आईएफटीएम विश्वविद्यालय, मुरादाबाद, उत्तर प्रदेश

IFTM University, Moradabad, Uttar Pradesh

NAAC ACCREDITED

E-Content

IFTM University, Moradabad

1. Subject Name: Molecular Biology

2. Topic Name: Mutation

3. Course: M.Sc (Biotechnology/Microbiology/Food Technology)

4. Year/Semester: I/I

5. Number of pages: 10 pages

6. Content Creator Name: Ms. Kanchan Lakhera

MUTATION

Introduction

- Sudden and heritable changes in the sequence of nucleotide of organism's genome or genotype is called as Mutation.
- The process by which mutation is produced is called as mutagenesis.
- An organism exhibiting a novel phenotype as a result of the +se of mutation is called a mutant.
- Such genetic changes includes ploidy, chromosomal aberrations and changes in individual genes.
- Generally the change in individual gene is known as gene mutation.
- Gene mutation at point level that involves the substitution of one base pair for another or deletion/addition of single base pair is described as point mutation.
- Mutation was first discovered by Wright in 1791 in male lamb which had short legs.
- Later on mutation was reported by Hugo de Vries in 1900 in Oenothera, Morgan (1910) in Drosophila (white eye mutant) and several others in various organisms. The term mutation was coined by de Vries.
- Mutations are generally recessive but dominant mutations also occur.
- Mutations are generally harmful to the organisms.
- Mutations are random, they can occur anytime and in any cell.
- Mutations are recurrent.

General Characteristics of Mutation:

Some of the important characteristics of mutations are briefly presented below:

i. Nature of Change:

Mutations may be permanent and heritable changes in the phenotype/genotype of an individual. Such changes occur due to alteration in number, kind or sequence of nucleotides of genetic material, i.e., DNA in most of the cases.

ii. Frequency:

Spontaneous mutations happen at a very low frequency. However, the mutation rate can be enhanced many fold by the use of physical and chemical mutagens.

iii. Mutation Rate:

Mutation rate varies from gene to gene. Some genes exhibit high mutation rate than others. These genes are called as mutable genes, e.g., white eye in Drosophila.

vi. Direction of Change:

Mutations usually occur from dominant to recessive allele or wild type to mutant allele.

v. Effects:

Mutation, occurring in the coding region of DNA or regulatory sequences of DNA can be harmful to the organism. In other words, most of these mutations have deleterious effects. Only about 0.1% of the induced mutations are useful in crop improvement.

vi. Site of Mutation:

Muton which is a sub-division of gene is the site of mutation. An average gene contains 500 to 1000 mutational sites. Within a gene some sites are highly mutable than others. These are generally referred to as hot spots.

vii. Type of Event:

Mutations are random events. They may occur in any gene (nuclear or cytoplasmic), in any cell (somatic or reproductive) and at any stage of development of an individual.

viii. Recurrence:

The same type of mutation may occur repeatedly or again and again in different individuals of the same population. Thus, mutations are of recurrent nature.

Role of Mutation:

- Ultimate source of all the genetic variations.
- Provides the raw material for evolution.
- Mutation results into the formation of alleles. Without mutation, all genes would exist in only one form.
- Organisms would be able to evolve and adapt to environmental change.

Molecular basis of gene mutation:

Mutations occur in two ways;

- **Spontaneous mutations:**
    - that occur without the treatment of organism with any exogenous mutagen.
    - Mutagen- It is an agent that leads to an increase in the frequency of occurrence of mutations
    - Spontaneous mutations are the ultimate source of natural genetic variation that is seen in populations
    - Spontaneous mutations may occur during the normal growth of cell because of
    - **Replication error**
    - **Spontaneous lesions**
    - **Transposition of transposable elements**
- **Induced mutations**:
    - Arise because a mutagen has reacted with the parent DNA, causing a structural change that affects the base pairing capability of the altered nucleotide

Spontaneous mutations:

1. Replication Error:

- Each of the common bases in the DNA can spontaneously undergo tautomeric shift changing from one form to the another.

