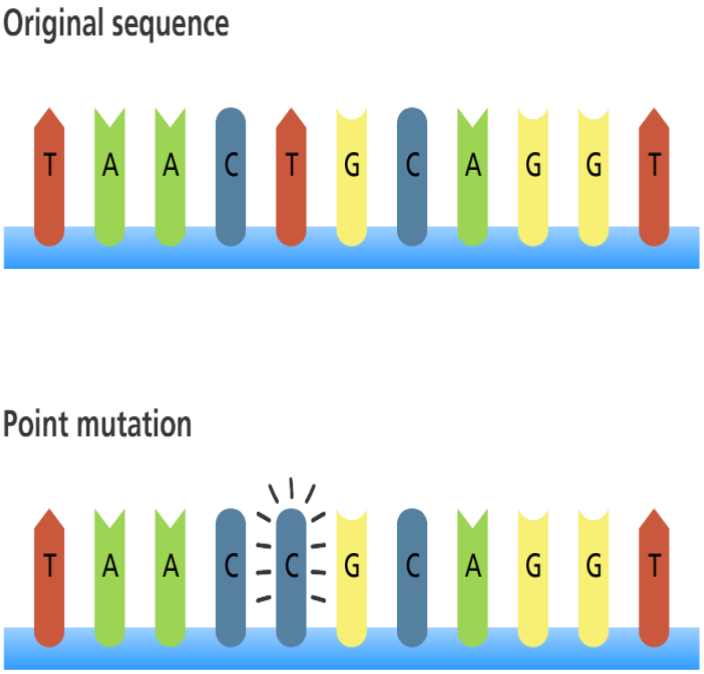
MUTATION



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INTRODUCTION: The word mutation was given by Hugo-De-Varies and in biology, a **mutation** is defined as sudden change in structure or function of gene. It is an alteration in the nucleotide sequence of the genome of an organism, virus or extra chromosomal DNA. Mutations result from errors during DNA replication, mitosis, and meiosis or other types of damage to DNA (such as pyrimidine dimers that may be caused by exposure to radiation or carcinogens), which then may undergo error-prone repair or cause an error during other forms of repair or else may cause an error during replication. Mutations may also result from insertion or deletion of segments of DNA due to mobile genetic elements. Mutations may or may not produce discernible changes in the observable characteristics (phenotype) of an organism. They play a part in both normal and abnormal biological processes including evolution, cancer, and the development of the immune system.

Mutation can result in many different types of change in sequences. Mutations in genes can either have no effect, alter the product of a gene, or prevent the gene from functioning properly or completely. Mutations can also occur in non genic regions. Due to the damaging effects that mutations can have on genes, organisms have mechanisms such as DNA repair to prevent or correct mutations by reverting the mutated sequence back to its original state. Depending on biochemical basis of mutations there are different types of mutations.

CAUSES OF MUTATIONS: Four classes of mutations are (1) spontaneous mutations (molecular decay), (2) mutations due to error-prone replication by passing of naturally occurring DNA damage (also called error-prone trans lesion synthesis), (3) errors introduced during DNA repair, and (4) induced mutations caused by mutagens. However, different causes of mutations include-

(1) Tautomerism, depurination, deamination and slipped stand mispair.

(2) Mutation arise by error-prone replication.

(3) Can arise due to defective DNA repair.

(4) Certain chemicals like hydroxylamine, base analogs, DNA intercalary agents, DNA cross linkage and oxidative damage.

(5) UV and ionizing radiations can cause mutations.

(6) Changes in chromosome structure can lead to deletion, duplication, translocation and inversion which are types of mutations.

(7) Changes in number of chromosomes can lead to aneuploidy (change in chromosome number) or euploidy (change in chromosome set.

(8) Loss of function of a gene can lead to defective gene products which can create mutations.

