Manipulating Genomes

Model Answers 1

Level	A Level
Subject	Biology
Exam Board	OCR
Module	Genetics, evolution and ecosystems
Topic	Manipulating genomes
Booklet	Model Answers 1

Time allowed: **63 minutes**

Score: **/47**

Percentage: **/100**

Grade Boundaries:

A*	A	B	C	D	E
>69%	56%	50%	42%	34%	26%

Question 1

Which of the following statements about gene therapy is **not** correct?

A. changes resulting from gene therapy cannot be passed on to offspring

B. germ-line gene therapy affects the whole organism

C. gene therapy is a form of genetic engineering

D. somatic cell gene therapy can only affect a limited number of cells

[1]

Germ line gene therapy involves inserting a gene at the embryonic stage so all the cells have a copy of the gene which can then be passed on the offspring. This technique is not licensed yet.

Question 2

Which statement correctly describes a difference between somatic and germ line gene therapy?

A. Germ line therapy involves the use of liposomes; somatic therapy involves use of viral vectors.

B. Somatic therapy can target specific tissues in need of treatment, germ line therapy cannot.

C Somatic therapy is most successful when targeting single gene defects, but germ line therapy can target multiple defects.

D Long term success is theoretically more likely with somatic cell therapy than germ line therapy.

[1]

Somatic therapy involves vectors such as liposomes and viruses delivering a gene into tissues lacking an effective gene. Germ line therapy delivers genes into embryos so that all cells contain the gene

Question 3

Fred Sanger developed an effective DNA sequencing technique in 1977.

(a) Define the term *DNA sequencing*. **[1]**

Working out the sequence of bases / nucleotides in DNA

(b) The speed at which DNA can be sequenced has been increasing rapidly since the introduction of DNA sequencing.

The length of DNA that can be sequenced in a given time is measured in base pairs or kilobase pairs.

In 1980, the speed at which DNA could be sequenced by a single machine was approximately 500 **base pairs** per hour. In 2016 that speed had increased to approximately 50 million **kilobase pairs** per hour.

Calculate how many times faster the speed of DNA sequencing is in 2016 compared with 1980.

[2]

1×10^8 or 1.0×10^8 or 100 million

500 base pairs is 5×10^2

50 million kilobases is 5×10^1 (50) $\times 10^6$ (million) 10^3 (kilobase) = 5×10^{10}

5×10^{10} is 1×10^8 greater than 5×10^2

(c) One technique that has allowed the speed of DNA sequencing to increase has been the development of nanopores.

Fig. 21 shows how nanopores can be used to sequence DNA.

