Full Name:	Civics group: 21S	Index no.:	Date:

Core Idea 2: Genetics & Inheritance

Gene mutation & Chromosomal aberration
Tutorial 10

MCQ
ANSWERS

1	2	3	4	5	6	7
A	D	C	D	B	D	C

1 A point mutation is a change to a single nucleotide and can occur anywhere in a gene.

Which statements are true?

1 A point mutation in an exon can result in a different amino acid sequence.

2 A point mutation in an exon can produce a shorter protein if a stop codon produced.

3 A point mutation in an intron can alter the binding site of a splicing enzyme.

A 1, 2 and 3
B 1 and 2 only
C 1 and 3 only
D 2 and 3 only

2 A mutation results in the substitution of thymine for cytosine in the base sequence ATC in a section of a template DNA strand. What are the base sequences on the tRNA corresponding to the new triplet?

template DNA: ATC
mutant DNA: ACC
mRNA: UGG
tRNA: ACC *(I,e same as mutant template DNA, except U instead of T)*

A ATC
B TAG
C UGG
D ACC

3 The diagram shows part of the normal sequence of an mRNA molecule.

5' – CCA AGU GGU CCG CUA AAA UGG C – 3'

Template DNA: GGT TCA CCA GGC G**AT T**TT ACC G
Polypeptide: gly - ser – pro – gly - ???

Mutant DNA: GGT TCA CCA GGC **ATT** TTA CCG
Polypeptide: gly - ser – pro – gly – ile – leu – pro

Mutation is a base deletion of 13th nucleotide guanine.

A mutation in the DNA resulted in a polypeptide beginning with the following sequence.

glycine – serine – proline – glycine – isoleucine – leucine – proline

The DNA triplets for some amino acids are

Glycine	Isoleucine	Leucine	Proline	Serine
CGA	ATA	TTA	CCA	TCA
GGT	ATT	CTT	CCG	TCG
GGC		CTC		

Which mutation has occurred in the DNA molecule?

A A reversal in the order of nucleotide
B An addition of an extra nucleotide
C The loss of a nucleotide
D The replacement of one nucleotide by a different nucleotide

4 Two enzymes X and Y, are each encoded by different alleles of the same gene. The amino acid seqwuences of the two enzymes differ between positions 87 and 91 of the polypeptides.

The amino acid sequences of enzymes X and Y, and the corresponding DNA sequence of enzyme X from position 86 to position 93 of the polupeptides, are shown in the table below.

	←N terminal end amino acid position C terminal end→							
	86	87	88	89	90	91	92	93
DNA triplet codes for enzyme X	TTT	TCA	GGT	AGT	GAA	TTA	CGA	CGA
amino acid sequence of enzyme X	lys	ser	pro	ser	leu	asn	ala	ala
amino acid sequence of enzyme Y	lys	val	his	his	leu	met	ala	ala

The actual mRNA codons for the amino acids in these positions for enzymes X and Y, are shown in the table below.

amino acid	lys	ser	pro	leu	asn	ala	val	his	met
mRNA codon (s)	AAA	AGU UCA	CCA	CUU UUA	AAU	GCU	GUC	CAU CAC	AUG

What could account for the difference in amino acid sequence of enzymes X and Y?

A A single frame shift by deletion in the DNA code at position 87.

B Frame shift mutations in the DNA codes at position 87 and position 90.

C A change in the sequences of the second and third nucleotides at positions 87 and 88 of the DNA codes and frame shifts at positions 89 and 91.

D A deletion in the DNA code at position 87 and an insertion into the DNA code at position 92.

DNA for enzyme X TTT TCA GGT AGT GAA TTA CGA CGA
mRNA for enzyme X AAA **A**GU CCA UCA CUU AAU GCU GCU
(A at position 87 is deleted)
mRNA for enzyme Y AAA GUC CAU CAC UUA AUG **G**CU GCU
(G at position 92 is inserted)

5 The diagram shows the banding pattern of two human chromosomes. **P** is a normal chromosome.

What accounts for chromosome **Q**?

