**3** Porphyria is a group of rare genetic diseases in which molecules called porphyrins accumulate in the body.

Three examples of porphyria are:

- X-linked protoporphyria
- variegate porphyria
- congenital erythropoietic porphyria (CEP).

**(a)** X-linked protoporphyria is caused by a mutant allele located on the X chromosome.

Fig. 3.1 shows the pattern of inheritance of X-linked protoporphyria in one family.

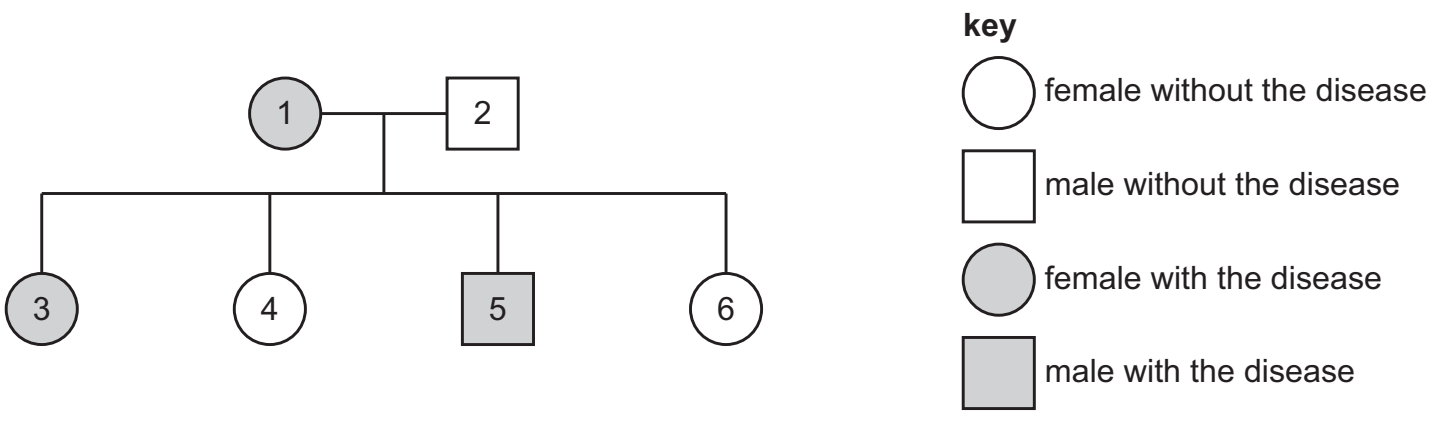


**Fig. 3.1**

X-linked protoporphyria is described as a sex-linked disease.

Use the information in Fig. 3.1 to make **one** other conclusion about the pattern of inheritance of X-linked protoporphyria.

Give evidence to support your conclusion.

conclusion .....

evidence .....

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[2]

**(b)** Variegate porphyria occurs in 1 in 100 000 people in Europe.

In the 1600s, approximately 100 Dutch people migrated from Europe to South Africa.

The population of people of Dutch descent in South Africa is now 2.5 million. Variegate porphyria occurs in 1 in 1000 people in this population.

Suggest **and** explain why variegate porphyria is more common among people of Dutch descent in South Africa than among people in Europe.

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**(c)** Microarrays can be used to detect various forms of porphyria caused by mutant alleles.

Describe how microarrays can be used to detect a disease by analysing gene expression.

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**(d)** The nucleotide sequences of alleles that cause rare genetic diseases, such as the various forms of porphyria, are stored in a database.

State **one** benefit of having a database of nucleotide sequences for alleles that cause rare diseases.

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..... [1]

**(e)** Congenital erythropoietic porphyria (CEP) is caused by a substitution mutation in a gene coding for an enzyme.

The mutant CEP allele codes for an enzyme with little or no function.

Scientists used gene editing in the laboratory to correct the nucleotide sequence of the mutant allele in cultured human cells.

The scientists introduced three molecules to the cells:

- an enzyme called Cas9 that causes breaks in DNA strands
- guide RNA (gRNA), attached to Cas9, that is complementary to the mutant CEP allele
- a short length of DNA, known as template DNA, that can replace the section of the allele where the substitution mutation has occurred.

The repair mechanism within the cell allows the template DNA to be inserted so that the mutation is corrected.

Fig. 3.2 shows part of the nucleotide sequence in the mutated CEP allele before and after the gene editing procedure.

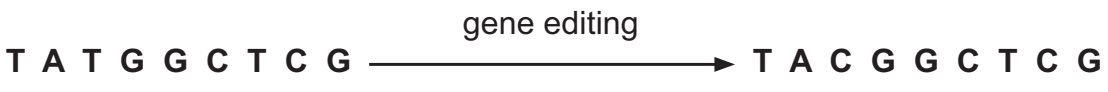


**Fig. 3.2**

In the future, this gene editing procedure may be used in a person with CEP to prevent the accumulation of porphyrins in the body.

Suggest **and** explain how this gene editing procedure will prevent the accumulation of porphyrins in a person with CEP without damaging other genes.

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[Total: 13]