

1. The bacterium *Escherichia coli* (*E. coli*) uses glucose as a respiratory substrate. In the absence of glucose, *E. coli* can use lactose. The use of a different substrate is determined by the interaction between genes and the environment.

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[Total 5 marks]

2. Cystic fibrosis (CF) in humans is caused by mutations of a gene coding for transmembrane protein (CFTR) which acts as an ion pump. A large number of different mutations of the gene have been found. Explain what is meant by a gene mutation.

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[Total 2 marks]

3. CFTR regulates the transport of chloride ions ( $\text{Cl}^-$ ) across the plasma (cell surface) membrane. Tissues that express the normal CFTR allele secrete alkaline fluids, whereas the secretions of tissues expressing some mutant alleles are acidic.

The transport of  $\text{Cl}^-$  by epithelial cells expressing the normal CFTR allele was compared with that by epithelial cells expressing one of 10 different mutant CFTR alleles. The results are shown in the table below.

In the table, normal digestive functioning of the pancreas associated with a particular allele is indicated with a tick (✓) and the absence of normal functioning by a cross (✗).

CFTR allele	percentage of Cl <sup>-</sup> transported in comparison with normal allele	normal digestive functioning in pancreas
normal	100	✓
mutation 1	6	✗
mutation 2	4	✗
mutation 3	0	✗
mutation 4	3	✗
mutation 5	1	✗
mutation 6	33	✓
mutation 7	41	✓
mutation 8	46	✓
mutation 9	37	✓
mutation 10	44	✓

With reference to the information given in the table, explain why some mutant CFTR alleles allow normal digestive functioning of the pancreas and others do not.

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[Total 3 marks]

4. A product manufactured using microorganisms is single cell protein (SCP).

Describe how a protein would be synthesised in the cell of a single celled fungus.



*In your answer, you should make clear the sequence of the steps in the process.*

[Total 10 marks]

- 5.
- DNA is found in the nucleus of a cell.
  - During interphase DNA replicates.
  - DNA is involved in the transcription stage of protein synthesis.

The following statements, **A** to **H**, refer to events that may take place during:

- ◆ DNA replication **only**
- ◆ transcription **only**
- ◆ **both** DNA replication **and** transcription
- ◆ **neither** DNA replication **nor** transcription.

Complete the table by marking the appropriate boxes with a tick (✓) if the event takes place or a cross (✗) if it does not take place.

		DNA replication	transcription
<b>A</b>	Nucleotides line up along an exposed DNA strand.		
<b>B</b>	The whole of the double helix 'unzips'.		
<b>C</b>	Uracil pairs with adenine.		
<b>D</b>	A tRNA triplet pairs with an exposed codon.		
<b>E</b>	Both DNA polynucleotide chains act as templates.		
<b>F</b>	Adjacent nucleotides bond, forming a sugar-phosphate backbone.		
<b>G</b>	The original DNA molecule is unchanged after the process.		
<b>H</b>	Adenine pairs with thymine.		

[Total 8 marks]

6. (a) Part of the **DNA** base sequence coding for a protein is shown below.

**A T G G C C T A A G T G**

- (i) State the corresponding base sequence of **mRNA**.