A crossing over between sister chromatids
(False as the banding patterns are different for P & Q. Crossing over does not affect banding pattern as it involves exchange of equivalent portions of non-sister chromatids of a homologous pair (both of which have the same gene loci and banding pattern)..)

B inversion of part of the chromosome
(True. See red box for comparison.)

C deletion of part of the chromosome
(False as length of chromosomes are the same. For deletion, we expect Q to be shorter than P.)

D translocation of part of another chromosome
(False as length of chromosomes are the same. For translocation, we expect Q to be longer the P.)

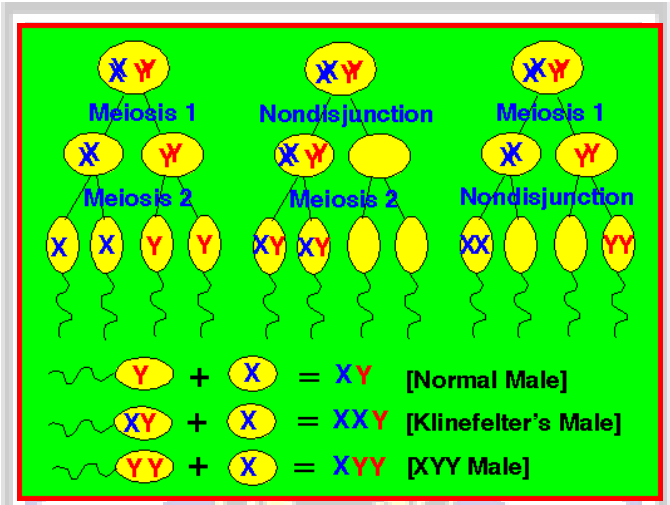
6 ***2019/9744/1/16***

A small proportion of men have the genotype XYY.

Such genotypes are usually the consequence of non-disjunction occurring during meiosis. Non-disjunction results from a failure of chromosomes to separate correctly.

In which gamete and at which stage of meiosis must this non-disjunction occur?

A An egg produced by non-disjunction in meiosis I
B An egg produced by non-disjunction in meiosis II
C A sperm produced by non-disjunction in meiosis I
D A sperm produced by non-disjunction in meiosis II



Explanation:

- Men with genotype XYY means they got YY from father's sperm & X from mother's egg (since mother does not have Y chromosome)
- To get an aberrant sperm with 2 Y chromosomes, this means that the sister chromatids of the duplicated Y chromosome failed to separate during Anaphase II. [See figure above]

7 A Robertsonian translocation is a type of chromosomal translocation in which the long arms of two chromosomes fuse together.

Fig. A shows this event occurring between chromosomes 14 and 21.

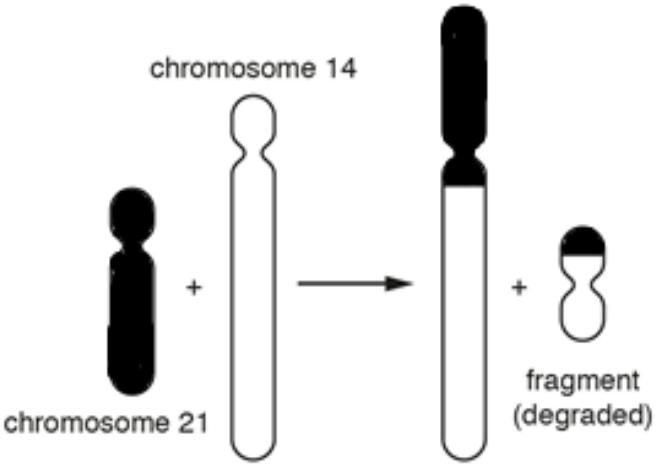


Fig. A

An individual who inherits the translocated chromosome in **Fig. A** will either have Down's syndrome or be a carrier of the disorder.

A couple has a child. The mother is a carrier and the father is genetically normal. The genetic material with respect to chromosomes 14 and 21 in the somatic cells of the parents are shown in **Fig. B**.