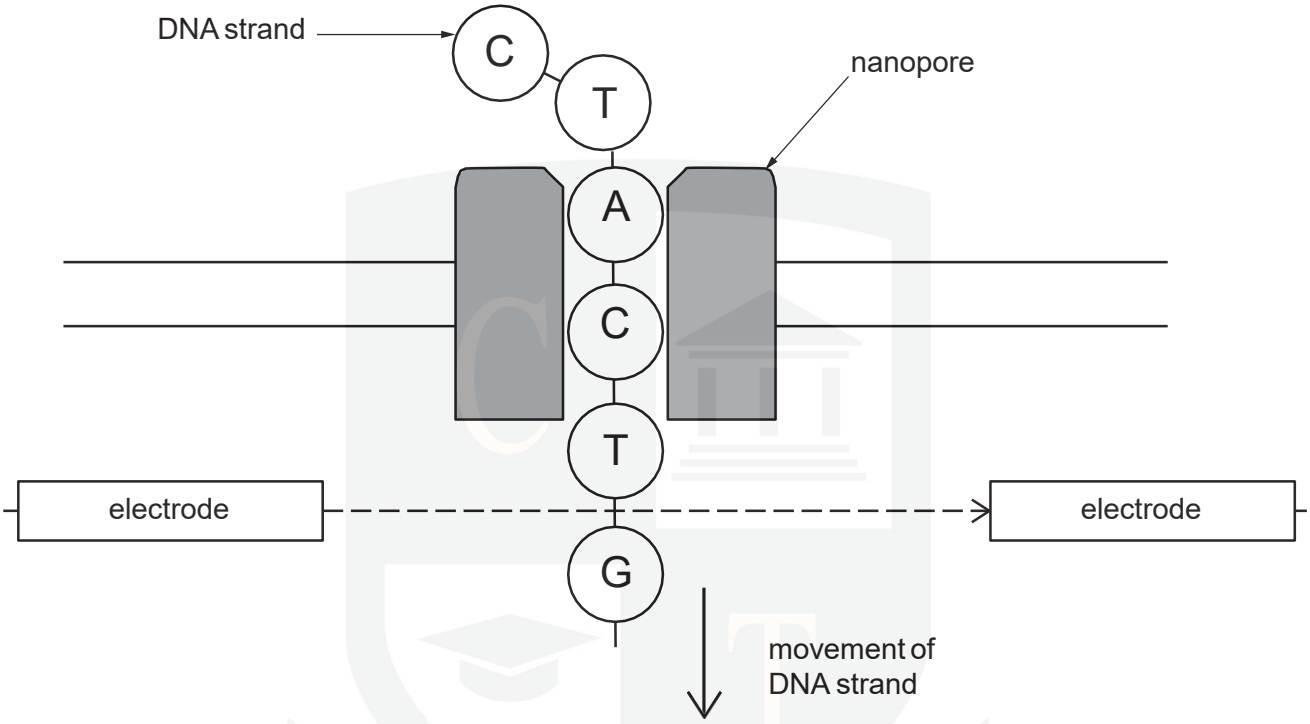


Fig. 21

(i) State one development, other than nanopore technology, that has led to an increase in the speed at which DNA can be sequenced.

[1]

High throughput or shotgun or next generation sequencing

You could also describe part of the technique, for example replacing radioactive tags with fluorescent tags

(ii) Part of Fig. 21 is labelled **G**.

Use the table below to identify two differences between the part labelled **G** and the structure of a molecule of ATP.

[2]

	G	**Molecule of ATP**
Difference 1	guanine deoxyribose sugar	adenine ribose sugar
Difference 2	1 phosphate phosphates on C3	3 phosphates no phosphates on C3

(iii) Explain how DNA sequencing allows the sequence of amino acids in a polypeptide to be predicted.

[2]

- DNA sequence allows the sequence of amino acids to be calculated
- As 3 bases code for each amino acid

(d) DNA sequencing can be used to determine the genome of an entire organism.

The first organism to have its entire genome sequenced was a virus.

Ebola is a virus that caused the death of over 11 000 people in West Africa between 2014 and 2016. The DNA of ebola virus has **a rapid rate of mutation**.

Since the first outbreak in 2014 scientists have been working to develop an **effective vaccination** against ebola.

Other scientists have developed a portable nanopore sequencing technique that could be used to sequence rapidly the entire ebola genome.

Outline how DNA sequencing and bioinformatics could be used to increase the effectiveness of a vaccination programme against ebola.

[4]

sequencing

- A high mutation rate means there are many strains or forms of the virus
- This allows us to predict the shape of the protein / antigen
- This means the vaccine contains the correct antigen

What is the theme of this question? The sequence of bases can be used to work out the sequence of amino acids. Antigens are protein so knowing the sequence of bases allows us to predict the primary structure of the protein. Note highlighted text in blue.

bioinformatics

- This gives access to large amounts of data
- Data such as DNA and proteins
- The format of data is universal
- The source of the outbreak can be identified
- Populations which are at risk can be predicted
- These populations can be targeted

Bioinformatics combines biological techniques, computer science, mathematics and statistics to analyse and interpret large amounts of biological data.