MOLECULAR BASIS OF MUTATIONS: Based on different types of mutations, it may be classified as following-

(1) BY EFFECT ON STRUCTURE: Viewing the effect on structure, mutation may result in structural changes in chromosome leading to deletion, duplication, inversion and translocation. These changes may lead to large scale mutations which includes amplifications, deletion of large chromosomes region and large scale changes to structure of chromosomes.

(2) BY EFFECT ON FUNCTION: Loss in functional aspect of a gene can lead to mutation and can aid to generate a defective gene product. These mutations are of different types-

DOMINANT NEGATIVE MUTATION: Such mutations contain an altered gene product which would act antagonistic to wild type allele, resulting in altered molecular functions.

NEMORPH MUTATION: If through mutation a new defective gene product is synthesized then it is known as nemorph mutations.

LETHAL MUTATIONS: If any mutation causes death of the organism then it is called lethal mutation.

REVERSION: In any mutation where mutation can revert itself back to normal then it is called reversion.

(3) BY EFFECT ON FITNESS: Depending on fitness of organism mutations may be of three types-

HARMFULL MUTATIONS: These decrease fitness of an organism

BENEFICIAL MUTATIONS: These increase fitness of an organism.

NUETRAL MUTATIONS: These mutations neither benefit nor harm the organisms.

(4) BY IMPACT ON PROTEIN SEQUENCE: Based on this parameter, mutations are classified differently as-

FRAMESHIFT MUTATIONS: It is a type of mutation caused by insertion or deletion of a number of nucleotides in a DNA. The added sequence is not in triplet, so it disturbs the codon sequence.

For eg-**AUG- AGA-GUA (original sequence)**

Mutated sequence- **AUG-A- AGA-GUA (Mutated sequence)**

POINT MUTATIONS: This type of mutation results in a change in a single nucleotide. It can be of following types-

SILENT MUTATIONS**:** In this type of mutations a codon is replaced by another codon, but both of them code for same amino acid. Such mutation is silent mutations.

NON-SYNONYMOUS MUTATIONS: In such type of mutation, codon is replaced by other codon but both code for different amino acids. This mutation can be further classified as-

MISSENCE MUTATIONS: These mutations changes a nucleotide to cause mutation by substitution of a different amino acid, this can result in a non-functional protein. Such mutations can cause diseases like epidermolysis bulosa, sickle cell anemia etc.

NON-SENSE MUTATIONS: It is a type of mutation in which DNA sequence results in a premature or non-sense codon, which further leads to development of non-functional protein product.

BY INHERITANCE: In multicellular organism mutations may be of two types-

GERMLINE MUTATIONS: These refer to mutations taking place in the germ cells which are heritable.

SOMATIC MUTATIONS: These refer to mutations taking place in somatic cells.

SPECIAL CLASS OF MUTATIONS: This mutation consist of basically one type of mutation-

CONDITIONAL MUTATION: It is a type of mutation in which a wild type phenotype under certain conditions and a mutant phenotype under certain restrictive conditions would show their effect while in other condition they will not show any effect. For eg. A temperature sensitive mutation can cause cell death at high temperature but might have no effect at low temperature.

MUTATION RATES: Mutation rates vary substantially across species and the evolutionary forces that generally determine mutation are subject of ongoing investigation.

DISADVANTAGES OF MUTATIONS: All mutations are not harmful but most of them are harmful. Changes in DNA lead to mutations generally. However, the disadvantages of mutation are-

(1) It can lead to cancer development and can also turn tumor cells into malignant cells.

(2) Mutation can lead to changes in gene product or resulting protein.

(3) Mutations in disease causing prions (protein which do not contain genetic material) can lead to diseases in the body.

(4) Mutation can cause duplication of large section of DNA through genetic recombination.

(5) Mutations can also lead to changes in chromosome number which can lead to disastrous effects.

BENEFICIAL ASPECTS OF MUTATIONS: Sometimes mutations can be beneficial, some of its benefits are following-

(1) They lead to evolution and generation of new species.

(2) In plants, somatic mutations can lead to seed production and grafting.

(3) Sometimes it aids in maintain the germ line of genome.