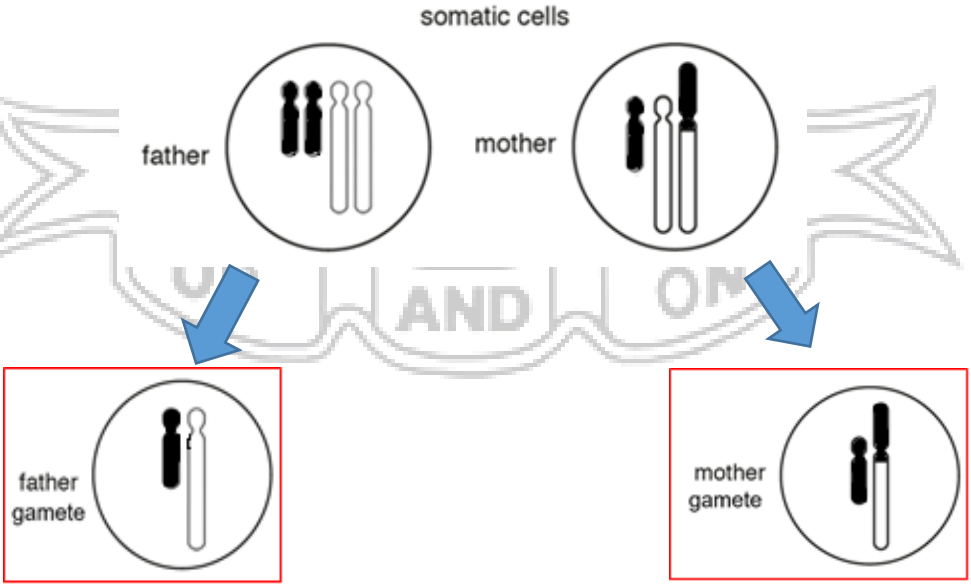
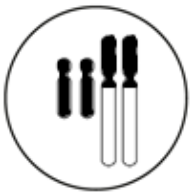
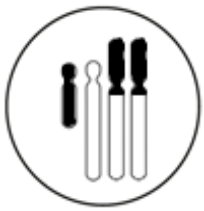
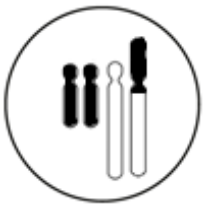


Fig. B

The child is born with Down's syndrome. ➔ implied child has the translocated chromosome.

Which of the following shows the correct genetic material with respect to chromosomes 14 and 21 in the zygote of the child? ANS: C

A  **B**  **C**  **D** 

STRUCTURED QUESTIONS

QUESTION 1 *[9747 / 2008 / Nov / P2Q2]*

Sickle cell anaemia is most commonly caused by the haemoglobin variant HbS.

In HbS the amino acid valine takes the place of glutamic acid at the sixth amino acid position of the beta globin polypeptide chain.

Table 1.1 shows the details of this change.

Take note that the actual DNA mutation that leads to sickle-cell anaemia is CTT → CAT (Thymine is replaced by Adenine)

Beta globin sequence in normal adult haemoglobin							
position of amino acid	3	4	5	6	7	8	9
DNA bases	CTG	ACT	CCT	GAG	GAG	AAG	TCT
amino acid	Leu	Thr	Pro	Glu	Glu	Lys	Ser
Beta globin sequence in mutant adult haemoglobin (HbS)							
position of amino acid	3	4	5	6	7	8	9
DNA bases	CTG	ACT	CCT	GTG	GAG	AAG	TCT
amino acid	Leu	Thr	Pro	Val	Glu	Lys	Ser

Table 1.1

(a) State the type of mutation responsible for this change in the amino acid sequence.

……[1]

1 (single base / base) substitution ;

REJECT: point mutation, missense mutation.

Reasons:
Point mutation describes the change in one base which could be brought about by a single base substitution, deletion or addition. The term "point mutation" is considered too vague in comparison to "base substitution". The information in Table 1.1 showed that there is substitution of 1 base from A to T.

