Genetics

Biology Dept.3rd stage

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Lec -7-

Centromeres and Telomeres

Centromeres and telomeres are two essential features of all eukaryotic chromosomes.

Each provide a unique function i.e., absolutely necessary for the stability of the chromosome.

Centromeres are required for the segregation of the centromere during meiosis and mitosis.

Teleomeres provide terminal stability to the chromosome and ensure its survival

Centromere

The joining point of a metaphase chromosomeis the centromere (primary constriction). The centromere is a constant zone ofeach chromosome and is present at the same site in all mitotic cycles. In some
hromosomes, the centromere is closer to one end and not necessarily in the middle. Specialized proteins bind to the outer faces of the two centromeres of
each duplicated chromosome to form laminar structures called kinetochores

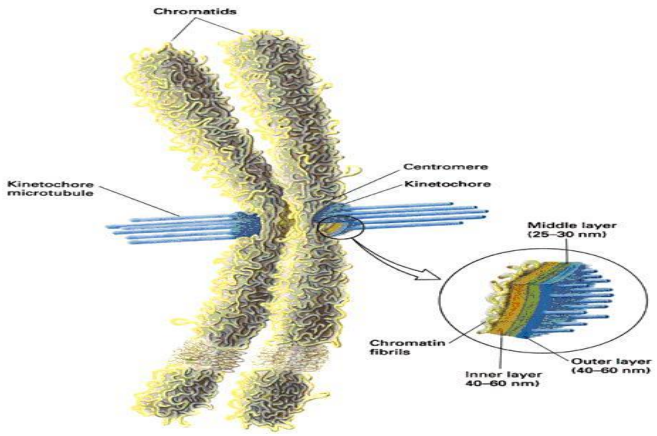
The region where two sister chromatids of a chromosome appear to be joined or "held together" during mitotic metaphase is called Centromere

When chromosomes are stained they typically show a dark-stained region that is the centromere. Also termed as Primary constriction During mitosis, the centromere that is shared by the sister chromatids must divide so that the chromatids can migrate to opposite poles of the cell.

On the other hand, during the first meiotic division the centromere of sister chromatids must remain intact whereas during meiosis II they must act as they do during mitosis. Therefore the centromere is an important component of chromosome structure and segregation.

Kinetochore

Within the centromere region, most species have several locations where spindle fibers attach, and these sites consist of DNA as well as protein.The actual location where the attachment occurs is called the kinetochore and is composed of both DNA and protein. The DNA sequence within these regions is called *CEN* DNA.



Telomere

The two ends of a chromosome are known as telomeres.

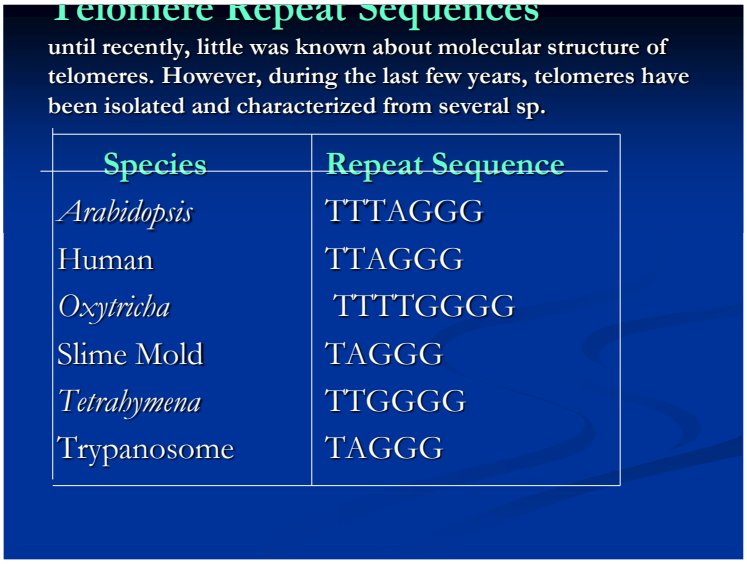
It required for the replication and stability of the chromosome.

When telomeres are damaged or removed due to chromosome breakage, the damaged chromosome ends can readily fuse or unite with broken ends of other chromosome.

Thus it is generally accepted that structural integrity and individuality of chromosomes is maintained due to telomeres.

McClintock noticed that if two chromosomes were broken in a cell, the end of one could attach to the other and vice versa.

Thus the ends of broken chromosomes are sticky, whereas the normal end is not sticky, suggesting the ends of chromosomes have unique features.



What is a mutation?

A mutation is any change in the DNA sequence. Mutations can lead to genetic disorders or disease. Most mutations are recognised because the phenotype, that is the characteristics displayed by an organism, have changed. There are many different types of mutation.

