H3

MINISTRY OF EDUCATION, SINGAPORE
in collaboration with
CAMBRIDGE INTERNATIONAL EDUCATION
General Certificate of Education Advanced Level

BIOLOGY **9816/01**

Paper 1 **For examination from 2026**

SPECIMEN INSERT **2 hours 30 minutes**

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INSTRUCTIONS

- This insert contains information for Question 1.
- You may annotate this insert and use the blank spaces for planning. **Do not write your answers** on the insert.

This document has **4** pages.

Singapore Examinations and Assessment Board

CAMBRIDGE International Education

Information for Question 1

The information provided in this insert is based on a number of published scientific articles. Other published articles may not agree with all of this information.

The cystic fibrosis transmembrane conductance regulator glycoprotein (CFTR)

CFTR contains a chain of 1480 amino acids, which has to be fully folded before being positioned in the cell surface membrane. The glycoprotein consists of two membrane-spanning domains (MSD1 and MSD2), two nucleotide-binding domains (NBD1 and NBD2) and a regulatory domain (RD). MSD2 contains glycosylation sites.

Figure 1.1(a) shows how CFTR is arranged when the ion channel is shut and Figure 1.1(b) shows how CFTR is arranged when the ion channel is open.

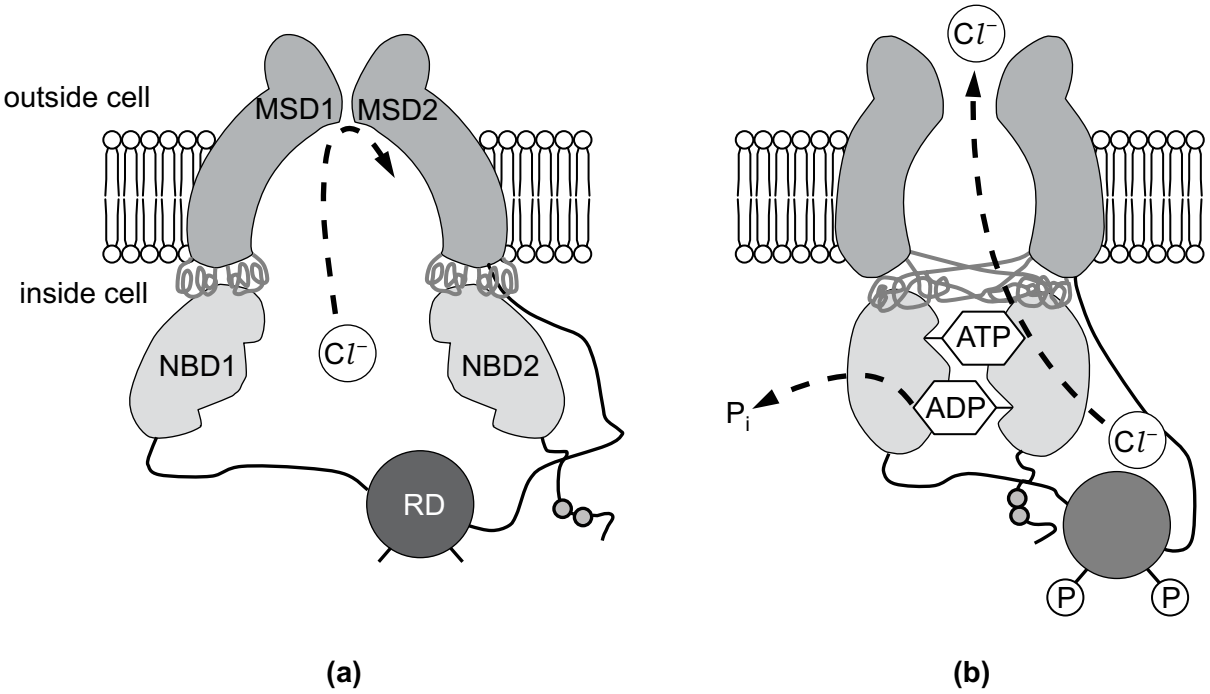

Figure 1.1

CFTR normally works by transporting chloride ions out of a cell. This usually decreases the water potential outside the cell, causing movement of water.

However, in the sweat glands CFTR assists in reducing the loss of NaC*l* by reabsorbing chloride ions.