Missense mutation describes the effect of mutation on amino acid sequence (at the protein level) i.e. the change of one amino acid for another, to form a non-functional protein. A missense mutation is not responsible for the change in amino acid sequence which is caused by changes at DNA level.

(b) Explain the significance of the change in amino acid to the properties of haemoglobin.

……[3]

1 Valine replaced glutamic acid in the polypeptide; Valine has non-polar / hydrophobic R group while glutamic acid has charged / hydrophilic R group

Protein folding

2 Changes the interaction between R-groups of amino acids, thus affecting protein folding to form a different tertiary structure (3-D conformation) for HbS;

Protein interaction

3 Effect on HbS occurs at low oxygen concentration, solubility of HbS decreases which leads to ;

4 HbS molecules stick to each other via their hydrophobic regions and polymerise into fibres.

Examiners' comments

A significant number of candidates incorrectly referred to haemoglobin as an enzyme and described the base substitution as causing a change in the active site so that oxygen could no longer be carried.

(c) Describe the effects of the change in the properties of haemoglobin explained in **(b)**.

……[3]

1 Affected red blood cells (**REJECT: HbS)** will adopt a sickle shape ;

2 Due to their shape, there is tendency of the sickled red blood cells to clump together and clog capillaries, preventing other cells from moving through capillaries ;

3 Obstructing blood flow to organs can cause organ damage (as a result of oxygen in RBCs not being able to reach the organs) ;

4 Sickled shaped RBCs have shorter lifespan, resulting in anaemia in patients.

Examiner's comments:

A large number of candidates thought that once the HbS had polymerised it could not carry oxygen again. This is incorrect.

Again, there was a failure to recognize the point of the question, that the change from HbA to HbS would result in changes to the red blood cells. Although some candidates referred to the sickle shape of the red blood cells, a large number referred to the HbS becoming sickle shaped. Rather than the sickle shaped cells

blocking capillaries, again many referred to HbS doing this. Resultant organ damage was rarely mentioned as was the fact that red blood cells have a shorter life. Often relevant points required in **(b)** were seen in **(c)** and vice versa, indicating that pupils did not understand the specific requirements of each question.

(d) Sickle cell anaemia may be treated with a drug called hydroxyurea which induces the formation of fetal haemoglobin (HbF). HbF is normally found in the fetus and newborn. When present in individuals with sickle cell anaemia, HbF helps to prevents sickling (i.e. formation of sickle shaped red blood cells).

(i) Suggest how formation of HbF would be induced.

……[2]

1 Gene for HbF would be transcribed / activated / expressed ;
2 resulting in translation of mRNA to produce HbF (protein).

[Actual mechanism, FYI only: hydroxyurea generates nitric oxide radicals, which increase cGMP levels, which upregulates specific transcription factors (such as CREB, TFII-I, c-Fos), which increases transcription of HbF gene (among many other genes)]

(ii) Suggest how elevated levels of HbF may reduce the symptoms of sickle cell anaemia.

……[2]

1 Presence of elevated HbF retards/hinders the polymerization of HbS into long fibres, hence red blood cells sickle less readily, hence less clogging of capillaries.

2 Cells with elevated HbF have longer life span / less prone to haemolysis, hence leads to reduced anemia effects.

3 HbF has a higher affinity for oxygen, hence oxygen can be transported more efficiently to reach the organs.

[Q1 Total: 11]

QUESTION 2 *[Adapted from 9744 / 2020 / Nov / P2]*

Fig 2.1 is an electron micrograph showing the complete set of chromosomes (karyotype) of a person.