Germinal and Somatic Mutations

Eukaryotic organisms have two primary cell types --- germ and somatic. Mutations can occur in either cell type. If a gene is altered in a germ cell, the mutation is termed a germinal mutation. Because germ cells give rise to gametes, some gamete s will carry the mutation and it will be passed on to the next generation when the individual

successfully mates. Typically germinal mutations are not expressed in the individual containing the mutation

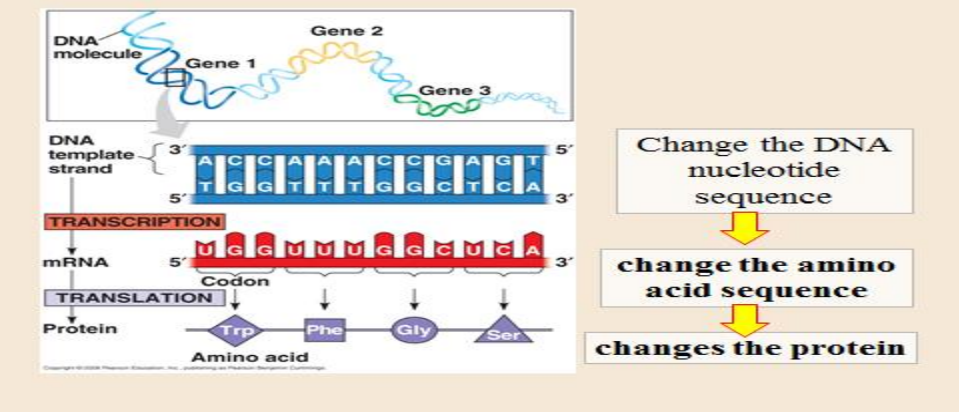
Somatic cells give rise to all non-germline tissues. Mutations in somatic cells are called somatic mutations. Because they do not occur in cells that give rise to gametes, the mutation is not passed along to the next generation by sexual means.

- According to origine
- 2 types of mutations:

1-Spontaneous Mutations: Some mutations arise as natural errors in DNA replication (or as a result of unknown chemical reactions); these are known as spontaneous mutations

  - occur in the natural environment without the addition of mutagens (agents that cause mutations)
  - Occur randomly and spontaneously
  - (without any known causal factors),
- Most common type of substitution
- Mistake during DNA replication, incorrect base incorporated into DNA

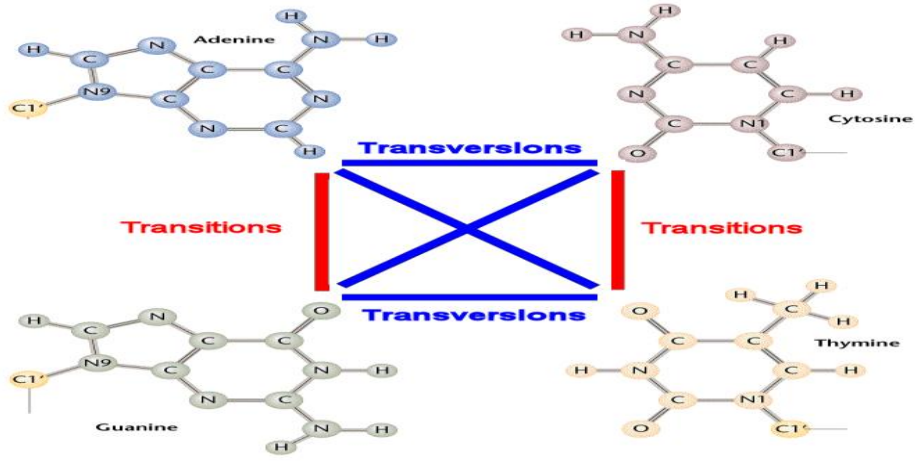
four types:



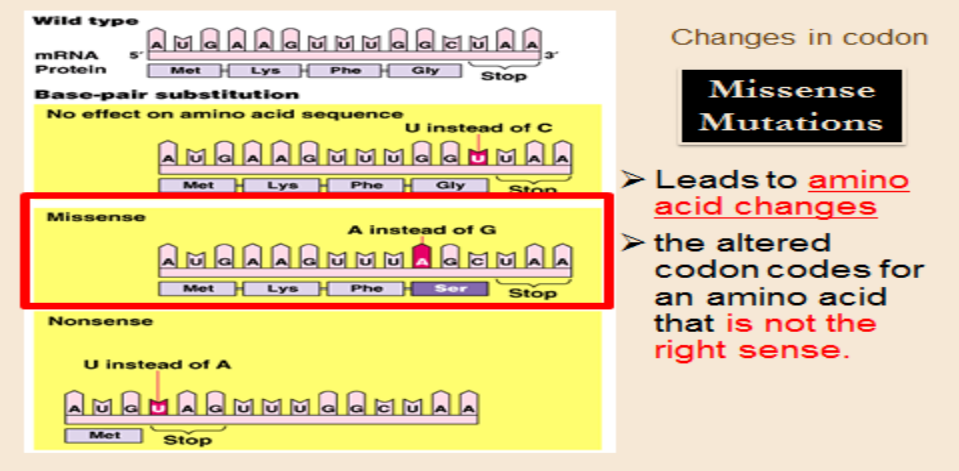
Single base substitutions

A single nucleotide base becomes replaced by another. These single base changes are also called point mutations. If a purine (a, t) replaces a purine or a pyrimidine

