TAMPINES MERIDIAN JUNIOR COLLEGE

JC2 PRELIMINARY EXAMINATION

CANDIDATE NAME	
CIVICS GROUP	

H2 BIOLOGY 9744

Paper 3 Long Structured and Free Response Questions

18 September 2020

2 hours

READ THESE INSTRUCTIONS FIRST

Write your name and Civics Group in the spaces at the top of the page.
Write in dark blue or black pen on both sides of the paper.
You may use an HB pencil for any diagrams, graphs or rough working.
Do not use staples, paper clips, glue or correction fluid.
The use of an approved scientific calculator is expected, where appropriate.

Section A
Answer **all** questions.

Section B
Answer **ONE** question.

You may lose marks if you do not show your working or if you do not use appropriate units.

At the end of the examination, fasten all your work securely together.

The number of marks is given in brackets [ ] at the end of each question or part question.

For examiner's Use	
Section A	
1	/ 32
2	/ 18
Section B	
3 or 4	/ 25
Total	**/ 75**

This document consists of **17** printed pages and **1** blank page.

Section A

Answer all questions in this section.

QUESTION 1

The cystic fibrosis transmembrane conductance regulator (CFTR) protein is an ion channel. In the lung, the CFTR ion channel moves chloride ions from inside the cell to outside the cell.

Cystic fibrosis (CF) is a serious genetic condition caused by recessive mutations in the gene for the CFTR protein. One of the most common mutated alleles of this gene is known as ΔF508, a deletion of the amino acid phenylalanine at the 508th amino acid position of the polypeptide. This mutation results in a CFTR protein that does not conduct chloride ions.

Features of CF, which are also observed in heterozygotes, include:

- a reduction in water loss through epithelial cell membranes
- a reduction in sweating.

When there is less water outside the cells, the mucus in the airways becomes dehydrated and thickens, as shown in Fig. 1.1. The cilia becomes unable to sweep properly when the mucus is thick as sticky mucus weighs them down.

Because the cilia are unable to move properly, mucus gets stuck in the airways, making it difficult to breathe. In addition, germs caught in the mucus are no longer expelled from the airway, allowing them to multiply and cause infections. Thick mucus in the lungs and frequent airway infections are some of the most common problems that people with CF face.

