Mutations (A2)

Errors can happen during DNA replication.
These are generally corrected by the cell's own mechanism.
Changes to the original DNA are known as mutations.
Mutations may also arise through exposure to particular chemicals, eg: some dyes and organic chemicals such as benzene and the chemicals in cigarette smoke.
Mutations may also be caused by ultraviolet light, X-rays, gamma rays, alpha and beta radition.
Because DNA is the template for mRNA, which carries the information for the primary structure of a protein, changes to the base sequence in DNA can cause a change in the primary structure of a protein.

Understanding genetic mutations

In some cases the change in the DNA is very small.
A single change in a base (for example C to T) is not uncommon and it will not always cause a change in protein structure and function.
There is more than one codon for many amino acids is beneficial.
If a mutation occurs and one of the bases is altered, there is still the possibility that the correct amino acid will be incorporated into the protein.
For example, if UCU is changed to UCG, serine will still be incorporated in its correct place in the polypeptide chain.
If the change results in a different amino acid being incorporated into protein there is still a chance that the effect will be small.
It will only alter protein structure and function if an amino acid essential for protein function is altered.
Example: an amino acid at the active site of an enzyme.

Mutations which results in a change in a stop or start codon are more serious.

A crucial protein may not be produced or may be so changed so that it cannot function properly.

The deletion of a base is also a serious matter.

It alters the way the message is read and produces a different sequence of amino acids in the protein chain.

Example:

the correct sequence in DNA is,

—ATA CGC TAG CAT G—

the mRNA will be,

—UAU GCG AUC GUA C—

which codes for,

Tyr Ala Ile Val ...

However, if the 2nd A is deleted, then the DNA will be,

—ATC GCT AGC ATG—

the new mRNA will be,

—UAG CGA UCG UAC—

which codes for,

stop Arg Ser Tyr

Alterations or deletions to bases in DNA may result in a genetically based condition such as sickle-cell anaemia or cystic fibrosis

Exercise 1

a. Explain why the sequence -AGC ATG ATC ACT- in the template strand of DNA making RNA codes for Ser Tyr stop stop.

b. Use the information in part a. to determine a possible base sequence on the anticodons of Ser-tRNA and Tyr-tRNA.
Use the wheel of genetic code to help you.

Workings

a. The template strand of DNA is translated to the complementary sequence in mRNA.

template strand of DNA	-AGC	ATG	ATC	ACT-
mRNA sequence	-UCG	UAC	UAG	UGA-
acid amino coded	Ser	Tyr	stop	stop

b.

codon base sequence	UCG	UAC
anticodon base sequence	AGC	AUG
tRNA	Ser	Tyr

Exercise 2

a. Use the information in genetic codes wheel to suggest the amino acid sequence corresponding to the following sequence of bases in DNA which form a template strand for mRNA.

-TAC TGC TTT AAG CCT ATG -

b. The final T in the DNA sequence in part a. is changed to a C.

i) What effect will this have on the amino acid sequence that is coded for?

ii) What do we call a change like this when it occurs in nature?

Workings

a.

template strand of DNA -TAC TGC TTT AAG CCT ATG-

mRNA sequence -AUG ACG AAA UUC GGA UAC-

amino acid coded Met Thr Lys Phe Gly Tyr

final amino acid sequence Thr-Lys-Phe-Gly-Tyr

-because the methionine coded for by the start codon AUG is removed.

b. i) original DNA base sequence ATG

changed DNA base sequence ACG

mRNA base sequence UGC

amino acid Cys

The final amino acid sequence becomes Thr-Lys-Phe-Gly-Cys

ii) mutation

Sickle-cell anaemia.

The red blood cells of patients with sickle-cell anaemia have a crescent (sickle) shape rather than the normal disc shape.

Sickle cells cannot bend as easily as normal red blood cells in order to get through small blood vessels.

The small blood vessels get blocked and oxygen transport to various organs can be reduced.

This can lead to severe pain and damage to the organs.

The disease arises from a single mutation in the DNA coding for the β polypeptide chain in haemoglobin.

A single amino acid at the 6th position of the polypeptide chain is altered.

Normal β chain	Val	His	Leu	Thr	Pro	Glu	Glu
Sickle-cell β chain	Val	His	Leu	Thr	Pro	Val	Glu

The abnormal haemoglobin sticks together to form rods inside the red blood cells, which become sickle-shaped.

Cystic fibrosis

Cystic fibrosis is a condition that affects the lungs, pancreas and sweat glands.