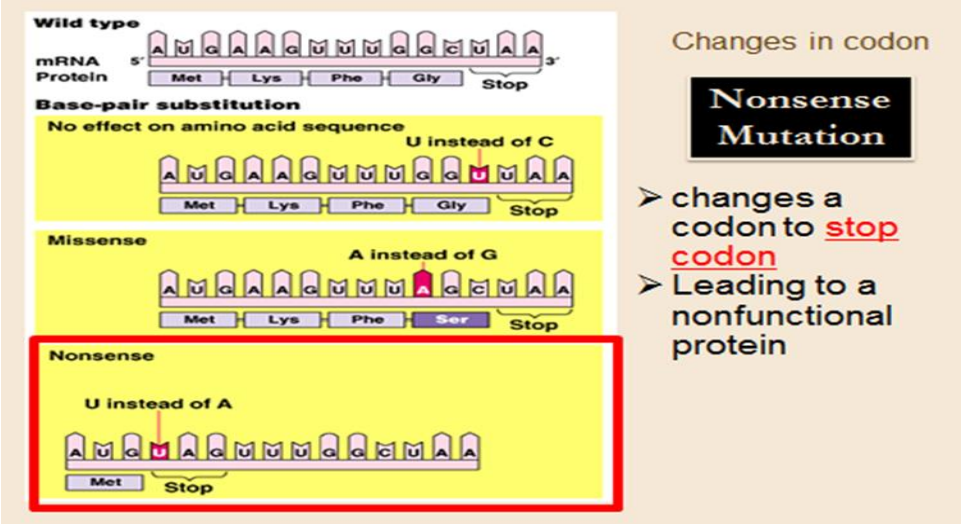
(c, g) replaces a pyrimidine, it is called a transition. If a purine replaces a pyrimidine or vice-versa, the substitution is called a transversion.



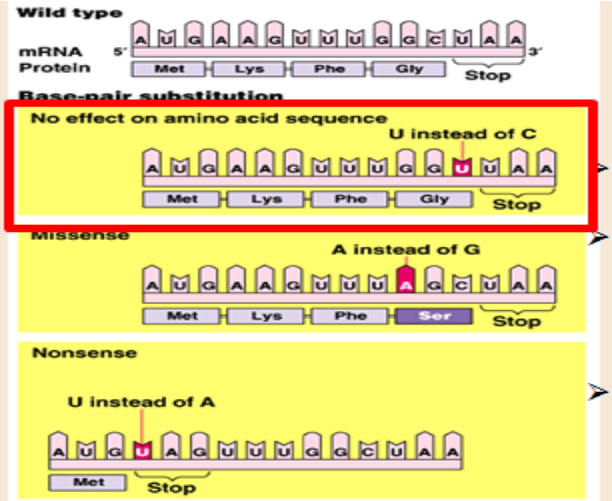
- **Missense mutations** - In a missense mutation, the new base alters a codon resulting in a different amino acid being incorporated into the protein chain. This is what happens in sickle cell anaemia. The 17th nucleotide of the gene for the beta chain of haemoglobin is changed from an 'a' to a 't'. This changes the codon from 'gag' to 'gtg' resulting in the 6th amino acid of the chain being changed from glutamic acid to valine. This apparently trivial alteration to the beta globin gene alters the quaternary structure of haemoglobin, which has a profound influence on the physiology and wellbeing of the individual.



Nonsense mutations - In a nonsense mutation, the new base changes a codon that specified an amino acid into one of the stop codons (taa, tag, tga). This will cause translation of the mRNA to stop prematurely and a truncated protein to be produced. This truncated protein will be unlikely to function correctly. Nonsense mutations occur in between 15% to 30% of all inherited diseases including, haemophilia, and duchenne muscular dystrophy.



- **Silent mutations** - Silent mutations are those that cause no change in the final protein product and can only be detected by sequencing the gene. Most amino acids that make up a protein are encoded by several different codons. So, if for example, the third base in the 'cag' codon is changed to an 'a' to give 'caa', a glutamine (Q) would still be incorporated into the protein product, because the mutated codon still codes for the same amino acid. These types of mutations are 'silent' and have no detrimental effect.



Changes in codon

Silent Mutations

- have no effect on the encoded protein.
- a change in a base pair transform one codon into another that translated into the same amino acid.
- happens because of redundancy in the genetic code.