Some of these answers are common sense if you read the question carefully

[Total: 12]

Question 4

Gene sequencing is an important technique in molecular biology.

Fig. 3.1, **of the Insert**, shows part of a computerised graph obtained from an automated gene sequencing machine.

- The section of the DNA molecule represented in Fig. 3.1 is from base position 117 (on the left of the graph) to base position 137 (on the right of the graph).
- The bases in the DNA sequence are labelled with four different coloured fluorescent dyes.
- The identities of some of the bases (117 to 119 inclusive and 129 to 137 inclusive) are indicated below the graph.

(a) Use Fig. 3.1 to identify the order of bases from positions 120 to 128. **[1]**

A	A	A	T	C	T	G	G	T
.....	.....	.....	.....	.....	.....	.....	.....	.....
120	121	122	123	124	125	126	127	128

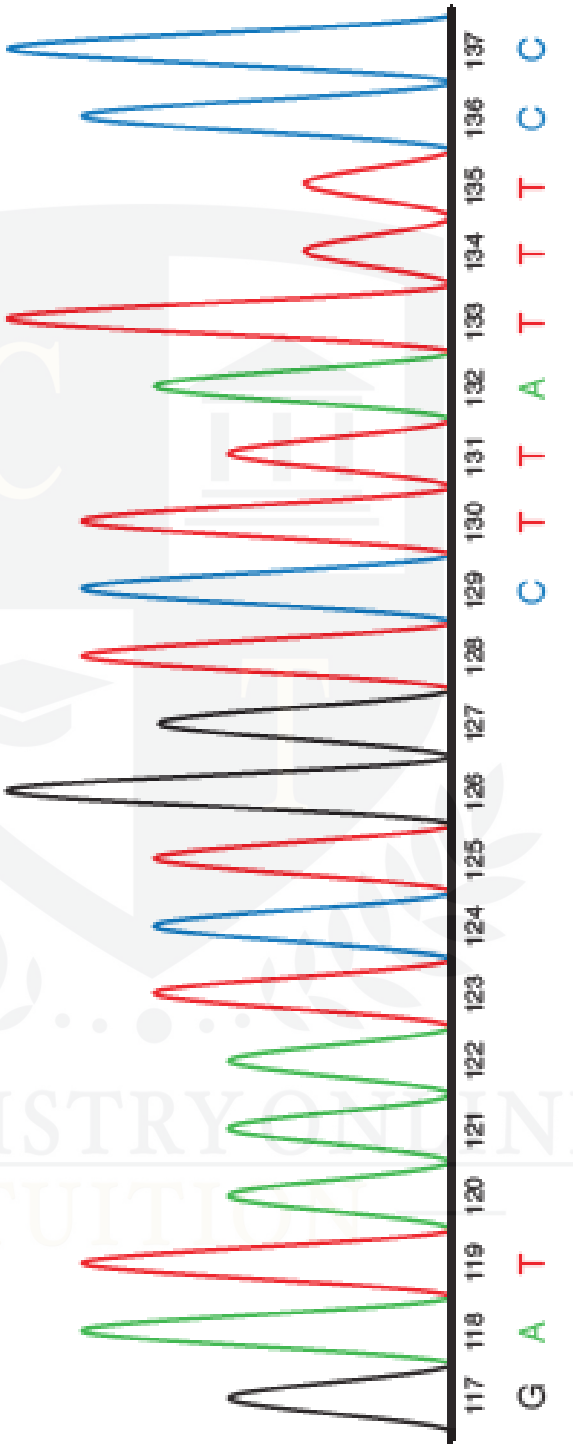


Fig. 3.1

(b) To produce the type of graph shown in Fig. 3.1, the automated gene sequencing machine needs to be loaded with the following:

- the DNA to be sequenced
- short primer sequences specific to the DNA to be sequenced
- many normal DNA nucleotides
- some chain-terminating DNA nucleotides labelled with coloured dyes
- the enzyme *Taq* polymerase.

