

I SEMESTER

PAPER – CELL BIOLOGY AND GENEICS

TOPIC – MUTAGENESIS – SPONTANEOUS AND INDUCED MUTATIONS

SOURCE – INTERNET

UNIT -IV

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4.1 MUTAGENESIS – INDUCED AND SPONTANEOUS MUTATIONS

Mutation : A heritable change in DNA sequence is called mutation.

When a DNA sequence is changed because of mutation, the amino acid sequence of a protein also changes.

When an amino acid sequence changes, the structure of a protein also changes. The change in structure of a protein may alter (or) abolish the function of protein.

Example:- Sickle cell anaemia

Type of mutation: point mutation (single base substitution) in the globin gene (HBB). Missense mutation DNA codon GAG → GTG.

Effects on amino acid sequence: Normal hemoglobin (HbA): 6th position Glutamic acid (Glu)
Sickle hemoglobin (HbS): 6th position Valine (Val)

Change: hydrophilic Glu → hydrophobic Valine.

Effects on protein structure: single amino acid substitution (Glu → Val). The hydrophobic valine creates a sticky patch on the B-globin surface.

Effects on protein function: Decreased solubility in low oxygen. Polymerization distortion RBC shape.

An agent which is called as causes "mutagen". a mutation is

Types of mutations

(1) mutations can be spontaneous (or) Induced.

(2) spontaneous mutations occur during the replication errors, due to Rare forms of bases, Metabolic errors etc....

(3) During replication mutations arise with a frequency of 10^{-4} to 10^{-6}

(4) Induced mutations takes place due to various mutagens like physical, chemical and Biological.

(5) Physical mutagens include ionising radiation like X-rays and non-ionizing radiation like UV rays. chemical mutagens include various alkylating agents, base analogs and Deaminating agents etc....

Biological mutagens include retroviruses and some others.

Point mutations:

(1) A mutation that involves a single nucleotide change is called as point mutation.

(2) point mutations are of two types.

Transition

Transversion.

Transition: An point mutation in which a purine is replaced by purine and a pyrimidine is replaced by pyrimidine.

Transversion: An point mutation in which a purine is replaced by a pyrimidine & viceversa.

Biochemical basis of mutations -

Mutation is a heritable change in the sequence of DNA.

Spontaneous Mutation:

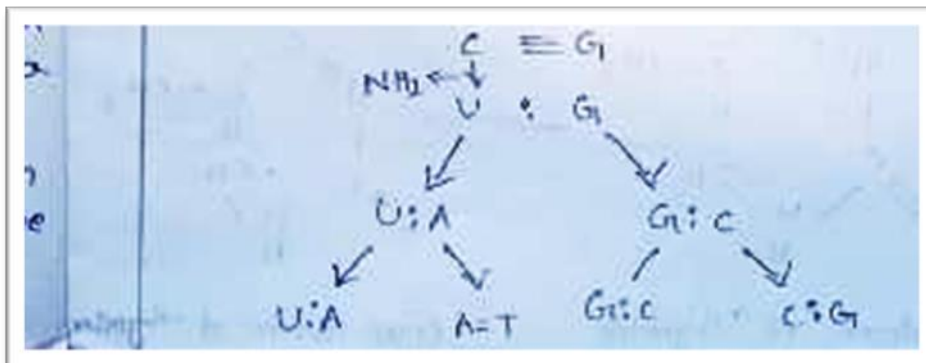
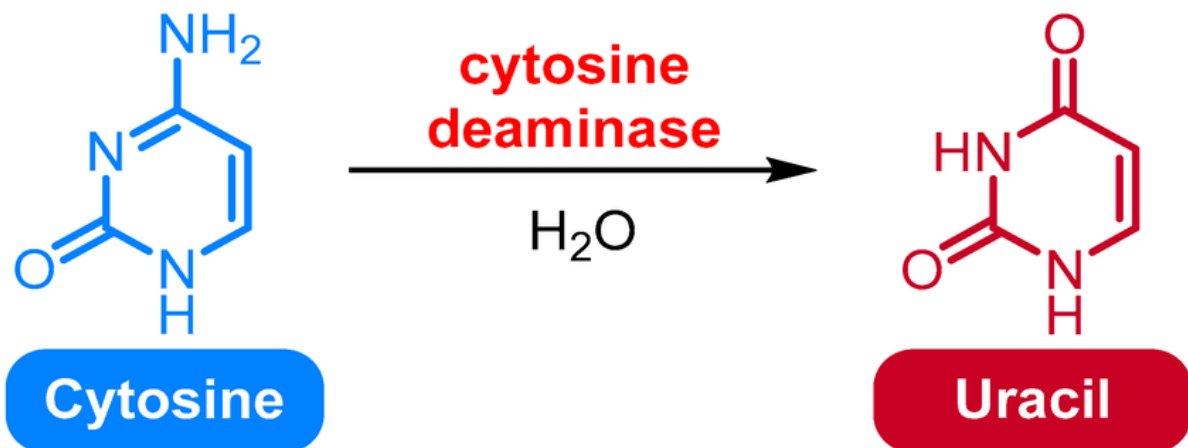
Spontaneous mutations takes place during the replication errors, spontaneous deamination of nitrogenous bases to the DNA and due to rare tautomeric forms of bases in the DNA.