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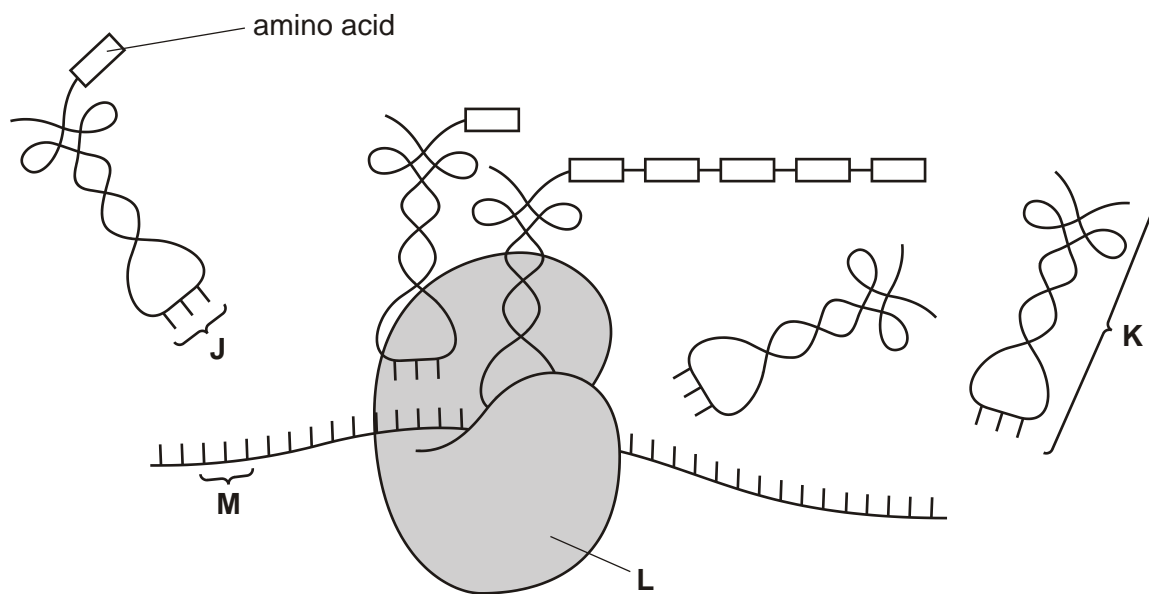
[2]

- (ii) Name the process by which the DNA code is transferred to mRNA.

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[1]

(b) The figure below is a diagram that shows the stage in protein synthesis when amino acids are joined in the correct sequence to make the primary structure of the protein.



(i) Name **J** to **M**.

The group of bases at **J** .....

**K** .....

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**L** .....

The group of bases at **M** .....

[4]

(ii) Using the information in the diagram to help you, explain how amino acids become arranged into the correct sequence in the primary structure of the protein.

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[4]

(c) Mistletoe is a parasitic plant that produces lectin 1, a ribosome-inactivating protein. Lectin 1 inhibits protein synthesis in the cells of the host plant.

Suggest how lectin 1 could inhibit protein synthesis.

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[2]

[Total 13 marks]

- 7. Liver cells damaged by hepatitis infection switch on a gene called Fas, which causes them to self-destruct. Pioneering research has produced a strikingly successful treatment for hepatitis in mice. The Fas gene was silenced by the technique of RNA interference.

RNA molecules, 21 to 23 nucleotides long, were injected into mice with hepatitis. The sequence of this 'small interfering RNA' (siRNA) matched part of the Fas gene. Once in the liver cell the two strands of the siRNA were separated so that one strand could bind to the mRNA transcript of the Fas gene. This caused the mRNA to be destroyed by enzymes, therefore preventing the gene product from being made.

This therapy prevented liver cell death and considerably increased the survival of mice with hepatitis.

- (a) (i) Describe a way in which the **function** of mRNA differs from that of DNA.

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[2]

- (ii) Describe **two** ways in which the **structure** of siRNA differs from mRNA.

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[2]

- (b) Describe how one strand of the siRNA can bind to the mRNA of the Fas gene.

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[3]

[Total: 7 marks]

8. The technique of RNA interference has been used to slow replication of HIV (Human Immunodeficiency Virus) *in vitro*. siRNA sequences that match the RNA genome of HIV can be used to trigger destruction of this RNA, preventing HIV from multiplying.

Another approach is to use RNA interference to silence genes for cell surface receptors, such as the CD4 and CCR5 molecules on human white blood cells. If these genes do not produce their protein antigens, HIV cannot bind to and infect the white blood cells.

The table below summarises some information about the two cell surface receptors used by HIV to bind to and infect white blood cells.

	cell surface receptor	
	CD4	CCR5
type of cell with this receptor	T lymphocyte white blood cells which divide by mitosis	macrophage cells which are long-lived and do not undergo mitosis
function of receptor	important roles in the immune system	limited, since 1% of people lack this receptor and show some resistance to HIV

Experiments have been carried out where,

- siRNAs matching the CD4 mRNA were introduced into test tube populations of T lymphocytes;
- siRNAs matching the CCR5 mRNA were introduced into test tube populations of macrophages.

In both cases HIV was present but the presence of the siRNAs reduced its replication.

(i) Use the table to suggest with reasons which of the two test tube experiments showed most reduction of HIV replication.

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- (ii) Explain which receptor would be the best target for RNA interference if the approach was used as a therapy for humans infected with HIV.

