Mutations

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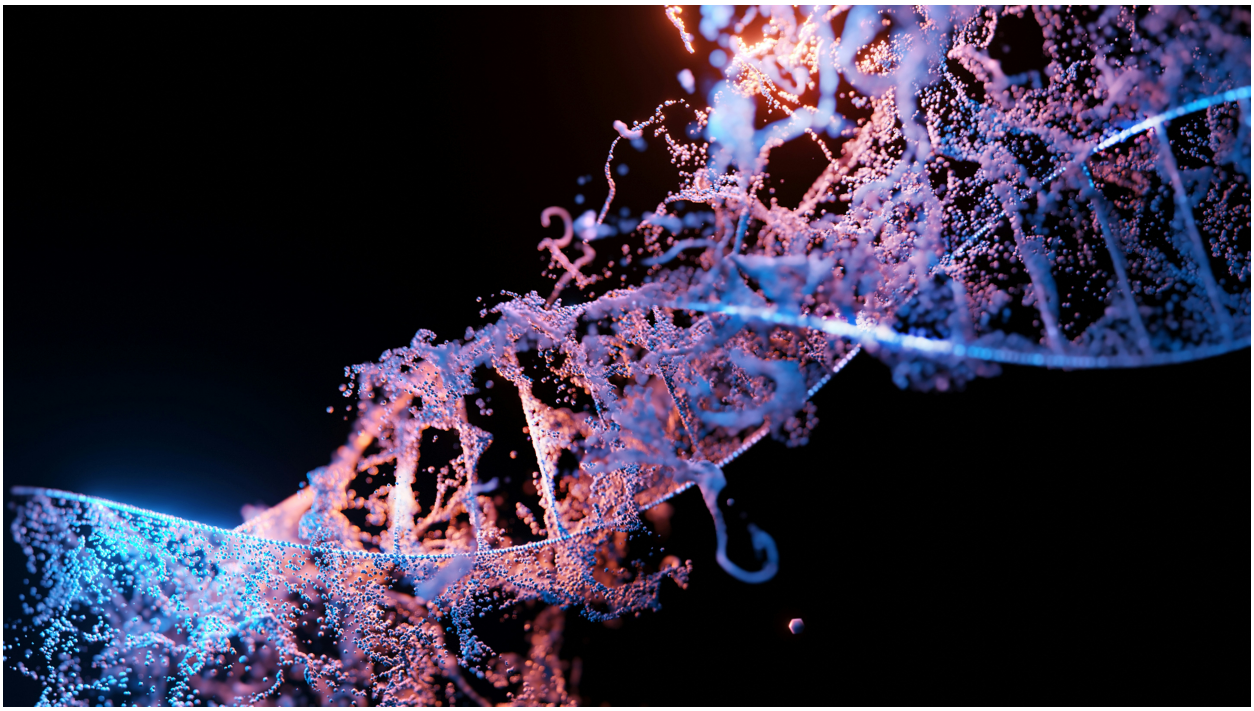

Difference between gene mutation and chromosomal aberrations

(i) Distinguish between gene mutations and chromosomal aberrations. [2]

Point of Comparison	Gene mutation	Chromosomal aberration
1. Definition	Change in nucleotide sequence	Change in chromosomal structure or number;
2. No. of genes affected	Affects a one gene	Usually affects many genes (because involves a segment or an entire chromosome hence);
3. Changes in chromosome number	No change in chromosome number	May have changes in chromosome number e.g. aneuploidy / polyploidy;
4. Mechanisms	Substitution, deletion or addition of nucleotides (any 2)	Translocation, deletion or inversion of chromosomal segments or non-disjunction events during nuclear division (any 2);
5. Frameshift	Frameshift is possible	No frameshift;

Any two pairs

▼ Notes

what recessive mutations mean

- Both copies of the gene must be mutated
- Mutations will result in non-functional protein/ no protein produced
- Normal allele will mask the effect of mutated allele if only one copy is mutated

Explaining how a point mutation can result in a non-functional protein/ disease/ any condition or effect

- Explain what the type of mutation given in the question means
  - Insertion mutation: adding of nucleotide into the nucleotide sequence
  - A single base substitution from original base to new base
- This will result in the change of sequence of mRNA and a change in codon

- Causing a different anticodon binding to the mutated codon, carrying a different amino acid with different R group chemical properties
- Changes in primary structure
- Change in specific 3D conformation
    - If an enzyme, can cause enzyme to no longer be complementary to substrate
    - Can cause enzyme to be non functional
- May introduce stop codon causing a shortened polypeptide and hence the protein won't be produced

Effect of mutations on haemoglobin sickle cell anaemia)

- A single base substitution from thymine to adenine
- Results in a change of sequence of mRNA and change in codon
- Change from GAG coding for amino acid glutamate to GUG which codes for valine
- Hydrophillic charged glutamic acid is replaced by hydrophobic non-polar valine
- This changes the primary, secondary and tertiary structure because polypeptide chain folds is affected by change in R group and bonds formed
- At low oxygen, loss of oxygen from HbS results in an unusual conformational change that causes a hydrophobic patch to stick out
- This hydrophobic patch attaches to a hydrophobic patch on an other HbS causing them to polymerise into insoluble fibres es
- Long insoluble HbS fibres within red blood cell causes its shale to be distorted from a normal biconcave to a sickle shape, resulting in them being more fragile, having a shorter lifespan
- This causes shortage of RBC and poor oxygen transport causing anaemia
- The RBC can also get lodged in small blood vessels, interfering in blood circulation causing organ damage

Explain why somatic mutations have a milder consequence than Germaine mutations

Explain why somatic mutation may have milder consequence than germline mutation.