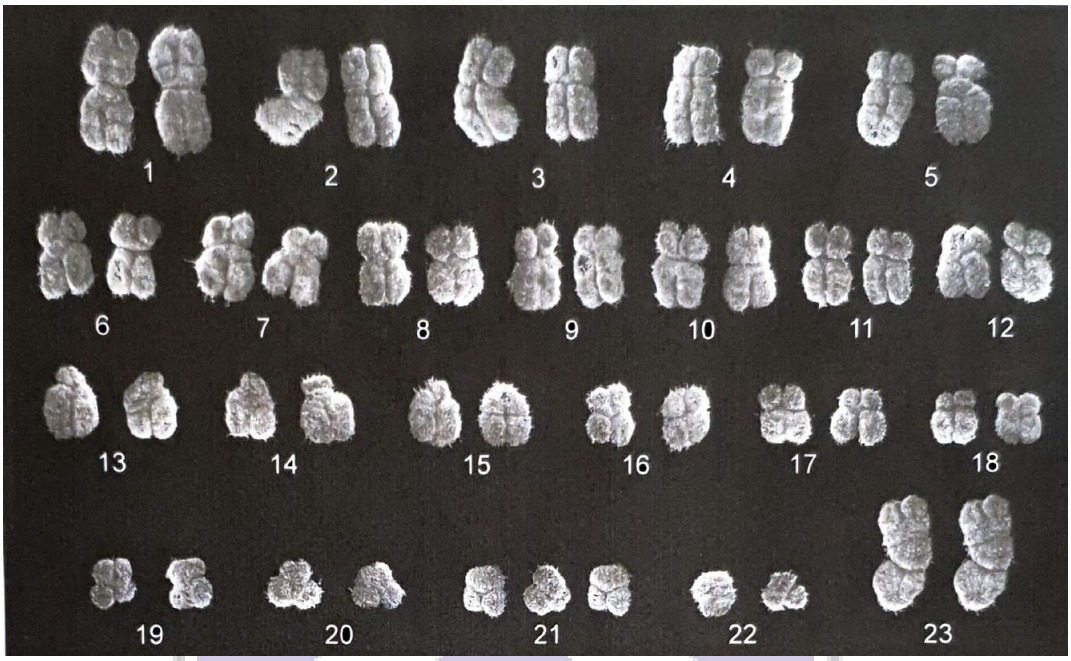


Fig. 2.1

(a) Identify, with reasons, two phenotypic features of this person that can be deduced from the karyotype shown in Fig. 2.1.

…… [4]

1 [Identify] The person has Down syndrome and the associated symptoms like mental retardation, facial deformities and compromised immune system
2 [Evidence] due to the presence of three chromosome 21.
3 [Identify] The person is phenotypically a woman
4 [Evidence] as she has two X chromosomes, as seen by the same size of her 23rd pair of chromosomes.

The age of a woman when she gives birth to a child affects the probability that the child will have a chromosomal aberration.

Fig. 2.2 shows this relationship.