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[1]

[Total: 3 marks]

9. A research team was investigating the properties of a newly-discovered enzyme, the product of which was a valuable drug.

This enzyme had been extracted from cells of a marine worm, found in the North Atlantic, where the temperature is always close to 5 °C. All the proteins of such animals are adapted to function at low temperatures.

Three water baths were set up at 15, 20 and 25 °C. Into each bath was placed a tube containing 1 cm<sup>3</sup> of the enzyme solution and a tube containing 10 cm<sup>3</sup> of concentrated substrate solution. On reaching the required temperature, the enzyme and substrate were quickly mixed and kept in the water bath.

There was a **large excess of the substrate**, so that substrate concentration was **not** a limiting factor.

Samples were taken from each tube at regular intervals and the concentration of the drug in these samples was determined. The results are shown in Fig. 1.

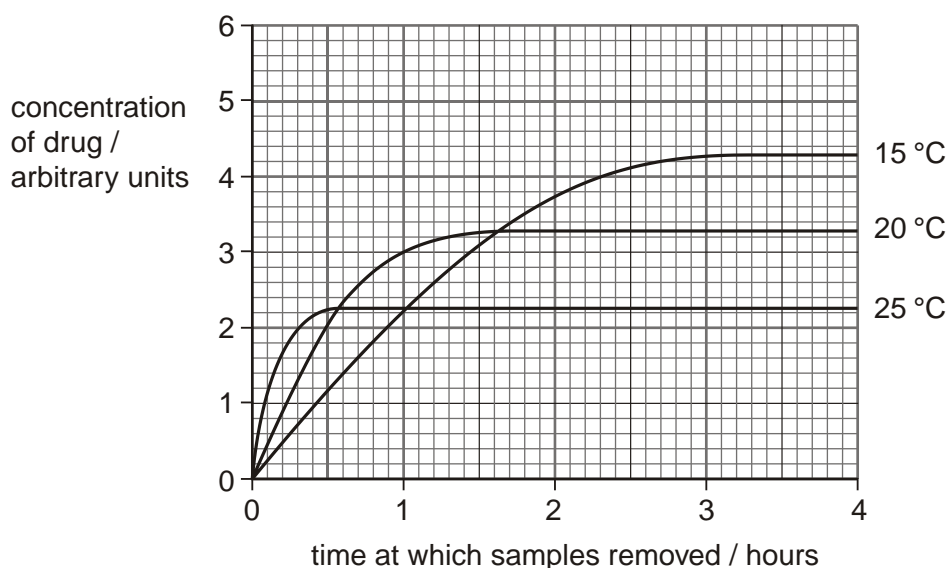


Fig. 1

(a) Using Fig. 1,

(i) describe what happened to the concentration of the drug in the tube at 15 °C;

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[2]

(ii) explain why the concentration of the drug changed in the way you have described.

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[2]

(b) State **one** factor, **not mentioned in the account of the investigation**, which would have been kept constant in all the tubes for the results to be valid.

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[1]

(c) Predict **and** explain the effect of carrying out the same procedure at 5 °C.

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[3]

Fig. 2 represents part of the primary and tertiary structure of the newly-discovered enzyme, including its active site. The amino acids are represented by circles, which are numbered to show their position in the primary structure.