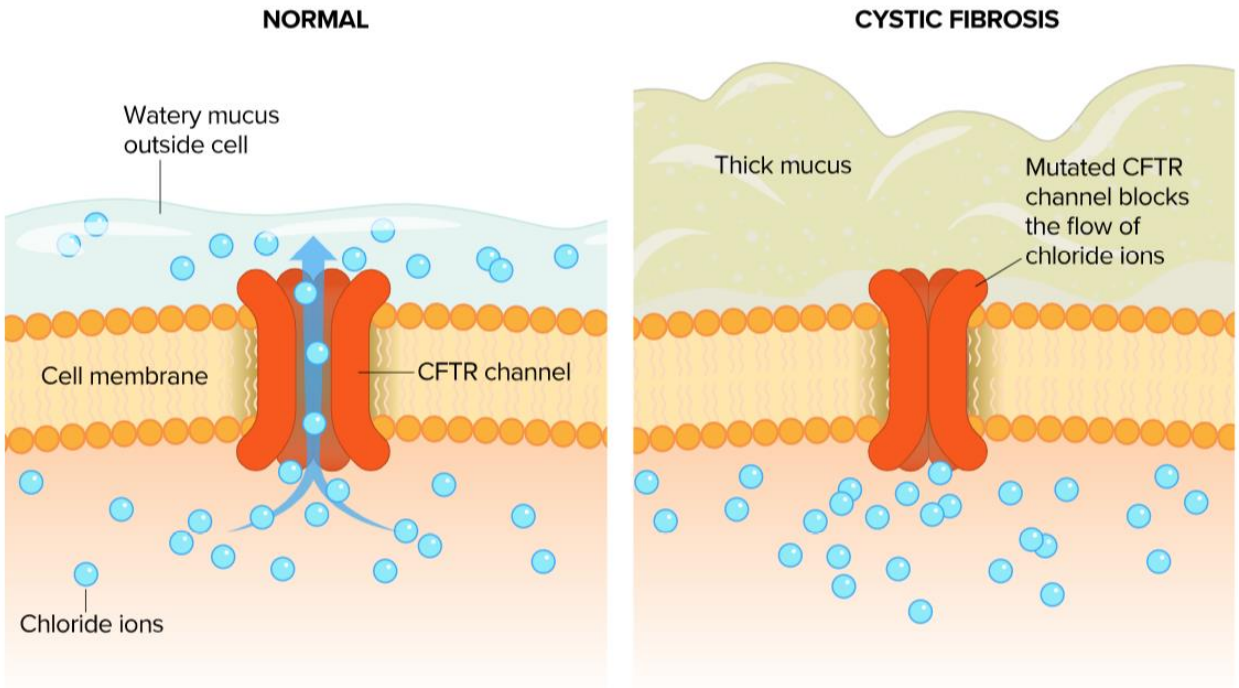

Fig. 1.1

a) Describe how the ΔF508 mutant CFTR protein may bring about a reduction in water loss through epithelial cell membranes. [3]

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b) Explain why inherited diseases, in general, have low occurrences in the general population.[3]

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c) CF is one of the most common inherited diseases. This unusually high occurrence has given rise to the suggestion that carriers of the ΔF508 allele may have a selective advantage over non-carriers.

Approximately 1 in 30 people in the European and North American populations are carriers of the defective allele ΔF508.

Within the European and North American populations, calculate the probability that a newly-born baby will be homozygous for this allele.

You should show your working. [2]

Probability = ……

d) There are at least 1500 different mutated alleles of the CFTR gene. These alleles have been classified into six classes according to the mechanism by which they disrupt the synthesis, trafficking and function of CFTR protein.

The six classes are described in Table 1.1.

Table 1.1

class of mutation	effect of CFTR mutation
class I	complete lack CFTR protein
class II	misfolded CFTR protein not transported to the cell surface
class III	reduced or lack of CFTR channel opening ('gating' defect)
class IV	a 'misshaped' CFTR pore that restricts the movement of chloride ions through the channel ('conductance' defect)
class V	splicing defect with a great reduction in normal CFTR proteins
class VI	decreased CFTR protein stability in the cell surface that leads to its removal and degradation

i) State the most likely class of mutation to which ΔF508 belongs. [1]

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ii) With reference to Table 1.1, explain why in the population of individuals who carry two recessive alleles, the symptoms of CF may range from mild to severe. [3]

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iii) Suggest how, in the class VI mutation, the unstable CFTR protein is removed from the cell surface membrane **and** subsequently degraded. [4]

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Cholera is caused by a toxin secreted by the bacterium *Vibrio cholerae* in the gut. This toxin enters the epithelial cells and activates an intracellular G-protein that leads to an excessive amount of cyclic AMP (cAMP). cAMP binds to CFTR to facilitate abnormally high movement of chloride out of the cell, increasing water loss from the gut epithelial cells. This results in severe diarrhea and may lead to death if untreated.

In an experiment carried out in 1994, it was shown that when mice that were heterozygous for ΔF508 were exposed to cholera toxin, they lost 50% less water than homozygous dominant mice also exposed to cholera toxin.

This supported a suggestion that the selective advantage of carrying the ΔF508 allele may be protection from the effects of cholera.

e) Suggest how the ΔF508 allele might be expected to convey a selective advantage in areas of the world where cholera is common. [4]

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f) In 2000, a further experiment to investigate the possible link between the ΔF508 allele and the severity of cholera in humans was conducted. To do this, the effect of prostaglandin was measured in human subjects including:

- some who had cystic fibrosis (homozygous for ΔF508)
- some who were carriers (heterozygous for ΔF508)
- a control group who did not have cystic fibrosis and did not carry ΔF508.

