MUTATIONS AND MUTAGENESIS

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Course: Molecular Biotechnology

MA Code408

Semester 8: Week 2

Date 8/2/2024

Mutation

Mutation refers to any change in the sequence of Nucleotides in DNA, which leads to changes in the genotype and phenotype of an organism. Mutations can either be beneficial or harmful.

Mechanisms of mutation

1. Substitution of a nucleotide.

2. Deletion or addition of a nucleotide.

Mutation

Mutations can be induced or spontaneous, result either fromerrors in DNA replication or from the damaging effects of mutagens, such as biological, chemicals and radiation.

Mutations occur due to deletion, insertion or substitution of one or more nucleotides.

When a purine nucleotide is replaced by a purine nucleotide it is known as **transition**, and when a purine is replaced by a pyrimidine, it is known as **transversion**.

Spontaneous Mutation

Spontaneous mutations occur naturally in the genome. They generally occur due to error during replication, mitosis, meiosis, etc. Mutations may also occur due to mobile genetic elements or transposons.

Difference between Spontaneous and Induced Mutation

Spontaneous Mutation	Induced Mutation
Spontaneous mutations occur naturally and mainly due to error in replication	Induced mutations occur due to physical or chemical agents
Occurs due to slippage in natural processes	Induced by mutagens
Caused due to replication error, tautomeric shift, transposable genetic elements, unequal cross overs, etc.	Caused due to base modification, base analogues, intercalating agents, base mispairing, radiations, etc.
E.g. sickle cell anaemia	E.g. skin cancer due to prolonged exposure to radiations

Mutations types

Mutations where only one nucleotides is exchanged are termed point mutations; other types of mutations include chromosome mutations or rearrangements when larger sequence sections are deleted or inserted, doubled, inverted. If such mutations occur within a transcription unit, they are referred to as gene mutations.

Deamination

In the human body, deamination of nucleotides also spontaneously arises with a rate of 100 deaminations per day and per cell. Cytidine is converted to uracil by deamination. If, following replication, U pairs with A instead of with G, as the original C had done, then the resulting CG pair is completely replaced with a TA pair

Depurination

The purine residues G and A can be removed spontaneously from DNA by hydrolysis. Depurination is considered as one of the most common spontaneous mutations and usually leads to transversions, but also to the deletion of individual bases; over 5000–10 000 purine bases are depurinated daily in every human cell.

