RAMA UNIVERSITY

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FACULTY OF ENGINEERING &TECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY

Mutation

What is mutation?

Mutation is defined as a change in nucleotide sequence due to errors of DNA replication, recombination, or repair or to radiation, chemical mutagens, viruses, or transposons. They can occur spontaneously or can be induced.

Categories and types of mutation

Three general categories of mutations exist: **genome**, **chromosome**, and **gene.**
Genome mutations result from **missegregration** (failure to properly segregate) during meiosis and produce changes in chromosome number.
Chromosome mutations are caused by rearrangements in the structure of a chromosome, such as translocations or deletions.
Gene mutations alter the base sequence of a gene.
Mutations occur in germ cells, somatic cells, and mitochondria.
Germ-line mutations affect DNA in all cells and are transmitted to offspring.
Mitochondrial mutations affect mitochondrial DNA, all of which is inherited from the mother's egg; accordingly, they are inherited maternally.
Somatic mutations affect cells in a single tissue, and are not transmitted to the next generation.
Mutations act, generally, by perturbing gene expression or the function of proteins, and they may do so from the earliest to the latest stages of life

Types of mutation

There are three types of DNA Mutations:

- base substitutions,
- deletions and
- insertions.

1. Base Substitutions

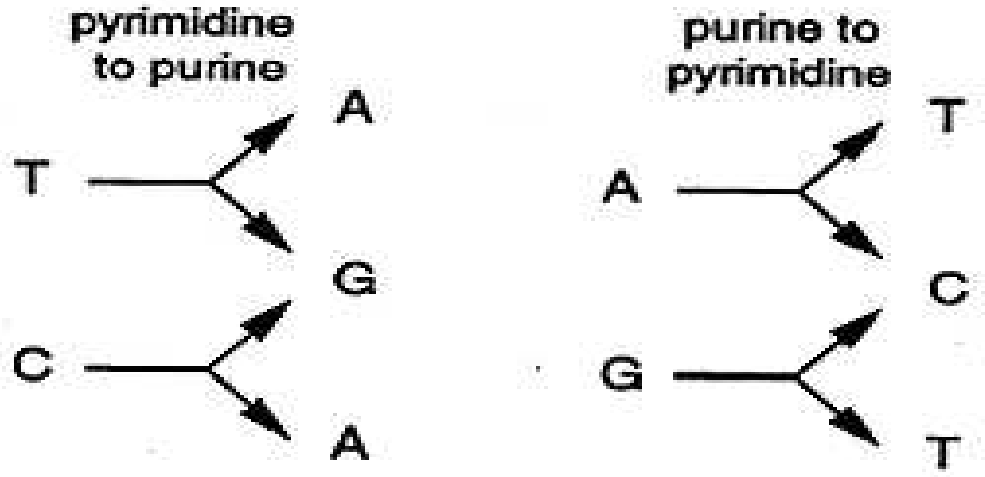
Single base **substitutions** are called point mutations, recall the point mutation Glu -----> Val which causes sickle-cell disease. The smallest mutations are point mutations, in which only a single base pair is changed into another base pair. Point mutations that occur in DNA sequences encoding proteins are silent, missense or nonsense. Point mutations are the most common type of mutation and there are two types.