Prostaglandin is a chemical that increases water loss from epithelial cells by increasing chloride secretion through the CFTR protein. The results are shown in Fig. 2.1.

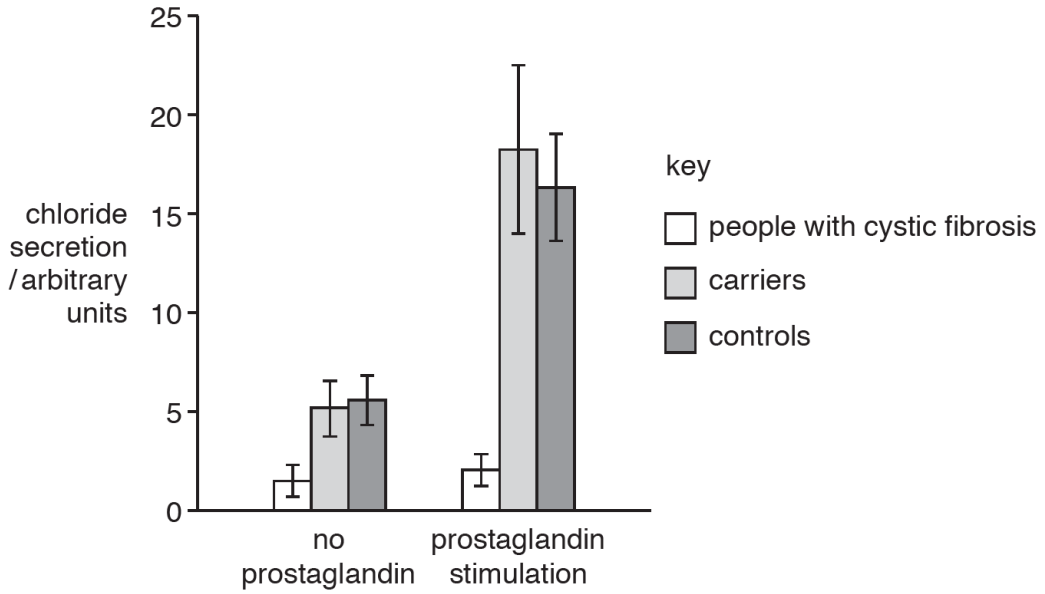

Fig. 2.1

i) Describe the results obtained in the study carried out in 2000. [3]

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ii) Suggest why a chemical (prostaglandin) was used to increase water loss from epithelial cells in the 2000 study. [2]

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iii) The studies carried out in 1994 and 2000 differ in various aspects, such as the results obtained, methodology and conclusions. One such difference is the lack of statistical data for 1994.

Comment on other differences between the studies carried out in 1994 and 2000. [3]

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g) In Europe and North America, the frequency of the Δ*F508* allele is relatively high, although there are now very few cases of cholera. In the past, cholera was very common throughout Europe.

Suggest how this may explain the present day frequency of the Δ*F508* allele in Europe. [2]

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h) In parts of Asia and Africa with hot climates, there are many cases of cholera but the frequency of the Δ*F508* allele is relatively low. Some scientists have therefore suggested that the distribution of the Δ*F508* allele is related to temperature, as well as the incidence of cholera.

Suggest an explanation for the relatively low occurrence of the Δ*F508* allele in hot climates. [2]

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[Total: 32]

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QUESTION 2

An investigation into a treatment for people who are infected with HIV was carried out involving a large number of people from over 70 countries. In September 1994, the patients began receiving a treatment called HAART (highly active antiretroviral therapy). They were monitored over the following years for helper-T cell counts and clinical outcomes. Data were analyzed within six-month periods.

Fig. 2.1, on the next page, shows the results of this investigation. The combined AIDS and death rate per six-month period is a measure of the number of patients who developed an illness characteristic of AIDS or who died.

a) HIV infects helper-T cells. If the infection progresses, the number of helper-T cells decreases. This decrease makes people more susceptible to opportunistic infections.

i) Helper-T cells are usually dormant unless activated.