Replication errors

Generally the mutation frequency during replication is 10^{-4} to 10^{-6} per generation

spontaneous De amination -

(1) loss of amino groups from the nitrogenous base is called as de amination. Spontaneous De-amination of cytosine leads to uracil



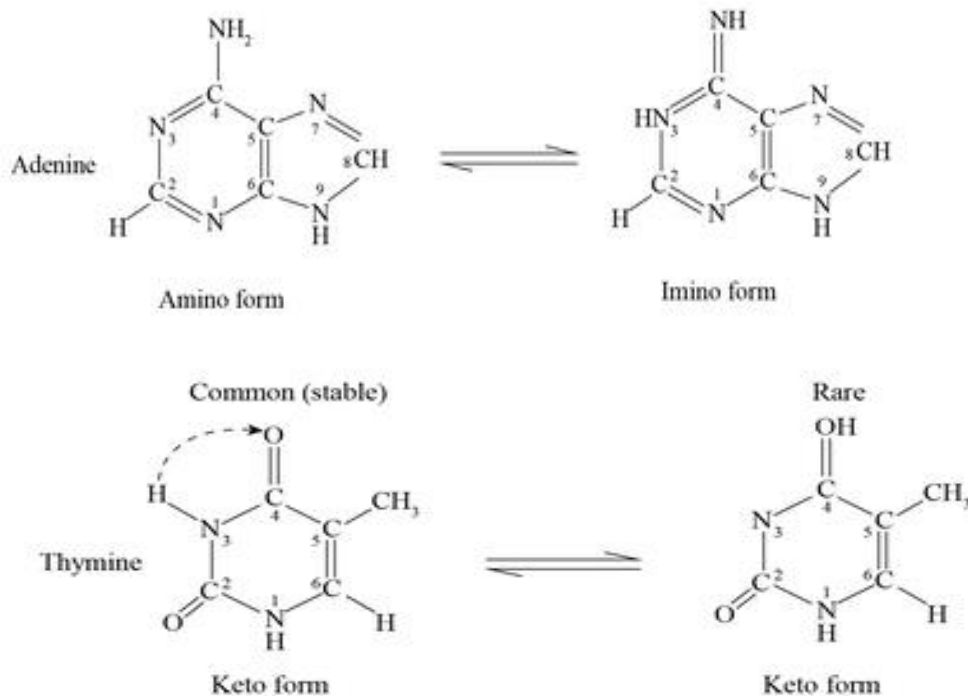
2) Due to deamination a C≡G pair would become an A=T pair.

Tautomeric forms :

- (1) Nitrogenous bases in DNA generally occurs in "ketoforms and Amino forms".
- (2) Occasionally the nitrogenous bases in DNA occurs in imino and rare tautomeric forms like Enol.
- (3) When these rare forms are incorporated into the DNA the base pairing between the nucleotide's changes, due to this the mutations incorporated into the DNA.

Ex: Imino form of adenine base pairs with cytosine rather than thymine. Due to this an A=T becomes a G≡C pair.

In the same manner, enol form of thymine pairs up with guanine and due to this again an A=T pair becomes a G≡C pair.



Induced Mutations

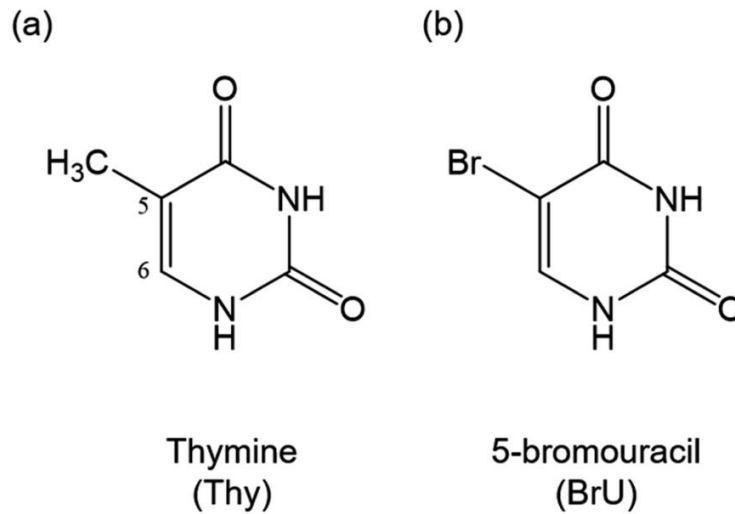
- 1) Induced mutations occur due to External agents known as mutagens.
- (2) these mutagens could be physical, chemical, Biological.

Chemical mutagens:

Various chemicals like base analogs, Alkylating agents and De-aminating agents can cause mutations in DNA.