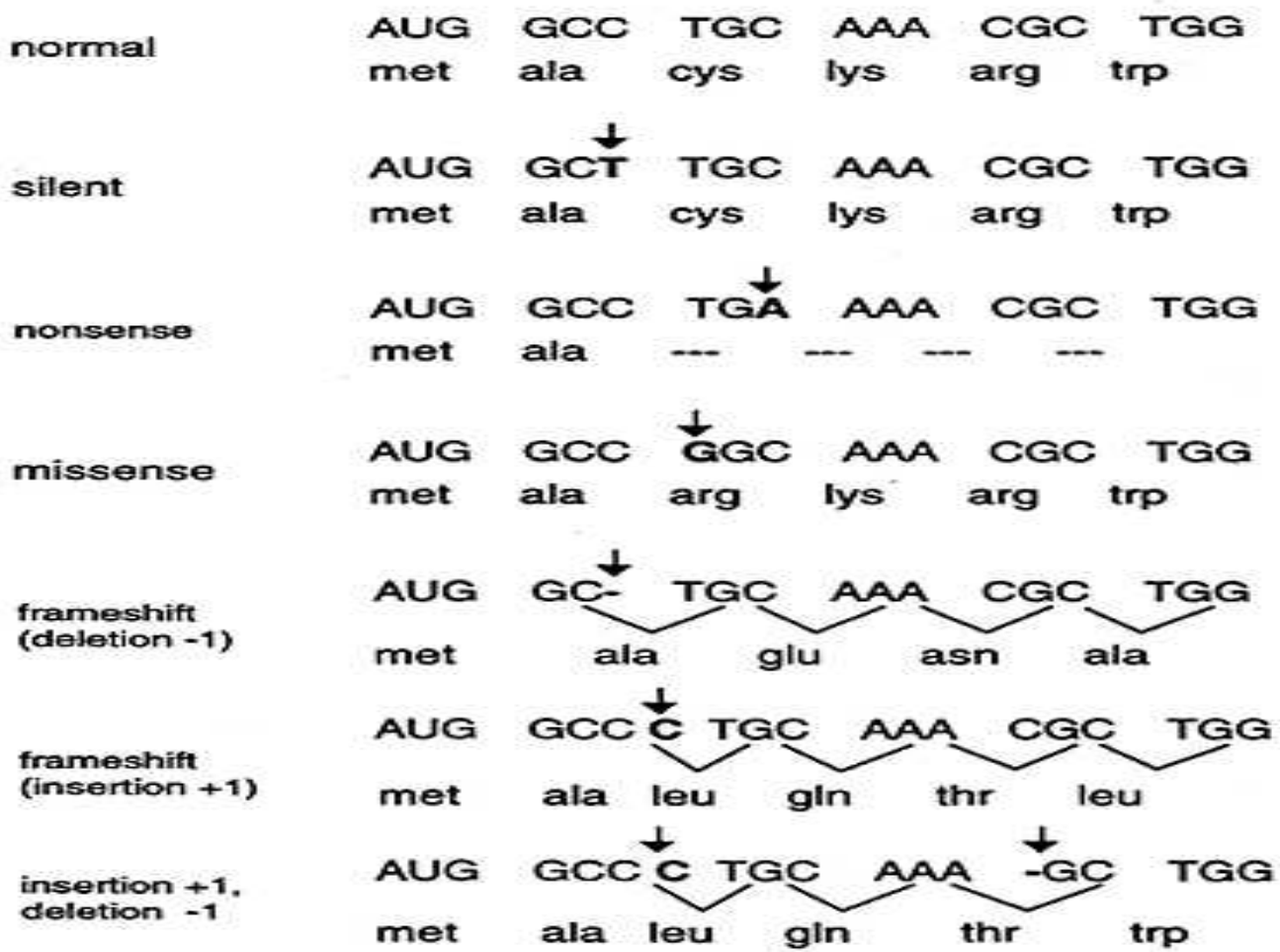
Transition: this occurs when a purine is substituted with another purine or when a pyrimidine is substituted with another pyrimidine.

Transversion: when a purine is substituted for a pyrimidine or a pyrimidine replaces a purine.

Transitions:

Transversions:




normal
AUG GCC TGC AAA CGC TGG
met ala cys lys arg trp
silent
AUG GCT TGC AAA CGC TGG
met ala cys lys arg trp
nonsense
AUG GCC TGA AAA CGC TGG
met ala --- --- --- ---
missense
AUG GCC GGC AAA CGC TGG
met ala arg lys arg trp
frameshift (deletion -1)
AUG GC- TGC AAA CGC TGG
met ala glu asn ala
frameshift (insertion +1)
AUG GCC C TGC AAA CGC TGG
met ala leu gln thr leu
insertion +1, deletion -1
AUG GCC C TGC AAA -GC TGG
met ala leu gln thr trp

Silent:

If a base **substitution** occurs in the third position of the codon there is a good chance that a synonymous codon will be generated. Thus the amino acid sequence encoded by the gene is not changed and the mutation is said to be silent.

Missence:

When base **substitution** results in the generation of a codon that specifies a different amino acid and hence leads to a different polypeptide sequence. Depending on the type of amino acid substitution the missense mutation is either conservative or non-conservative. For example if the structure and properties of the substituted amino acid are very similar to the original amino acid the mutation is said to be conservative and will most likely have little effect on the resultant proteins structure / function. If the substitution leads to an amino acid with very different structure and properties the mutation is non-conservative and will probably be deleterious (bad) for the resultant proteins structure / function (i.e. the sickle cell point mutation).

Nonsense: When a base **substitution** results in a stop codon ultimately truncating translation and most likely leading to a nonfunctional protein.

2. Deletions

A deletion, resulting in a frameshift, results when one or more base pairs are lost from the DNA. If one or two bases are deleted the translational frame is altered resulting in a garbled message and nonfunctional product. A deletion of three or more bases leaves the reading frame intact. A deletion of one or more codons results in a protein missing one or more amino acids. This may be deleterious or not.

3. Insertions

The insertion of additional base pairs may lead to frameshifts depending on whether or not multiples of three base pairs are inserted. Combinations of insertions and deletions leading to a variety of outcomes are also possible.