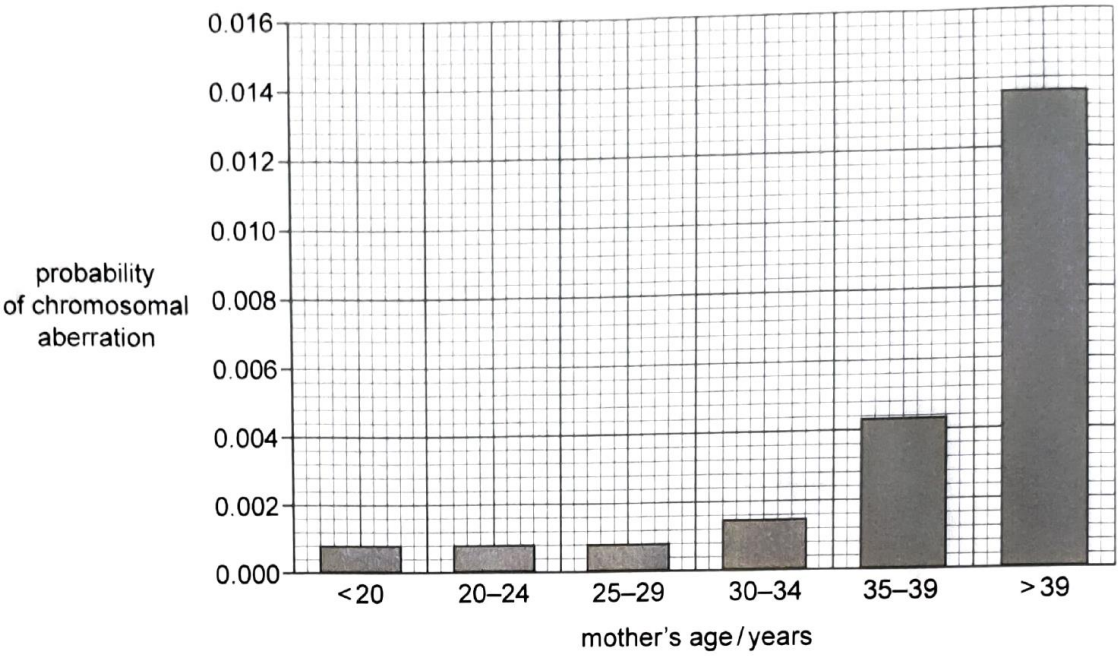


Fig. 2.2

(b) With reference to Fig. 2.2, describe how the age of a woman when she gives birth to a child affects the probability that the child will have a chromosomal aberration.

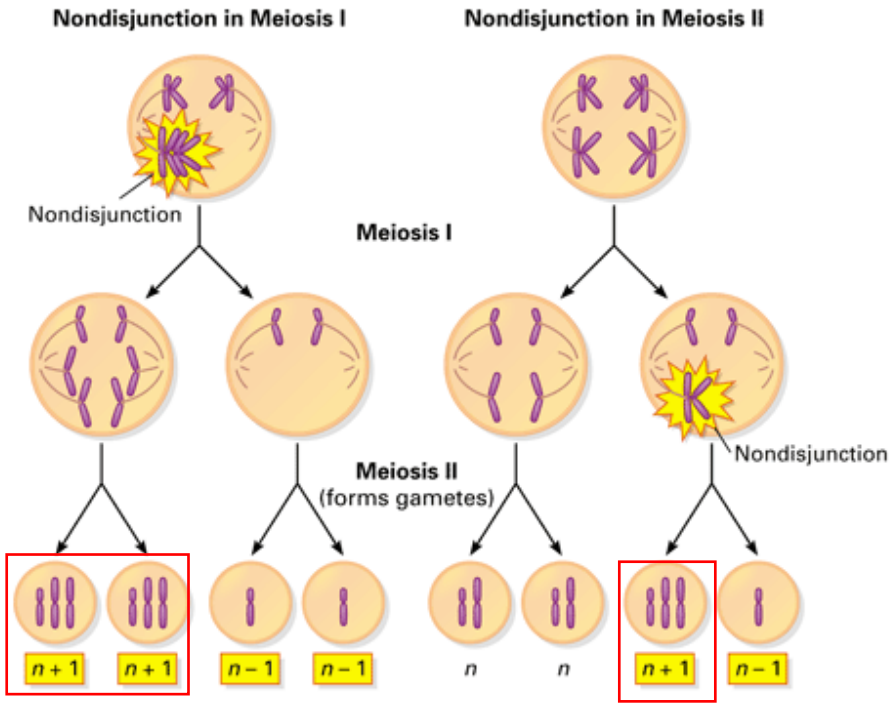
…… [3]

1 The older the woman when she gives birth to a child, the higher the probability the child will have a chromosomal aberration.
2 Below the age of 29, a woman has a very low probability of having a child with chromosomal aberration of 0.0008.
3 This increases exponentially from 0.0008 to 0.0136 when the woman's age increases from 29 to >39 years old when she gives birth.

(c) Down's syndrome is one such condition in humans that results from a chromosomal aberration leading to aneuploidy. Outline how this occurs.