Outline how helper-T cells are activated **and** the roles they play in the immune system. [3]

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ii) Suggest what is meant by *opportunistic infections*. [1]

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b) Explain why HIV-infected individuals are usually also put on oral antibiotic treatment, despite the fact that antibiotics have no effect on viruses. [1]

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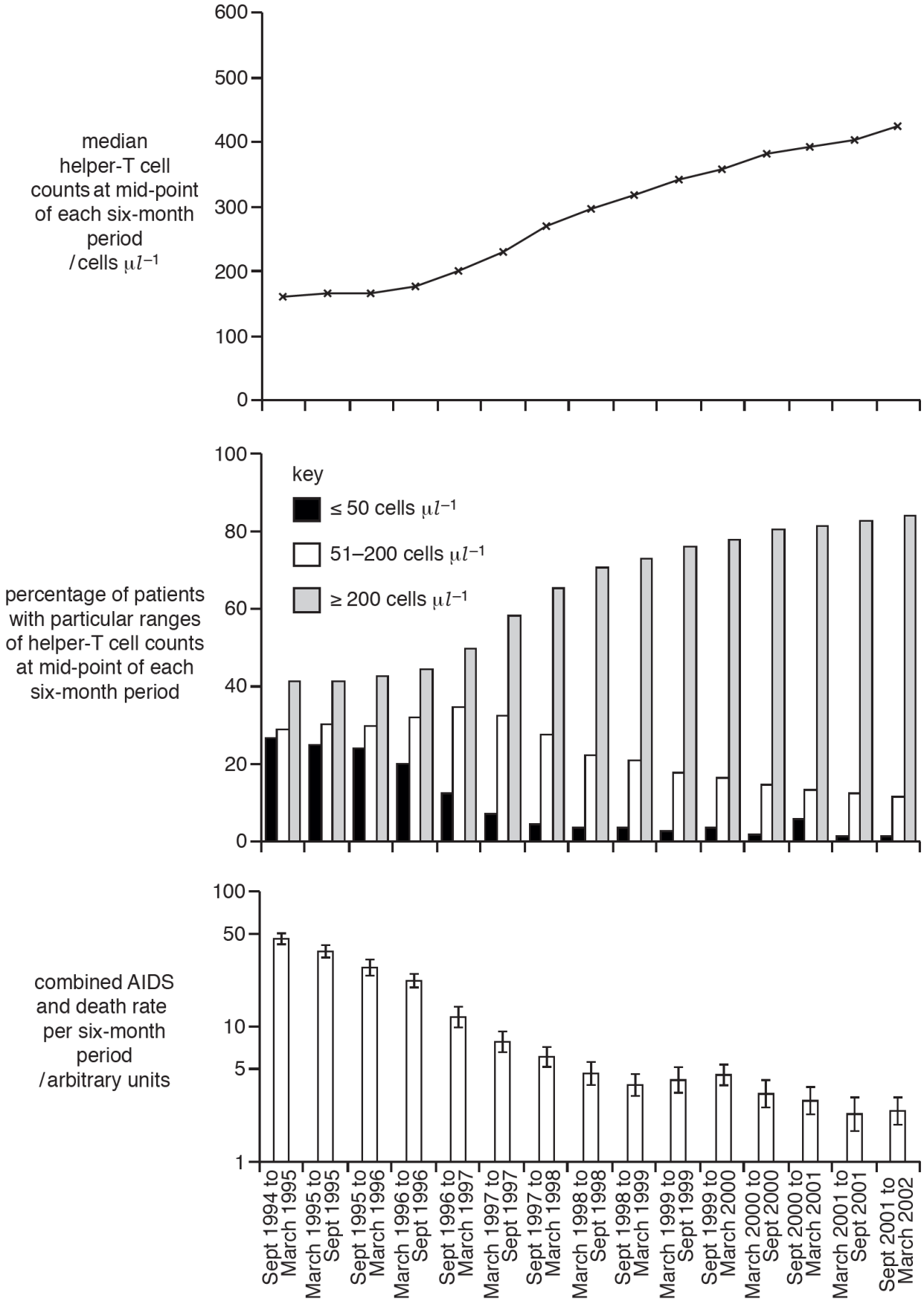
median helper-T cell counts at mid-point of each six-month period /cells μl⁻¹
600
500
400
300
200
100
0
percentage of patients with particular ranges of helper-T cell counts at mid-point of each six-month period
100
80
60
40
20
0
key
≤ 50 cells μl⁻¹
51–200 cells μl⁻¹
≥ 200 cells μl⁻¹
combined AIDS and death rate per six-month period /arbitrary units
100
50
10
5
1
Sept 1994 to March 1995
March 1995 to Sept 1995
Sept 1995 to March 1996
March 1996 to Sept 1996
Sept 1996 to March 1997
March 1997 to Sept 1997
Sept 1997 to March 1998
March 1998 to Sept 1998
Sept 1998 to March 1999
March 1999 to Sept 1999
Sept 1999 to March 2000
March 2000 to Sept 2000
Sept 2000 to March 2001
March 2001 to Sept 2001
Sept 2001 to March 2002