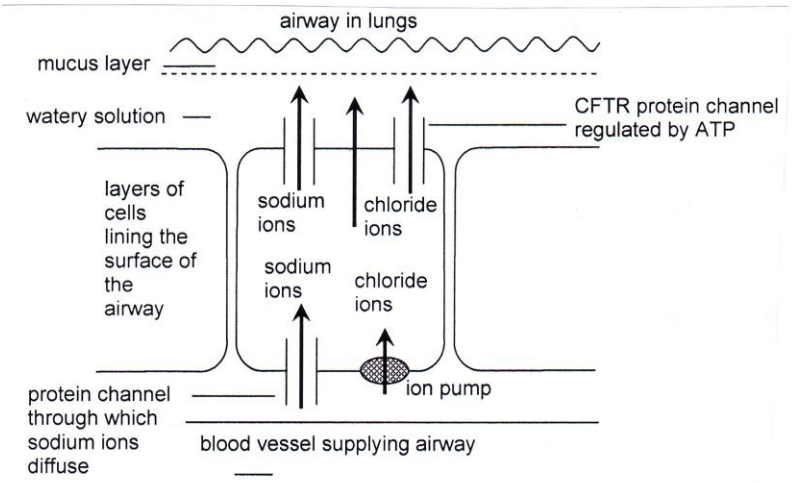
Instead of normal watery fluid (mucus) coming out from the cell, a thick sticky mucus is produced.

- The thick mucus stops digestive enzymes from the pancreas getting to the digestive system, so nutrients cannot be absorbed into the bloodstream.
- The thick mucus blocks the lungs, so sufferers (especially young children) are more likely to get chest infections.

In healthy cells, a protein called CFTR protein in the cell membrane controls the movement of Cl^- ions into and out of the cells.

In a normal cell, Cl^- ions are pumped into the cells from the blood and are pumped out through protein channels in the cell membrane.

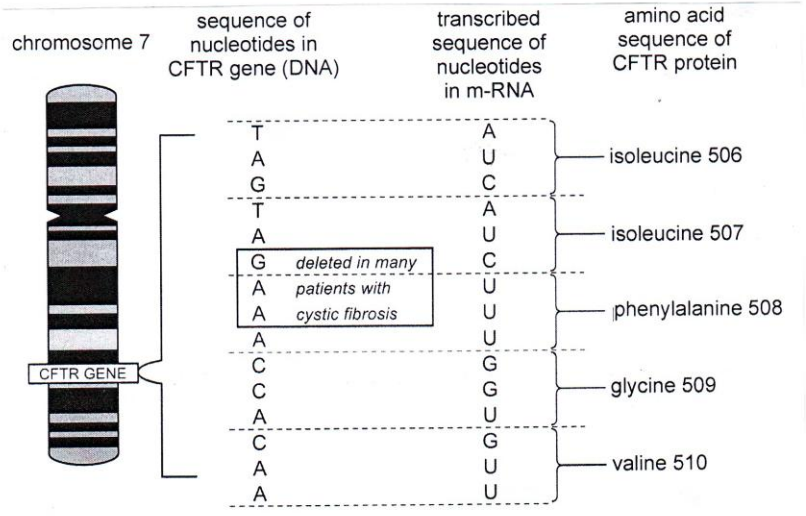
This is part of the process for keeping a running layer of watery mucus on the surface of the cells.



the movement of ions across cell membranes in the lungs

In patients with cystic fibrosis:

- there is a mutant gene for the CFTR protein, which has a sequence of three bases deleted.
- these bases would normally code for phenylalanine (Phe), the 508th amino acid in the structure of the protein.



the site of the commonest mutation that causes cystic fibrosis

- the CFTR protein is therefore missing or, if present, does not work properly.
- Cl^- ions are still pumped into the cells but are not pumped out.
- this causes the Cl^- ion concentration to build up in the cells.
- water moves into the cells by osmosis to try to equalise its concentration inside and outside the cells.
- as a result, the mucus on the outside of the cell becomes thick and sticky.

Exercise 3

The normal amino acid sequence is part of the enzyme lysozyme. Explain how the mutation may affect the activity of the enzyme.

Workings

The amino acid sequence is considerably different.
Amino acids with different types of side chain are in equivalent positions.
So the protein will not fold up in the correct way for catalysis and the amino acid residues in the active site will not be correct.
The enzyme is unlikely to function at all.

Exercise 4

a. Mutation of the mRNA of a T4 bacteriophage leads to the deletion of one base near the beginning of the sequence of 15 bases shown below.

5'—AGUCCAUCACUUAUU—3'

↑
this base deleted

i) Write down the base sequence of the mutant mRNA.

ii) Use the genetic code wheel to translate each of these base sequences into amino acid sequences in the normal and mutant protein.
The first codon starts with the A at the 5' end.

b. Write down the sequence of bases in the piece of DNA which would produce the normal mRNA sequence after transcription.

Workings

a. i) mutant mRNA —AUCCAUCACUUAUU—

ii) normal mRNA —AGU|CCA|UCA|CUU|AUU—

normal amino acid sequences— Ser–Pro–Ser–Leu–Ile–

mutant mRNA —AUC|CAU|CAC|UUA|UU—

mutant amino acid sequences —Ile–His–His–Leu–5th aa–

5th a.a. could either be Phe or Leu

b. normal DNA base sequences,

—TCAGGTAGTGAATAA—