……..…[3]

1 Non-disjunction occurred during meiosis / gamete formation
2 Resulting in failure of homologous chromosomes for chromosome **21** to separate in anaphase I of meiosis
OR
Failure of chromatids for chromosome **21** to separate in anaphase II of meiosis
3 Results in formation of an **ovum** with two chromosomes 21 (n+1) ;
4 When this ovum fuses with a normal haploid sperm (n) during fertilization, the resultant zygote will have 3 chromosomes 21. [during fusion of egg (n+1) and sperm (n)] ;


Nondisjunction in Meiosis I
Nondisjunction in Meiosis II
Nondisjunction
Meiosis I
Meiosis II
(forms gametes)
Nondisjunction
n + 1
n + 1
n – 1
n – 1
n
n
n + 1
n – 1

[Q2 Total: 6]

QUESTION 3

In eukaryotes, membrane proteins are synthesized, from the N-terminus to the C-terminus, by ribosomes bound to the rough endoplasmic reticulum in a process called translation.

Fig. 3.1 below shows an example of such a membrane protein embedded in the cell surface membrane. This protein is known to function as a receptor in a cell-signalling pathway.

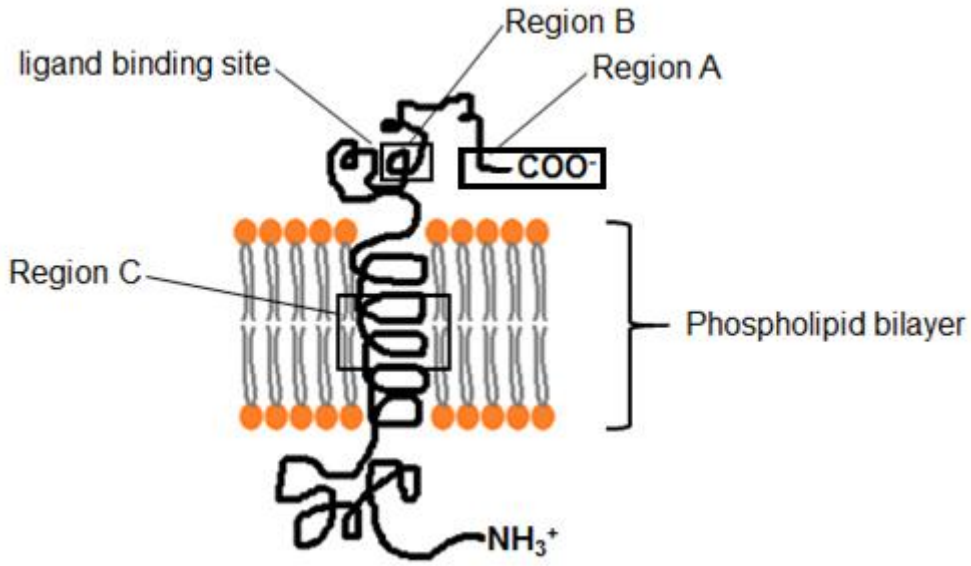


Fig. 3.1

DNA sequences at the locus coding for the membrane protein were isolated from 2 different individuals. A total of 4 different sequences were obtained. One of them is known to be the non-mutated sequence that gives rise to a fully functional membrane protein, while the other three, termed Mutations **A**, **B** and **C**, carry a single mutation **corresponding** to the Regions **A**, **B** and **C** respectively in **Fig. 3.1**.

These three mutations, together with their respective corresponding regions of non-mutated DNA sequences, are shown in **Fig. 3.2**. The sequences shown in **Fig. 3.2** are from the template DNA, presented in triplet codes.

Non-mutated sequence	3' – CTT AGA CTT ACT – 5'
Mutation A	3' – CTT AGT ACT TAC – 5'
[single base insertion]	
Non-mutated sequence	3' – CTC CTA CTT CTT – 5'
Mutation B	3' – CTC CCA CTT CTT – 5'
[single base substitution]	
Non-mutated sequence	3' – CAT CAA CAA TAA – 5'
Mutation C	3' – CTT CAA CAA TAA – 5'
[single base substitution]	

Fig. 3.2

(a) With reference to **Fig. 3.2**, state which of the 3 mutations led to a frameshift.