1. (idea of) Somatic cells are not inherited but gametes are inherited;
2. When mutated gamete fuse with another gamete, the resulting zygote contains the mutation;
3. When the zygote undergoes mitosis, the mutation is transmitted to (idea of) all cells and may be significant for the future of the species;
4. Somatic mutation is lost on the death of the organism;

[2]

▼ Notes

mtDNA mutation

(d) Mitochondrial complex I deficiency is the most common mitochondrial disorder present in childhood. It can be caused by mutation in mitochondrial DNA (mtDNA) or mutation in nuclear DNA.

The characteristics of the deficiency caused by mutations in mtDNA are:

- a cell in an ovary produces gametes with different proportion of normal mitochondria and mitochondria that contains the mtDNA mutation
- a person has disease symptoms when the proportion of mutant mitochondria in their cells exceed a certain threshold
- the severity of disease symptoms, and the age at which they appear, can vary greatly in the children of one woman.

In a family with history of mitochondrial complex I deficiency that is caused by mutation in a nuclear DNA, the probability of a child inheriting the mutation can be predicted.

Suggest why, in families where mitochondrial complex I deficiency is caused by mtDNA mutation, it is not possible to predict the probability of a child inheriting the mutation.

1. Different children have different amount of mutant mtDNA/mitochondria;
2. Only mother/siblings, with proportion of mutant mitochondria in their cells exceed a certain threshold will show symptoms;
3. (idea of) Does not show typical patterns of inheritance;
4. mtDNA is inherited only from mother/maternally;

[2]

▼ Notes

Describing effect of mutation

- Ref to nucleotide substitution/ insertion/ mutation (mechanism)
- Ref to missense/nonsense/frameshift mutation/extensive missense and may result in nonsense mutation (effect)

- Ref to different amino acid added, changing 3D structure of protein/ premature termination of translation/ synthesis of truncated protein

effect of mutations in inter-ionic region

- Creates a new alternative splice site within interionic region
- As a result, alternative splicing, both normal splice and incorrectly spliced mRNA are produced

Effect of mutation in upstream region

- Mutation occurs in the promoter region/enhancer/silencer
- Reduces binding efficiency of general transcription factors/ RNA polymerase/activator OR increases binding efficiency of repressors
- Less mRNA synthesised/ less gene expression/ transcription and hence less protein produced

Describe how gene mutations may affect the protein coded for by a gene

- A gene mutation is a change in the nucleotide/ base sequence in DNA
- Substitution mutation is where a nucleotide is replaced by a different nucleotide, resulting in a change in sequence of mRNA and a change in codon, causing a different Sequence of amino acid which leads to different folding of polypeptide to 3D conformation of same folding of polypeptide to 3D conformation as new amino acid coded is chemically similar
- Insertion or addition occurs when one or several nucleotides are inserted in a sequence and deletion occurs when one or several nucleotides are removed from a sequence of bases, resulting in a frameshift mutation and different sequences of amino acid, leading to different folding of polypeptide to 3D conformation or a truncated polypeptide and hence non functional
- Inversion is a segment of nucleotide sequence separated from the allele and rejoins at the original position but it is inverted causing in different codons on

mRNA and a different amino acid leading to different folding of polypeptide to 3D conformation or truncated polypeptide hence non Functional polypeptide

For a named genetic disease, describe the mutation and effect of phenotype

Sickle cell anaemia

- a result of a point substitution mutation where thymine is replaced with adenine in a gene coding for the beta globin chain
- A change in a single base in the 6th triple codon results valine to replace glutamine amino acid
- Valine being non-polar compared with charged glutamine results in a change in properties of polypeptide chain causing change in primary, secondary and tertiary structure leading to different folding of polypeptide to 3D conformation and normal haemoglobin becomes sickle cell haemoglobin
- When oxygen levels are low in the blood, the Hb Scmolecule undergoes an unusual conformation change that allows Hb S to polymerise/ crystallise to form rigid fibres
- This causes rbc to change from a circular biconcave shape to sickle shape
- Sickled RBC May obstruct blood vessels and interfere with blood circulation causing organ failure
- It is also more fragile and susceptible to lysis and active destruction of spleen results in reduction in rbc numbers causing anaemia
- It is a recessive condition requiring both alleles to the Beta globin chain to be mutated in order for the symptoms to appear

How to know phenotypic features of an individual from its karyotype

- 3 copies of chromosome 21
    - Person has Down syndrome and should have characteristics facial features such as short stature, hear defects, susceptibility to respiratory infection and mental retardation

- Having 2 homologous chromosome 23 (same height, size)
    - Female with female reproductive structure such as ovaries