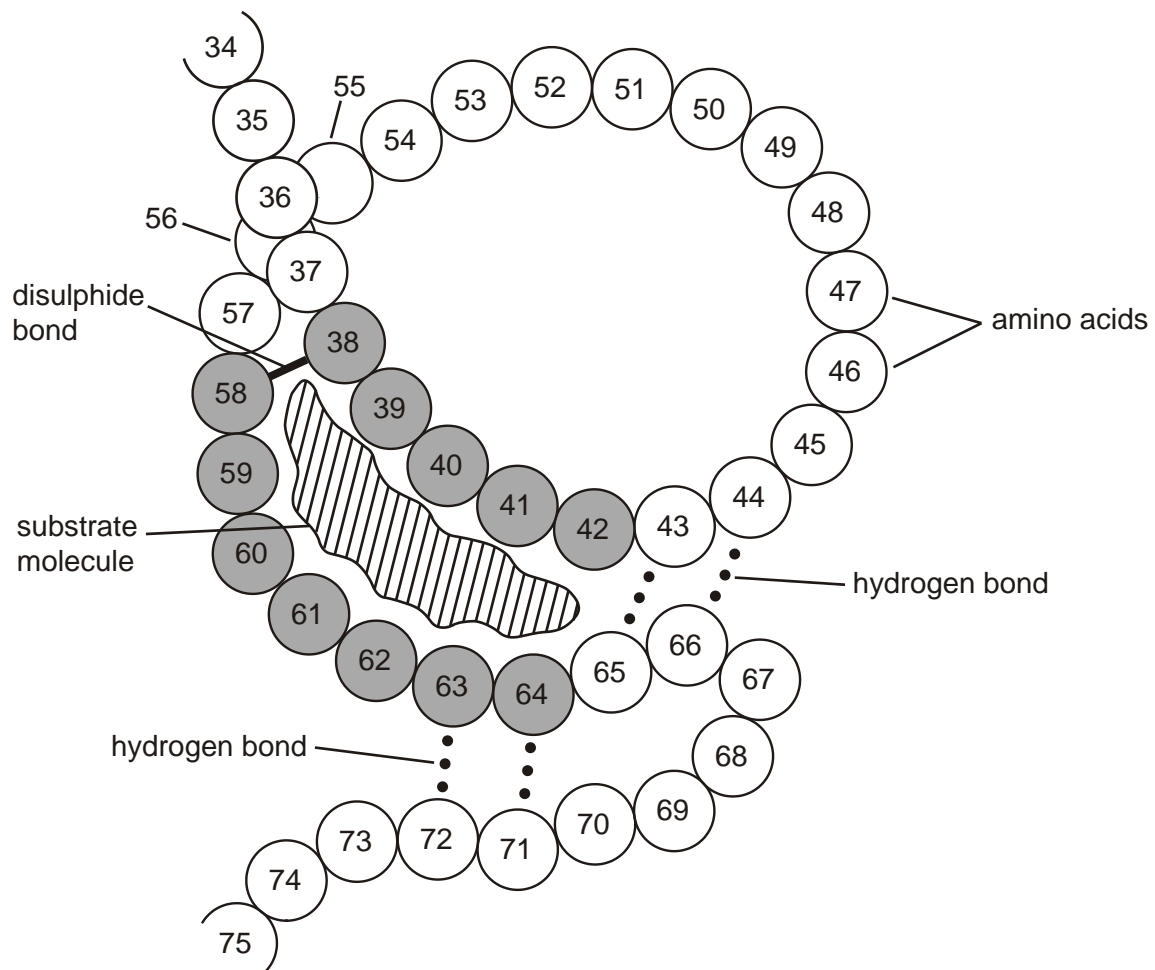


Fig. 2

(d) The research team wanted to change the structure of the enzyme so that it would function at higher temperatures to produce greater yields of the drug. They used a technique called **site directed mutagenesis**. In this technique:

- single changes to the amino acid sequence of the enzyme are planned
- the gene coding for the enzyme produced by the worm is isolated
- specific changes to the gene are made, in order to achieve the planned changes to the amino acid sequence
- the modified gene is introduced into a bacterium
- the offspring of the bacterium produce the changed enzyme molecules

(i) Suggest why it would be important that this procedure did **not** change any of the amino acids shaded grey in Fig. 2.

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[1]

(ii) The amino acids numbered 44 and 66 have side chains that link by hydrogen bonding.

Suggest why the research team might plan to replace these two amino acids with the amino acid cysteine, which forms disulphide bonds.

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- (e) Explain why the technique of site directed mutagenesis involves changing nucleotide sequences.

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[Total 13 marks]

- 10. (a) Explain what is meant by *heritability*.

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[2]

- (b) Rice plants may have, in addition to a main stem, a number of side shoots (tillers) growing from ground level. These tillers may also branch. The ability to grow tillers is controlled by a single gene with two alleles, **T/t**. Plants with the genotype **tt** have a single grain-bearing stem and no tillers.

Explain why the heritability of rice tiller growth is likely to be high.

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[2]

- (c) Allele **T** codes for a protein which regulates transcription. Expression of allele **T** allows stimulation of mitosis in the buds which become tillers.

Allele **t** has a 'stop' triplet within its DNA sequence as well as at its end.

- (i) State what is meant by a 'stop' triplet.

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[2]

- (ii) Describe the effect of the 'stop' triplet **within** the DNA sequence of allele **t**.

