "ANTIGEN" epitope in the BCG vaccine acted as the first exposure, and same epitope was also in SARS CoV-2 virus during the second exposure, what result would you have expected for the concentration of antibodies in the two groups? (2 marks)

We would have expected that the BCG vaccinated group would show higher concentration of antibodies than the un-vaccinated group.

10) Your actual results are below.

	Group 1: Covid patients, previously vaccinated with BCG	Group 2: Covid patients, previously not vaccinated with BCG
Concentration of antibodies that recognize the "ANTIGEN" epitope in arbitrary units (mean of the samples is given)	130	130

From this result, do you think that the "ANTIGEN" epitope in the BCG vaccine acts as a protective vaccine against SARS Cov2? Explain briefly. (1 mark for correct answer and 1 mark for explanation)

ANTIGEN is not a protective epitope. As the concentration of antibodies is the same in both groups, the BCG vaccination did not cause the memory B cells to proliferate and release antibodies. The T cell response also was not triggered. No marks will be given if the explanation is simply a restating of the answer from (9).

11) You are interested in the "ANTIGEN" epitope in the SARS CoV-2 virus and decide to study it further. You have SARS CoV-2 virus samples the were taken during different years of the pandemic (March 2020, April 2021, March 2022 and March 2023). You isolate the genome of the viruses from these samples and sequence them in the region that codes for the "ANTIGEN" epitope. You find that this region has changed in over the 4 years shown below.

March 2020: ANTIGEN (in all samples)
April 2021: ANTIGEN (in 80% samples) and ANTIPEN (in 20% of the samples)
March 2022: ANTIGEN (in 50% samples) and ANTIPEN (in 50% of the samples)
March 2023: ANTIPEN (in all samples)

It appears that this protein sequence is evolving. Circle the correct answer(s) among the choices below. (2 marks)

A) The ANTIGEN epitope gives the virus a survival advantage in humans
B) The RdRP enzyme does not give rise to any errors while replicating the virus genome
C) The ANTIPEN epitope gives the virus a survival advantage in humans
D) The viruses having the "ANTIPEN" sequence will retain that sequence forever

The ANTIGEN epitope is being lost in the population so it does not give the virus a survival advantage. The RdRP enzyme must give rise to errors for evolution. The viruses

having ANTIPEN will continue to evolve based on new selection pressures. This explanation is not required for getting marks.

Part B:

12) After working on the SARS Cov2 virus and making some interesting discoveries, you now decide to start working on cancer. You have a chemical molecule that you think may be an anti-cancer drug. You call this molecule CanCure. Before proceeding further on CanCure, you study two known anti-cancer drugs. The first one, Taxol, blocks the action of microtubules. Circle the stage(s) of the eukaryotic cell cycle will be acted upon by Taxol. (1 mark)

A) G1
B) S
C) G2
D) M

13) Another anti-cancer drug, Methotrexate, blocks the synthesis of DNA precursors. Circle the stage(s) of the cell cycle will be acted upon by Methotrexate. (1 mark)

A) G1
B) S
C) G2
D) M

Anyone who gave G1 as an answer, either alone or with S, gets full marks.

14) You take cancer cells, treat them with CanCure and study what happens to glucose metabolism. Write down three stages of glucose metabolism. (1 mark for each correct answer)

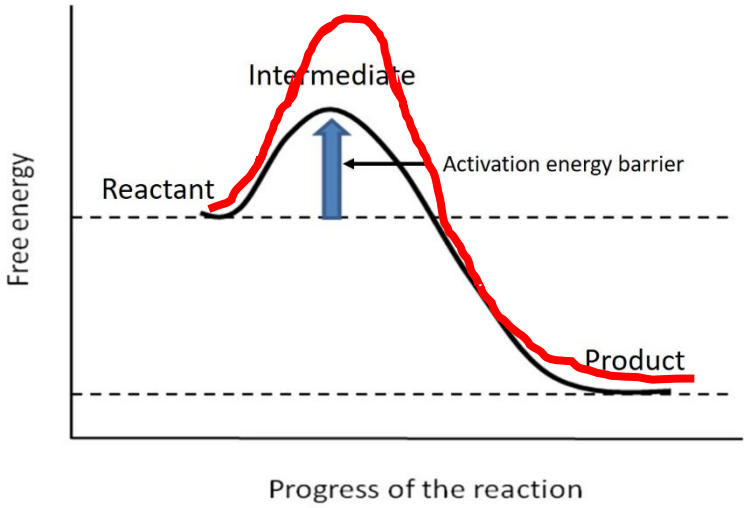
Glycolysis, TCA cycle and Electron Transport Chain (ETC). Anyone who wrote fermentation instead of one of these gets marks.

15) Which stage out of the three you mentioned above is used primarily by cancer cells when they have less oxygen? (1 mark)

Glycolysis. Anyone who wrote fermentation also gets marks.

16) You test CanCure and find that the cancer cells are being killed by this chemical molecule. The mechanism of CanCure is that it blocks one of the enzymes of glycolysis. The graph below shows the enzyme reaction. On this graph, draw the reaction in the presence of CanCure. (2 marks)

Enzymes are biological catalysts and so they would lower the activation energy of the reaction. An inhibitor of the enzyme would result in the activation energy being higher, as shown on the graph. Explanation not required for marks.



17) Although non-cancerous cells also carry out glycolysis, CanCure is more effective at killing cancer cells. Explain this briefly using your knowledge of metabolism. (2 marks)

If CanCure is not a complete inhibitor of the enzyme, non-cancerous cells may be able to generate some products of glycolysis and these could proceed into the TCA cycle and ETC for generating more ATP. Cancerous cells are entirely dependent on glycolysis so they would be killed.

Acceptable answers: Cancer cells show higher rate of glycolysis than non-cancerous cells.

Give 0 marks for any factually incorrect answers. Could be other answers also. Please send an email to all of us with potentially correct answers.

18) After successfully applying your knowledge from BB101 to different diseases you feel that you may wish to start-up a new company based on biology. What name would you give this company? (1 mark)

1 mark for any answer!