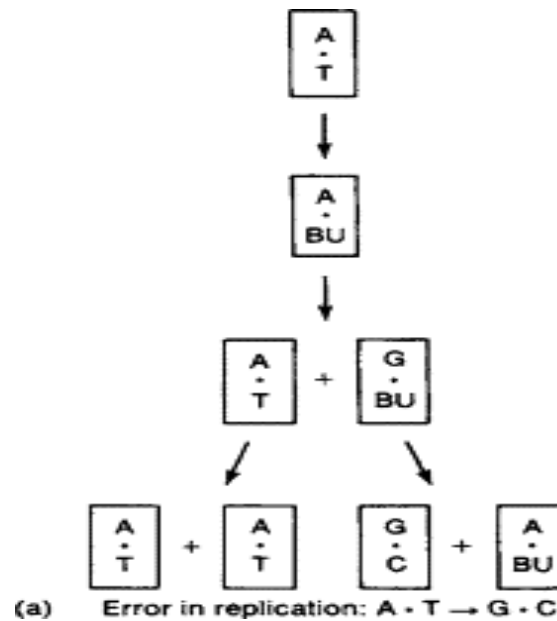
Base analogues:

Base analogs resemble nitrogen bases and incorporated into DNA during replication.



2) 5-Bromouracil is similar to thymine in the structure.

3) When 5-BU is incorporated into the DNA in place of thymine, it pairs with Guanine instead of adenine. Due to this an A=T pair becomes G=C.

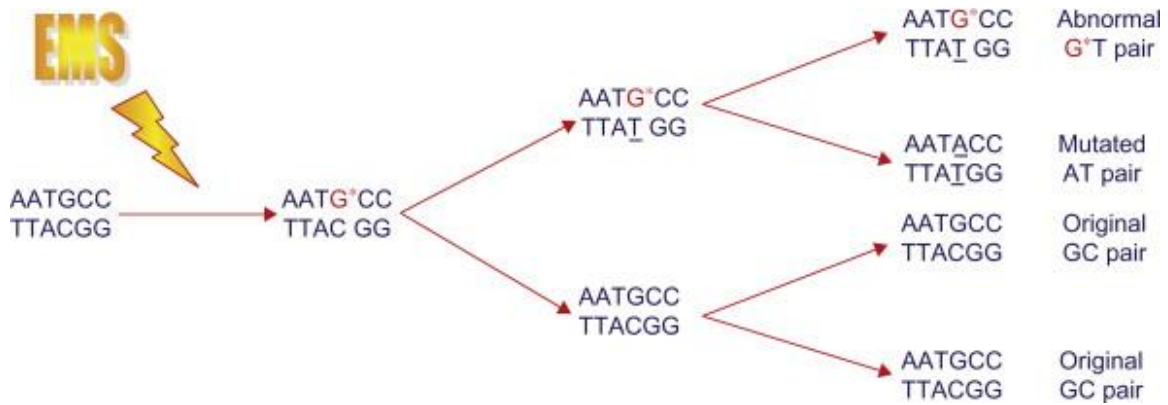


Alkylating agents:

They add Alkyl groups to the nitrogenous bases in the DNA, thereby altering the base pairing capacity of the nitrogenous bases.

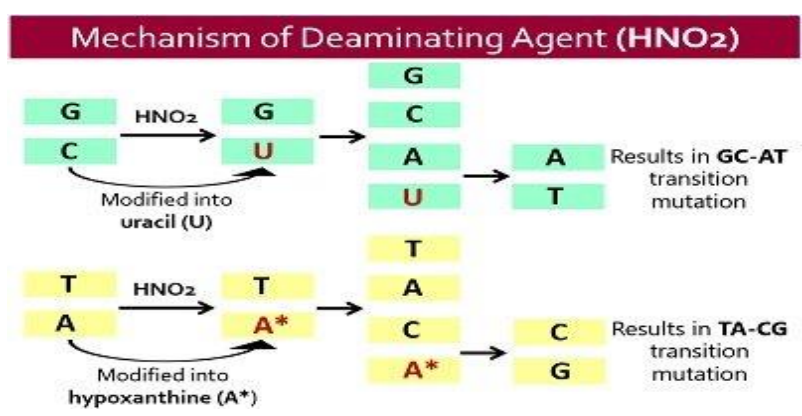
Ex:- Ethyl methanesulfonate [EMS] and Nitroso Guanidine [NG]

EMS add methyl group to guanine and methylated guanine now pairs with thymine instead of cytosine. Due to this a G=C pair becomes A=T pair.



De-aminating agents:

Chemicals like "nitrous acid" de-aminates cytosine to uracil and adenine to hypoxanthine, thus leading to mutations.



Induced mutations due to physical agents:

(1) Non-ionizing radiations like UV light causes mutations by producing pyrimidine dimers.

When a pyrimidine dimer is form, the DNA cannot act as a normal template and produces errors during the replication.