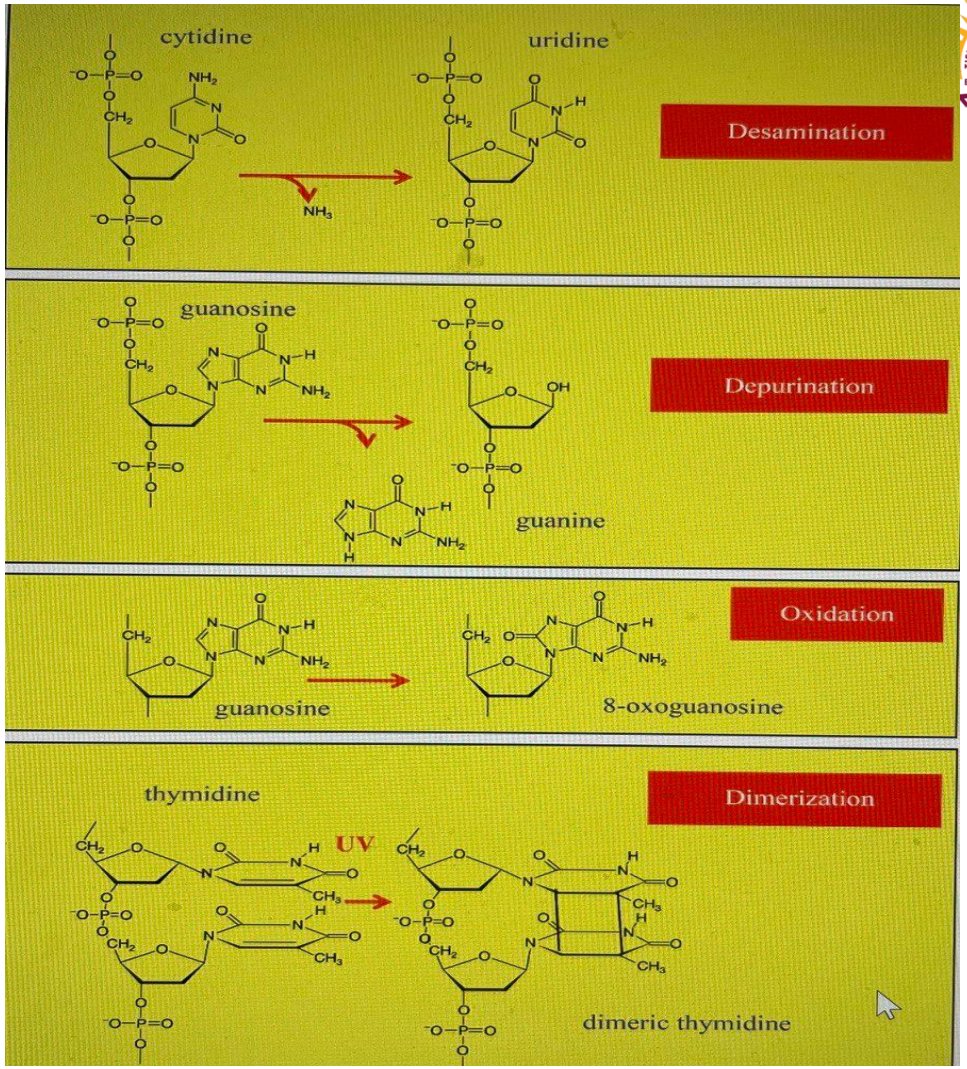
Dimerization

Under UV radiation (e.g., from extensive sunbathing) neighboring T and C residues can be activated, which then form dimers (dimerization)