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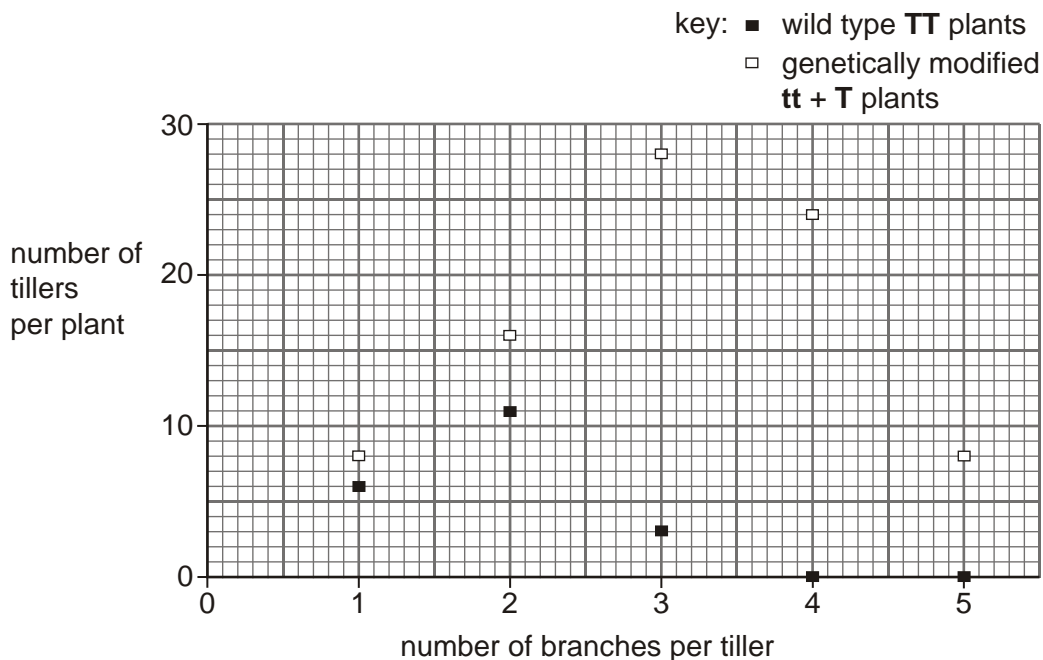
- (iii) Suggest how the protein encoded by allele **T** may regulate transcription.

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[2]

- (d) The number of tillers per plant and the number of times each tiller branched were recorded for wild type **TT** plants and for **tt** plants which had been given a copy of allele **T** by genetic engineering.

The results are shown below.



- (i) With reference to the figure above, compare the effect of the two rice genotypes on tiller growth.

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- (ii) Suggest why the expression of allele **T** may be changed when it is transferred by genetic engineering into rice plants with the genotype **tt**.

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[2]

[Total 15 marks]

11. When eaten by insects such as the larvae known as earworms, celery plants produce the chemical signal jasmonate (**J**). This stimulates insecticide production. Insecticide begins to build up in the leaves after 24 hours and reaches maximum concentration after 4 to 5 days.

However, earworms become resistant to this insecticide by switching on a gene in the gut lining that codes for an enzyme (**E**) to break it down.

Newly hatched earworms were divided into four groups:

- **not** exposed to **J** but fed on celery leaves containing insecticide
- **not** exposed to **J** but fed on celery leaves with **no** insecticide
- exposed to **J** and fed on celery leaves containing insecticide
- exposed to **J** and fed on celery leaves with **no** insecticide.

The earworms continued to feed on these diets until they pupated.

The percentage mortality of the different groups of earworms and the relative expression of the gene coding for enzyme **E** are shown below. In the table, a tick (✓) indicates the presence of insecticide in the celery leaf diet and a cross (✗) indicates its absence.

group of earworms	presence of insecticide in celery leaf diet	relative expression of gene coding for enzyme <b>E</b>	mortality / %
<b>not</b> exposed to <b>J</b>	✓	1.0	86.7
	✗	0.0	15.6
exposed to <b>J</b>	✓	6.5	48.3
	✗	5.5	6.7



Using the information given, explain the differences in percentage mortality of the different groups of earworms.