Fig. 2.1

c) Suggest what might be concluded from the data in Fig. 2.1 about HAART as a means of controlling the consequences of HIV infection **and** comment on the validity and limitations of the data. [5]

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d) Nucleotide Analogue Reverse Transcriptase Inhibitor (NtARTi) drugs are used to treat HIV infection. These molecules resemble the four deoxyribonucleotides used to make DNA. However, the 3' carbon of the sugar in NtARTi is linked to two hydrogen atoms.

State the role of reverse transcriptase in HIV **and** explain how NtARTi drugs interfere with the role of reverse transcriptase. [5]

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e) A technique called RNA interference has also been shown to interfere with the replication of HIV. Double-stranded RNA molecules, 21 to 23 nucleotides long, were added to a culture of helper-T cells infected with HIV. The sequence of this small interfering RNA (siRNA) matches part of the HIV protease gene. Once inside the helper-T cell, the two strands of the siRNA separate into single strands. One of the strands is identical in sequence to part of the mRNA of the HIV protease.

Using the above information, explain how this siRNA is able to interfere with HIV replication. [3]

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[Total: 18]

Section B

Answer **ONE** question.

Write your answers on the lined paper provided at the end of this Question Paper.
Your answers should be illustrated by large, clearly labelled diagrams, where appropriate.
Your answers must be in continuous prose, where appropriate.
Your answers must be set out in parts (a) and (b), as indicated in the question.

QUESTION 3

a) The Central Dogma of Molecular Biology depicts the unidirectional flow of genetic information to synthesize polypeptides, using DNA as the blueprint.

Outline the processes governed by the Central Dogma of Molecular Biology **and** explain, using specific examples, why the Central Dogma may not always hold true. [13]

b) Inorganic ions have an electrical charge, owing to the loss or gain of electrons. Despite playing a diverse role in cells, from regulating a variety of processes to being part of cellular structures, some inorganic ions are toxic to cells.

Discuss the important roles played by various inorganic ions **and** suggest why some inorganic ions are toxic to cells. [12]

[Total: 25]

QUESTION 4

a) Restriction endonucleases are enzymes that cut at specific nucleotide sequences within a DNA molecule. Total DNA isolated from human cells, when digested by restriction endonucleases, produces tens of thousands of DNA fragments of varying length.

Describe how the presence of insulin gene from a human cell can be detected after restriction digestion **and** explain the theoretical basis behind the procedures. [13]

b) Lactose catabolism and tryptophan synthesis are regulated in similar manner in bacterial cells.

Describe how the metabolism of lactose in bacterial cells is regulated **and** explain the advantages of such a regulation system in the context of tryptophan synthesis. [12]

[Total: 25]

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☺ End of Paper 3 ☺