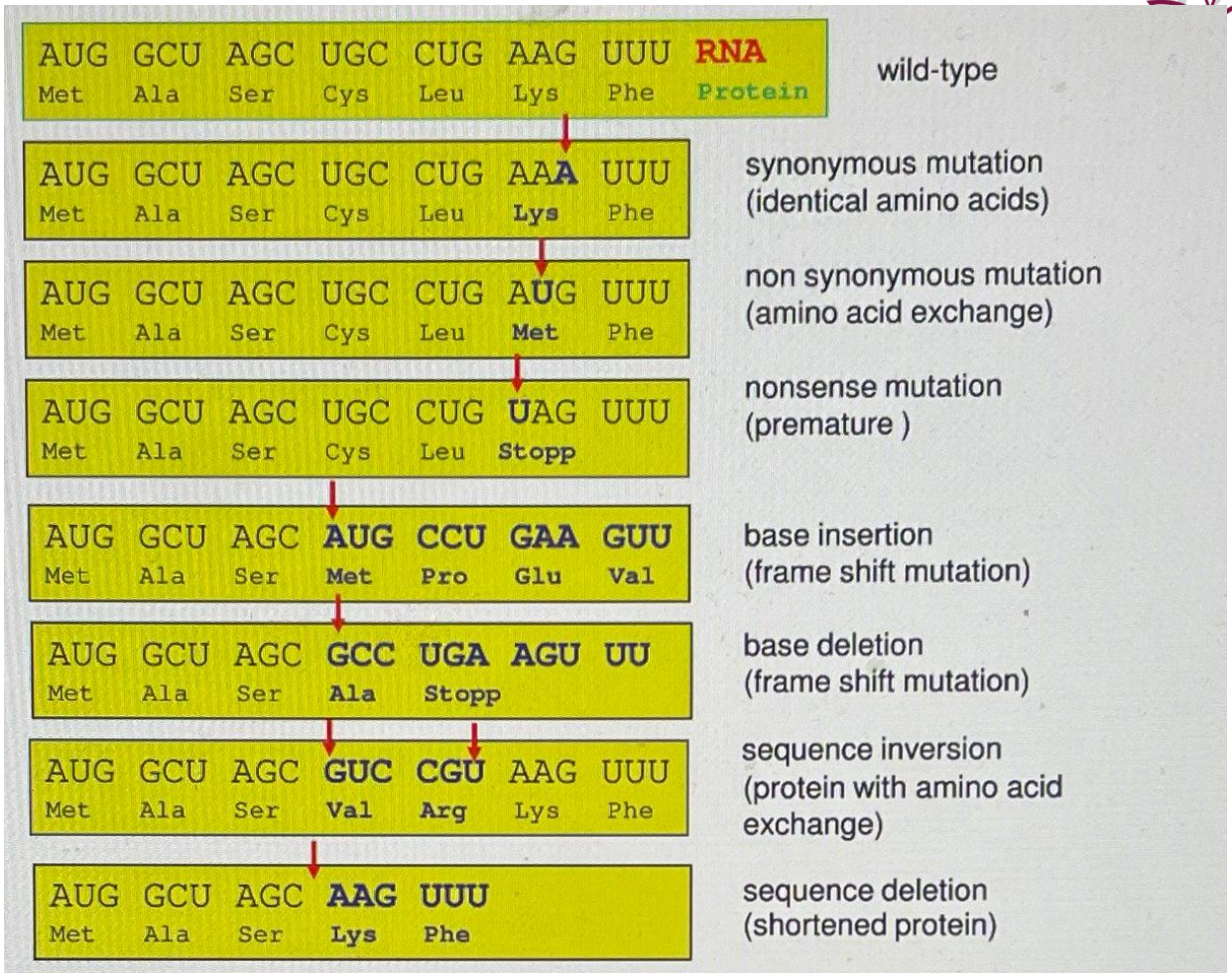
Oxidation

The oxidation of G to 8-oxoguanosine by reactive oxygen species (ROS) can also induce point mutations.

Major mutation mechanisms.



Consequences of gene mutations



Significance of mutation

1. Discovery of a mutation in a gene can help in identifying the function of that gene.
2. Mutations can be induced at a desired region to create a suitable mutant, especially to produce vaccines.
3. Spontaneous mutations can result in emergence of antibiotic resistance in bacteria.

Mutagens

Mutagens are substances that alter or change the genetic material of an organism, hence they are termed genotoxic. In most cases, the mutagens can incite carcinogenic responses or impair the functions of certain genes, thereby causing various medical conditions. However, the effects of most mutagens cannot be substantiated from a scientific perspective. For instance, a mutagen that shows a possible carcinogenic effect on one organism may not hold true for another organism.

Mutagens and Induced Mutation

Induced mutations do not occur spontaneously. They are induced through various chemical and physical agents known as mutagens. Mutagens greatly enhance the frequency of mutation. Induced mutagens can be **chemical**, **physical** or **biological** mutagens.

Biological mutagens (Transposons and viruses).

Transpozons are DNA units that carry out the DNA fragment's self-directed relocation and multiplication. The functionality of the genes is disrupted when transposons are inserted into chromosomal DNA. The insertion of viral DNA into the genome may lead to the disruption of genetic function.

Chemical Mutagens

Chemical mutagen is a chemical agent that causes mutations. Many chemicals that occur naturally in the environment have mutagenic properties and these have been supplemented in recent years with other chemical mutagens that result from human industrial activity.

Chemical mutagen mechanisms

1. Some act as base analogs and are mistakenly used as substrates when new DNA is synthesized
2. Some react directly with DNA, causing structural changes that lead to miscopying of the DNA.
3. Some mutagens act indirectly on DNA by synthesize chemicals that have a direct mutagenic effect.

Types of physical mutagens

1. UV radiation induces dimerization of adjacent pyrimidine bases, which results in a deletion mutation.

2. Ionizing radiation has various effects on DNA depending on the type of radiation and its intensity.

3. Heat stimulates the water-induced cleavage of the β-N-glycosidic bond that attaches the base to the sugar component of the nucleotide.

Next lecture

Gene Expression

Questions and comments?