A mutation in the *CFTR* gene can cause the disease known as cystic fibrosis. There are approximately 1500 known mutations of this gene, all of which are inherited in an autosomal recessive manner.

Table 1.1 shows the percentage of people who are carriers of cystic fibrosis in different ethnic groups.

Table 1.1

ethnic group	percentage of carriers
Ashkenazi Jews	4.17
European / North American	4.00
African–American	1.54
Asian	1.06

Figure 1.2 shows the distribution of the more common *CFTR* gene mutations among the four ethnic groups from Table 1.1. For example, Figure 1.2 shows that three of these more common gene mutations are unique to the Asian ethnic group.

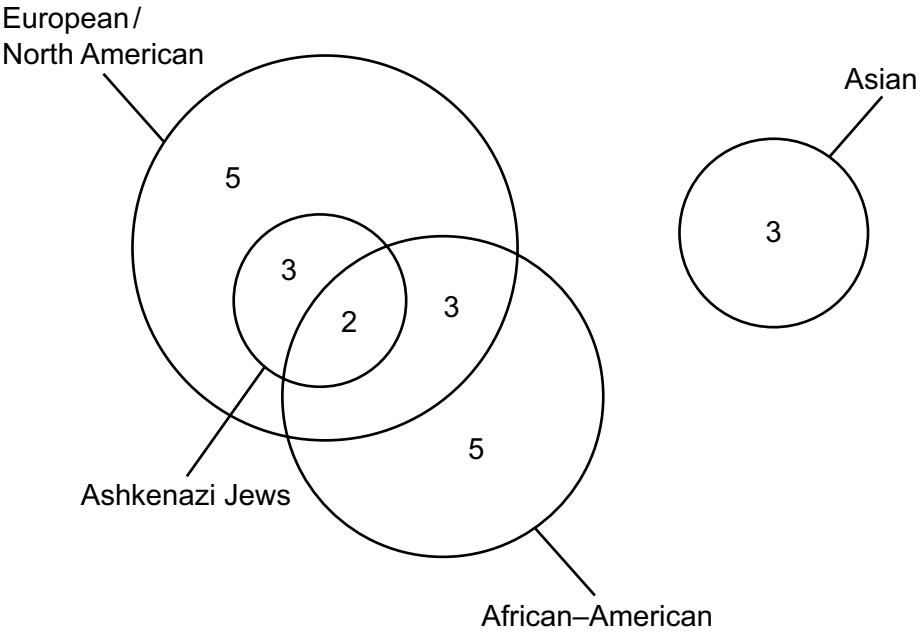

Figure 1.2

The 1500 different CFTR gene mutations have been classified into six classes, dependent on how each type of mutation may disrupt the normal functioning of CFTR. The six classes are described in Table 1.2.

Table 1.2

class of mutation	**effect of *CFTR* mutation**
class I	no CFTR produced
class II	defect in CFTR processing and transport through cell
class III	defective channel regulation
class IV	reduced chloride transport through CFTR
class V	splicing defect with reduced production of normal CFTR
class VI	decreased CFTR stability

When a person inherits two mutated *CFTR* alleles, these mutated alleles may be the same or different. The interaction of varying combinations of *CFTR* mutated alleles results in the disease having a complex range of phenotypes depending on the extent to which the function of CFTR is affected.

The most common mutation of the *CFTR* gene also results in the most severe symptoms and, up until the 1960s, it was rare for individuals with this phenotype to survive into their mid-teens. In recent years, life expectancy has increased greatly.

Research has suggested that this gene mutation arose about 50 000 years ago. It is unlikely that such a lethal mutation would survive unless there was some selective advantage.

One suggested selective advantage is that *CFTR* mutations result in a reduction in the effects of cholera. Cholera is caused by infection of the small intestine with the bacterium *Vibrio cholerae*. The bacterium releases a toxin that binds to a glycosylated region of a cell surface membrane receptor, resulting in an increase in cyclic AMP (cAMP). cAMP causes the CFTR ion channel to open more, which eventually results in excess chloride ion secretion and the consequent loss of large amounts of water in diarrhoea. This can result in death. Carriers of *CFTR* gene mutations would have fewer functional CFTR glycoproteins and so would **not** be as likely to die from cholera.