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[Total 4 marks]

12. Read the passage below and answer the questions which follow.

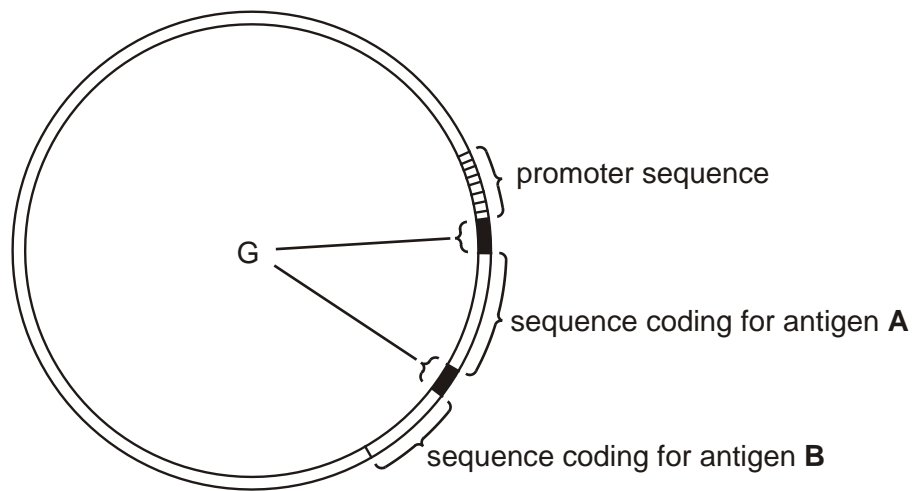
### **DNA vaccines**

Mice and monkeys have been successfully immunised against several important infectious diseases using experimental DNA vaccines, in the form of plasmids. Plasmids are small circular DNA molecules.

During the 1990s, researchers found that mouse muscle and other mouse tissues were able to absorb plasmids which had been injected into the animals. Any genes that were part of this plasmid DNA were transcribed and translated. The resulting proteins were transferred to the plasma membranes (cell surface membranes) of the mouse muscle cells. The proteins were exposed on the muscle plasma membranes together with receptor molecules that allow the immune system to recognise cells as self or non-self. Proteins that are presented at the cell surface in this way stimulate the lymphocytes of the immune system very effectively.

This discovery allows plasmid DNA to be used as a vaccine, even though the DNA does not itself act as an antigen. Most vaccines contain proteins, or fragments of proteins, that are extracted from the surface of pathogens. It is a complex and costly procedure to purify these protein antigens.

The figure below shows a simplified diagram of a DNA vaccine. This plasmid codes for two antigens, **A** and **B**.



(a) State **three** ways in which the structure of plasmid DNA differs from the structure of a protein molecule.

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[3]

(b) (i) Define the term *antigen*, as used in the passage.

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[1]

- (ii) Suggest why proteins presented at the cell surface are able to stimulate an immune response more effectively than proteins dissolved or suspended in the blood or tissue fluids.

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[1]

- (c) (i) Explain why a promoter sequence is needed as part of the plasmid if the vaccine is to work.

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[2]

- (ii) Suggest why it may be desirable to include nucleotide sequences coding for more than one antigen in a DNA vaccine.

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[2]



- (iii) Sequences of nucleotides, labelled G on the figure, code for groups of amino acids at the beginning of each polypeptide. These amino acid sequences direct the newly synthesised polypeptides to the Golgi apparatus of the muscle cell.

Explain how this makes the vaccine effective.

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[2]

(d) Suggest **three** reasons why researchers may be more concerned about the potential risks of DNA vaccines as compared with protein-based vaccines.

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[Total 14 marks]

13. (a) Cats with either black or white fur are common in Britain; brown fur is rarer. The dominant allele, **B**, of one gene gives black fur and the recessive allele, **b**, brown fur.

Many of the white cats carry a dominant allele, **A**, of a second gene which inhibits pigment production no matter which pigment-producing alleles are present in the genotype. The recessive allele, **a**, has no effect on fur colour.

Genes **A/a** and **B/b** are not linked and neither is on the X chromosome.

- (i) State the fur colour of cats with the following genotypes:

**AaBB** .....

**aaBB** .....

**Aabb** .....

**aabb** .....

[4]

- (ii) State the name given to this type of gene interaction.

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[1]

(iii) Suggest how one gene may inhibit the action of another.

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[3]

- (b) Two white cats produced a litter of kittens with three different coat colours: white, black and brown.
  - (i) State **one** possible genotype for **each** of the two white parents and explain the reasons for your choice.