……[1]

1. Mutation A (Thymine insertion between 5th and 6th nucleotide.)

Fig. 3.3 shows the triplet codes that code for the different amino acids.

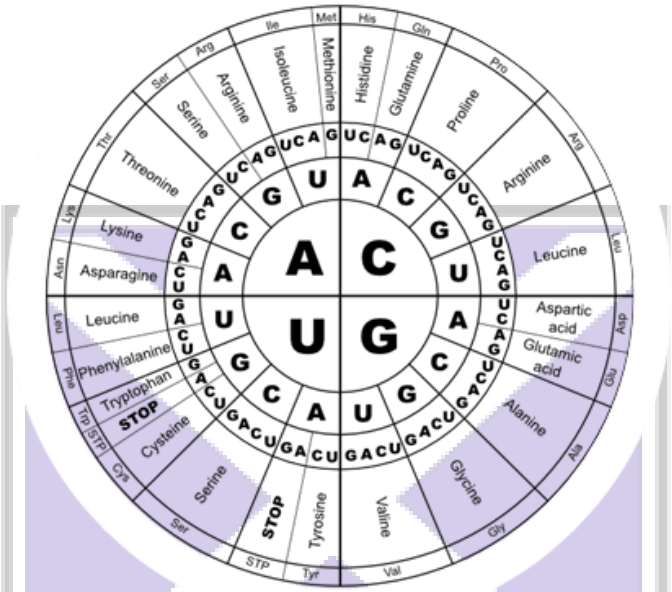


Fig. 3.3

It was found that out of the 3 mutations, only Mutation **A** produced an equally fully functional form of the membrane protein in the membrane. Mutation **B** led to the production of a non-functioning form of the protein in the membrane. Mutation **C** caused the receptor protein (of any form) not to be found in the membrane.

(b) With reference to **Fig. 3.1**, **3.2** and **3.3**, suggest and explain:

(i) how Mutation **A** can still lead to the production of a functioning membrane protein.

……[3]

1. Ref. to only a **loss of one amino acid** – glutamic acid (the 3rd codon is changed from glutamic acid to STOP codon);
2. Frameshift mutation (single base insertion) occurred near the end of the coding sequence. This led to only a **small / insignificant change** in primary structure of protein at the C-terminus;
3. **Majority** of the primary structure of protein (**from N-terminus to Region A**) is **unchanged,** thus, secondary (α-helix) and tertiary/globular/3D structure of protein is generally still intact / minimal change;
4. AVP (eg. 3D conformations of ligand-binding site and segment facing cytoplasmic side are still intact / unchanged);
5. AVP (eg. Segment / region / final amino acid of glutamic acid at C-terminal does not serve an essential function for the receptor);

(ii) how Mutation **B** led to the production of a non-functioning form of the protein in the membrane.

……[3]

1. Single base substitution mutation (T changed to C) led to change in amino acid from aspartic acid to glycine
2. Results in a change in **3D conformation** of ligand-binding site;
3. Ligand-binding site is no longer complementary to its ligand; ligand can no longer bind to receptor on the extracellular side.
4. Thus, signal can no longer be relayed to target molecules within cell / no signal transduction;

(iii) how Mutation **C** caused the protein not to be found in the cell surface membrane.

……[3]

1. Single base substitution mutation (A changed to T) led to a change in amino acid from valine [GUA] to glutamic acid [GAA]
2. Changing hydrophobic valine into hydrophilic glutamic acid alters the interactions between R groups
3. This changes the tertiary structure (3D conformation) of the receptor molecule, causing the protein to not be inserted into the membrane

   OR

   hydrophobic valine is required for **anchoring** of the protein in the membrane via hydrophobic interactions with **hydrophobic fatty acid chains** of phospholipid bilayer of membrane
4. AVP (eg. protein secreted instead of being embedded in the membrane)

[Q3 Total: 10]

~ THE END ~