- Formation of the tautomer of any of the base alters its base pairing capabilities
- Thymine and Guanine have more stable keto forms.
- Adenine and Cytosine have more stable amino forms.
- But these bases may undergo tautomeric shift to less stable enol (from keto) and imino (from amino form).
- If the bases exist in their less stable tautomeric form during the DNA replication, a mutation might result.
- When bases are +nt in their rare imino or enol states, they can form adenine - cytosine and guanine - thymine base pairs.
- The net effect of such an effect and the subsequent replication required to seggregate the mismatched base pairs is an AT or GC or GC to AT base pair substitution (transition).
-

Errors in DNA Replication:

The low overall rate of mutation during DNA replication (1 base pair change in one billion base pairs per replication cycle) does not reflect the true number of errors that take place during the replication process. The number is kept so low by a proof-reading system that checks newly synthesized DNA for errors and corrects them when they are found. Errors in DNA replication can take different forms, but usually revolve around the addition of a nucleotide with the incorrect base, meaning the pairing between the parent and daughter strand bases is not complementary. The addition of an incorrect base can take place by a process called tautomerization. A tautomer of a base group is a slight rearrangement of its electrons that allows for different bonding patterns between bases. This can lead to the incorrect pairing of C with A instead of G, for example.

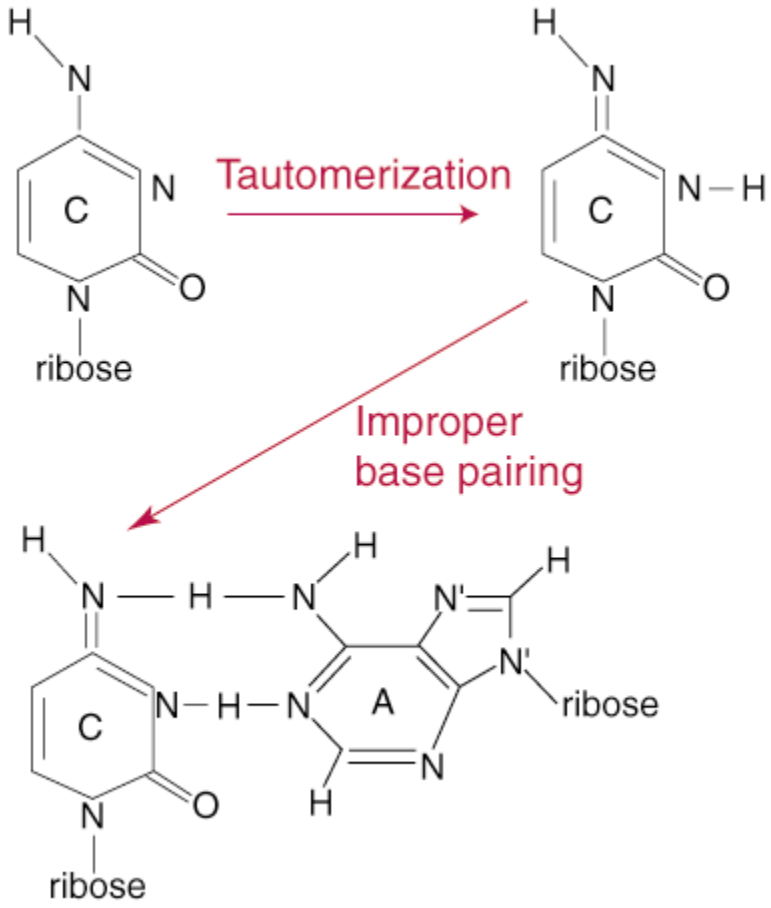

Figure : Tautomerization of Cytosine

- **Error during the replication may result in Point or Gene Mutations which includes :**
    - **1. Substitution mutation**
    - **2. Frameshift mutation**
- ***Point or Gene Mutations***

  A **point mutation** is when a single base pair (or just a few) is altered, an alteration at a "micro" level. There are two general types of point mutations: **substitutions** or **insertions** and **deletions**.