A regular cycle of temperature changes allows many DNA fragments of different lengths to be built up by the polymerase chain reaction (PCR).

Fig. 3.2 (**on the next page**) shows the end parts of the sequences of seven of these different length fragments, labelled 1 to 7. The end parts of the sequences for fragments 1 to 4 are complete but those for fragments 5 to 7 are not.
These seven fragments correspond to the **last seven peaks** on the right hand side of the graph in Fig. 3.1.

The letters in boxes represent labelled chain-terminating DNA nucleotides.
The letters not in boxes represent normal DNA nucleotides.

(i) Use the information in Fig. 3.1 to fill in the missing nucleotide bases on fragments 5 to 7 on Fig. 3.2.

You should distinguish between the normal and labelled nucleotides in the sequence for each fragment.

[2]

1 – **T**

2 – **T** **A**

3 – **T** **A** **T**

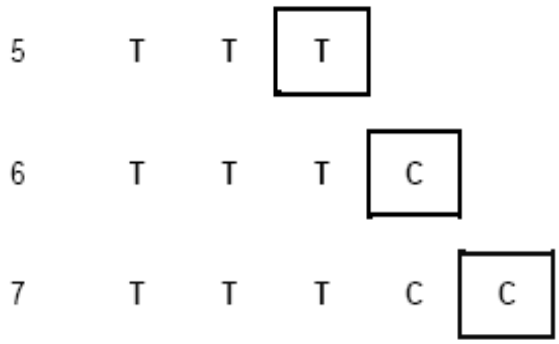
4 – **T** **A** **T** **T**

5 – **T** **A**

6 – **T** **A**

7 – **T** **A**

Fig. 3.2



(ii) Explain how the automated sequencing machine orders the DNA fragments from the PCR reaction into the size order shown in Fig. 3.2.

[3]

- The fragments of DNA are separated by electrophoresis
- The negatively charged DNA moves towards the positive electrode or anode
- The smaller fragments move fastest

DNA profiles compare the distance moved, width and number of fragments after electrophoresis

(c) Gene sequencing can help us to understand how an individual's genome affects their body's response to drugs.

One research study has looked at the effectiveness of drugs used to treat asthma in children. Asthma is a condition in which the bronchioles become reduced in diameter. This results in the child finding it difficult to breathe.

(i) Using your knowledge of the structure of bronchioles, suggest how their diameter might become reduced.

[2]

- The diameter of the bronchioles will become reduced by contraction of smooth muscle in the walls
- It would be the circular muscle which would cause the diameter to reduce
- Extra production of mucus could also reduce the diameter of the bronchial
- The diameter might also become reduced as a result of inflammation

(ii) Explain why it is difficult to expel air from the lungs if the bronchioles become reduced in diameter.

[1]

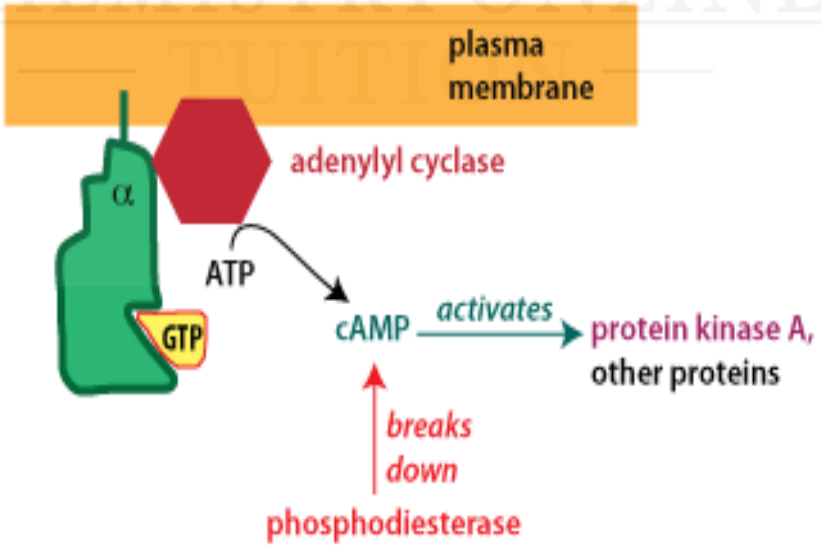
- A reduced diameter makes it difficult to expel from the lungs because the resistance to earth flow increases as a result of friction
- Breathing out is a passive process so muscular force would be needed to exhale to create additional pressure