You may use the space below for rough work, if needed.

genotypes of parents .....

explanation .....

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[5]

- (ii) State the ratio of phenotypes this pair of cats would be expected to produce in time, when the fur colour of several litters of kittens could be recorded.

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[2]

[Total 15 marks]

14. Research is taking place to see if chemicals can be added to toothpaste that block the expression of the genes responsible for the synthesis of the sticky gel and therefore stop plaque forming.

**RNA interference** is one method used to block the expression of genes.

This uses RNA molecules that are complementary to the messenger RNA of the gene.

(i) Explain how RNA interference affects the expression of a gene.

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[3]



- (ii) Unfortunately, adding complementary RNA to toothpaste has not proved successful in controlling plaque. Suggest why.

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[2]

[Total 5 marks]

15. The bacterium *Escherichia coli* uses glucose as a respiratory substrate. In the absence of glucose, *E. coli* can use lactose.

Explain how lactose induces the enzyme system involved in its uptake and metabolism.

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[Total 5 marks]

16. Muscle fibres may become torn and damaged.

Damaged muscle fibres have an increased messenger RNA (mRNA) concentration and a higher rate of oxygen consumption, **at rest**, than undamaged muscle fibres.

Explain these observations:

*increased mRNA concentration;*

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*higher rate of oxygen consumption.*

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[Total 5 marks]

17. (a) Repeating nucleotide sequences are common in the genomes of eukaryotes, for example in the centromeres and in the regions, called introns, which appear to interrupt the genes. Repeating sequences have been referred to as 'junk DNA'.

Suggest why the term 'junk DNA' is misleading.

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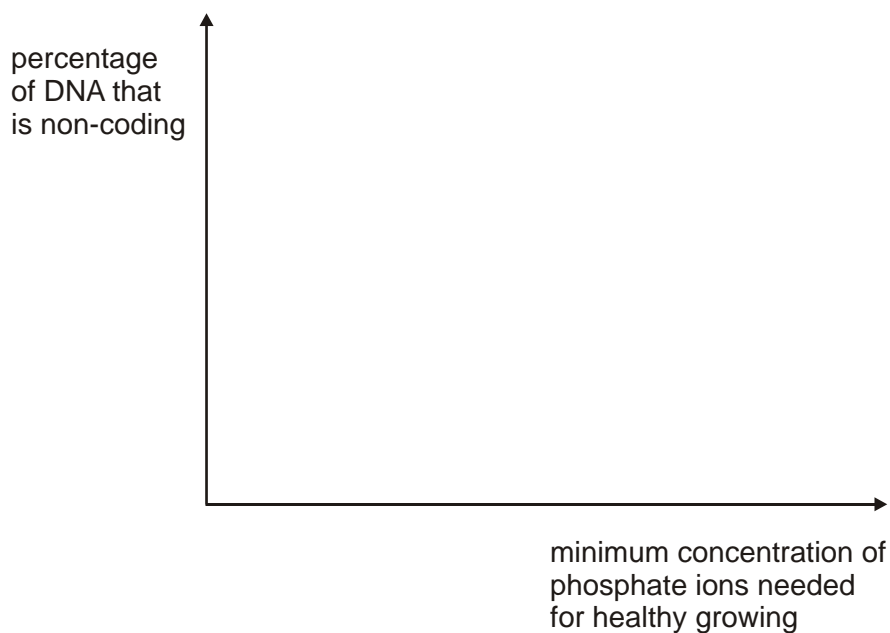
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[2]

- (b) Some species of plant are able to grow on soils that contain very little phosphate, while other species, for example stinging nettles, can only grow well in soils that are rich in phosphate. Each nucleotide in a DNA molecule includes a phosphate group.

If much of the non-coding DNA can be correctly regarded as functionless 'junk', there may be a correlation between the percentage of DNA that is non-coding and the minimum concentration of phosphate ions needed for healthy growth.

Draw a straight line graph, using the axes in the figure below, to show the correlation that you would predict.



[1]

- (c) Name a substance **other than DNA** that is found in cells and has one or more phosphate groups as part of its chemical structure.

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[1]

[Total 4 marks]

18. An enzyme, such as amylase, has a specific 3-dimensional shape.

Explain how DNA structure determines the specific shape of enzymes.

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[Total 4 marks]