  1. Base pair substitutions- It involve an alteration of a single nucleotide in the DNA. A substitution mutation can entail either a **transition** or a **transversion**. Some substitution mutations have no effect on the protein coded for. One reason is because of the redundancy of the genetic code (recall that about one fourth of all base pair substitutions code for the same amino acid; such mutations are

termed **silent mutation** since there is no change in amino acid that results from the substitution). Another reason for lack of effect is that even if a change in amino acid occurs (termed **missense mutation**), it may have no actual influence on the function of a protein. Also any mutation located within a non-coding region of the chromosome will not be translated into a protein. Lastly, an altered gene may be masked by other normal copies of the gene present in the genome.

In certain cases, point mutations can have a significant effect—particularly when a substitution produces a stop codon so that the alteration causes the protein synthesis to halt before the protein is entirely translated, altering the entire structure. These are called **nonsense mutations**.

- **Transition**: Purine replaced by a different Purine or Pyrimidine by a different Pyrimidine
- **Transversion**: Purine replaced by a Pyrimidine or Pyrimidine by a Purine

2. Frameshift mutations:

- Base pair insertions and deletions are additions or losses of one to several nucleotide pairs in a gene. Mutations that are insertions and deletions tend to have a much greater effect than do mutations that are base pair substitutions because they disrupt the normal reading frame of trinucleotides. Recall that each group of three bases corresponds to one of 20 different amino acids used to build a protein. Mutations involving base pair insertions and deletions are often therefore referred to as **frameshift mutations**. Under these circumstances the DNA sequence following the mutation is read incorrectly.

2. Spontaneous lesions:

- Naturally occurring damage to the DNA is called spontaneous lesions also can generate mutations.
- Most common spontaneous lesions are:
    - **a. Deamination**

- **b. Depurination and Depyrimidination**
- **c. Oxidative damage**

- **a. Deamination:**
  - Three of the four bases normally +nt in DNA Cytosine, Adenine and Guanine; also 5-methylcytosine contain exocyclic amino groups.
  - The loss of these groups (deamination) occurs spontaneously in pH and Temp. dependent reactions of DNA and results in the conversion of:
    - 5-methylcytosine---→deamination--→thymine
    - cytosine----------→deamination----→uracil
    - adenine----→deamination------→hypoxanthine
    - guanine----→deamination----→xanthine
- **b. Depurination and depyrimidination:**
  - The loss of Purine and Pyrimidine by the breaking beta-N-glycosidic bond of nucleotides of DNA has been most extensively studied at acidic pH
  - However depurination and depyrimidination may also occur at appreciable rates at neutral or alkaline pH but the mechanism of hydrolysis of nucleoside at neutral or alkaline pH is less well characterized.
  - Pyrimidine nucleosides are more stable than purine nucleosides with respect to the glycosidic bond of the bases to the deoxyribose
  - The mechanism of Depurination and depyrimidination is same
  - Cytosine and Thymine are lost at a rate of 1/20 of that for Adenine and Guanine

c. Oxidative damage:

- Damage to DNA may also occur due to attack by Reactive Oxygen Species
- Radicals like:

- Peroxide radicals
- Hydrogen peroxide
- Hydroxyl radicals

- Attack by these radicals may produce a variety of products

  For e.g.:

  (a) 8-oxo-7-hydrodeoxyguanosine (8-oxodG)

  (b) Thymidine glycol is the product of oxidative damage

- These products results in mispairing etc.

  For e.g.

  (a) 8-oxodG cause G to T transversion

  (b) Thymidine glycol halts (blocks) the DNA replication

3. TRANSPOSITION:

- A transposon is a DNA sequence able to insert itself (or a copy of itself) at a new location in the genome
- Insertion of a transposable element into or near to functional gene can alter its expression by causing:
  - Loss of gene function.
  - Changing gene's tissue specific or temporal expression.
  - Or by inducing the gene's inappropriate over expression.

REFERENCES :

- http://www.sparknotes.com/biology/molecular/dnareplicationandrepair/section3.rhtml
- https://masters.agron.iastate.edu/classes/527/lesson08/08.04.html
- https://www.khanacademy.org/science/biology/dna-as-the-genetic-material/dna-replication/a/dna-proofreading-and-repair
- https://www.boundless.com/biology/textbooks/boundless-biology-textbook/dna-structure-and-function-14/dna-repair-104/dna-repair-439-12942/