(d) Asthma in children may be treated with drugs. One of the most commonly used drugs is salmeterol.

Salmeterol acts by binding to protein receptors in the lining of the bronchioles. However, in approximately 14% of children with asthma, salmeterol is not very effective. This is thought to be the result of a genetic mutation in these children.

Suggest why this mutation reduces the effectiveness of salmeterol. **[3]**

- A mutation results in a change in the sequence of bases in DNA
- This causes a change in the amino acid sequence or the primary structure of a protein
- As primary structure changes so does the tertiary structure or 3-D shape which will also change the shape of the receptor to the drug
- The drug would be unable to bind
- There would be no response triggered in the cell and no second messenger



(e) In a recent medical trial, 62 children with this genetic mutation were studied.

- Their asthma was not controlled well by salmeterol.
- 31 children continued using salmeterol and the remaining 31 were given an alternative drug, montelukast.
- Montelukast is not routinely prescribed because salmeterol is far more effective for most children with asthma.

(i) After one year, the children taking montelukast had better control of their asthma and were able to reduce their use of montelukast.

Suggest why these children responded better to montelukast than to salmeterol. **[2]**

- The mutation resulted in a receptor having a **complementary shape** to montelukast
- Montelukast was able to bind to the receptor
- Whereas salmeterol could not
- Montelukast may have a different receptor entirely

This question is referring to the specificity between receptors and the chemicals they combine with, to trigger a response. In which case, 'complementary shapes' is a key term to get the marks.

(ii) Comment on the reliability of the results of this medical trial. **[1]**

- The results of this medical trial are not reliable because the sample size was too small, there were only 62 children in study

Repeating an investigation at least 3 times provides reliability, it helps to highlight any anomalies and allows you to calculate a mean. A large sample also makes the investigation more reliable and allows you to do a statistical test

(iii) It is proposed that a simple saliva test could identify those children who have the mutation.

What would be the source of the genetic material used in this test? **[1]**

- The source of the genetic material in the test was the cells lining the cheek

[Total: 16]

Question 5

This question is about genetic engineering and the techniques used for making multiple copies of genes (gene cloning).

(a) Genetic engineering uses the following:

A. an enzyme that synthesises new DNA
B. an enzyme that cuts DNA at specific sequences
C. an enzyme that reseals cut ends of DNA
D. small circular pieces of DNA found in bacteria; these pieces of DNA have antibiotic resistance genes
E. an enzyme found in some viruses with an RNA genome; this enzyme converts RNA into DNA.

Name **A** to **E**. **[6]**

A DNA or Taq polymerase Taq polymerase is thermally stable at very high temperatures

B restriction endonuclease Cuts DNA at specific sequences

C DNA ligase Joins sugars to phosphates by phosphodiester bonds

D plasmid Small circles of DNA used as vectors to deliver genes

E reverse transcriptase Found in retro viruses, it converts RNA back to DNA

(b) Genes are cloned for a number of reasons. For example,

- one group of research scientists at a hospital wanted to sequence a disease-causing mutation to learn more about a human disease; these scientists started their research using white blood cells;
- another group of scientists at a biotechnology company wanted to clone the insulin gene in order to manufacture its protein product to treat diabetes; these scientists started their research using cells from the pancreas.

Suggest **and** explain the biological reasons why the two groups each started with a different cell. **[4]**

- White blood cells were used because they are easy to collect
- White blood cells are a good supply of DNA
- Pancreatic cells are where insulin is made
- Pancreatic cells would therefore be a good source of the mRNA

(c) A gene can be cloned *in vitro* (in a test-tube) by the polymerase chain reaction (PCR). Alternatively, a gene can be cloned *in vivo* (in living cells) by introducing the gene into bacterial host cells.

Table 5.1 identifies some of the key steps in each process.

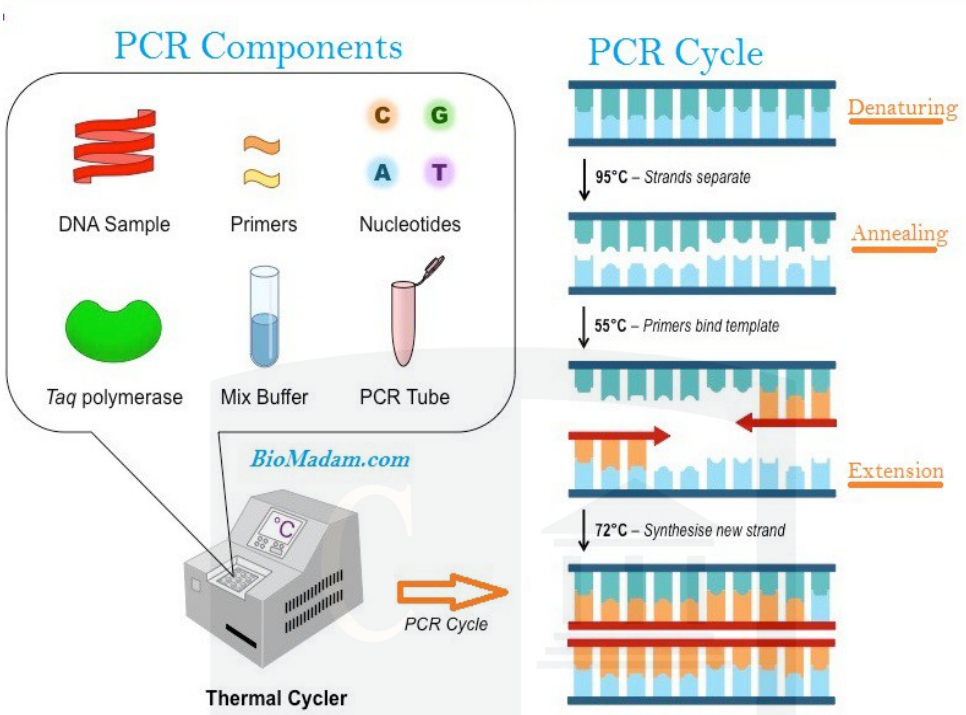
Table 5.1

in vitro gene cloning (PCR)	*in vivo* gene cloning
At 95 °C, DNA extracted from a cell separates into two strands.	A library of gene fragments is produced and introduced into host bacteria.
At 50 °C, specially-made primer sequences attach to the ends of the desired gene only.	Bacteria are screened for antibiotic resistance to identify those with recombinant DNA.
At 72 °C complementary copies of both DNA strands are made.	A gene probe is used to select the bacterial colony containing the desired gene.
The cycle of temperature changes is repeated and more copies of the gene are made.	This colony is grown on in nutrient broth and the DNA is then purified.

Compare the two processes of gene cloning by explaining the advantages of each.

In your answer you should ensure that clear comparisons between the two processes are made and explained.

- PCR is faster **[8]**
- PCR only takes a few hours compared to a few weeks
- PCR uses less equipment
- Only a thermal block whereas in vivo cloning needs lots of test tubes and petri dishes
- PCR is less labour intensive
- PCR can be set up and then left to run
- PCR is safer
- PCR doesn't use microbes which could cause contamination
- In vivo is less expensive,
- In vivo does not need expensive chemicals such as DNA polymerase and primers



[Total: 17]