MUTAGENS

Mutagens

Mutagens are substances that change the genetic material of an organism, which is why they are also called genotoxic. In many cases, mutagens can trigger cancer or damage the function of certain genes. They may even completely disable a gene, leading to different health problems.

Some mutagens cause silent mutations, where there are no noticeable effects because they affect parts of DNA that don't code for proteins. Other mutations are more noticeable and can cause serious health issues for the organism.

Types of Mutagens

Mutagens can be classified into 3 types based on their origin. They are as follows: Physical mutagens, Chemical mutagens, and Biological mutagens.

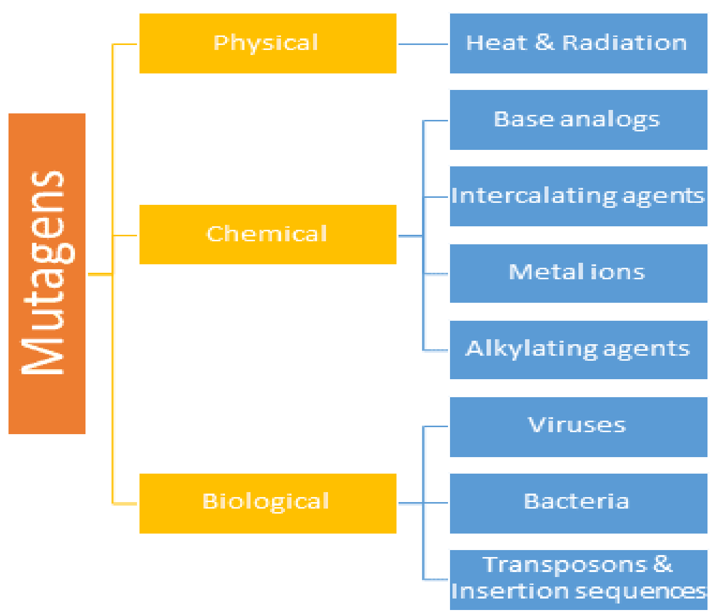

Figure 1: Types and Examples of Mutagens

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Physical Mutagens

1. Radiations were the first known mutagenic agents. Both ionizing (like X-rays and gamma rays) and non-ionizing (like UV rays) radiations can cause mutations. These radiations usually have lethal (killing the cell) or sub-lethal (damaging cell function) effects by directly harming the DNA or its building blocks. The damage can happen in several ways:

A - Causing DNA or protein to link together

B - Breaking chromosomes

C - Breaking DNA strands or losing chromosomes

D - Deleting bases or breaking DNA strands

Ionizing radiation, such as X-rays and gamma rays, mainly affects dividing cells, damaging not only DNA but also lipids and proteins. These rays create free radicals, which cause DNA or chromosome breakage.

A dose of 350-500 rems of X-rays is considered lethal because it breaks the bonds that hold DNA together, causing strand breaks. UV rays, which have less energy than X-rays, cause mutations through mechanisms like base deletion, strand breakage, cross-linking, and the formation of dimers between nucleotides.

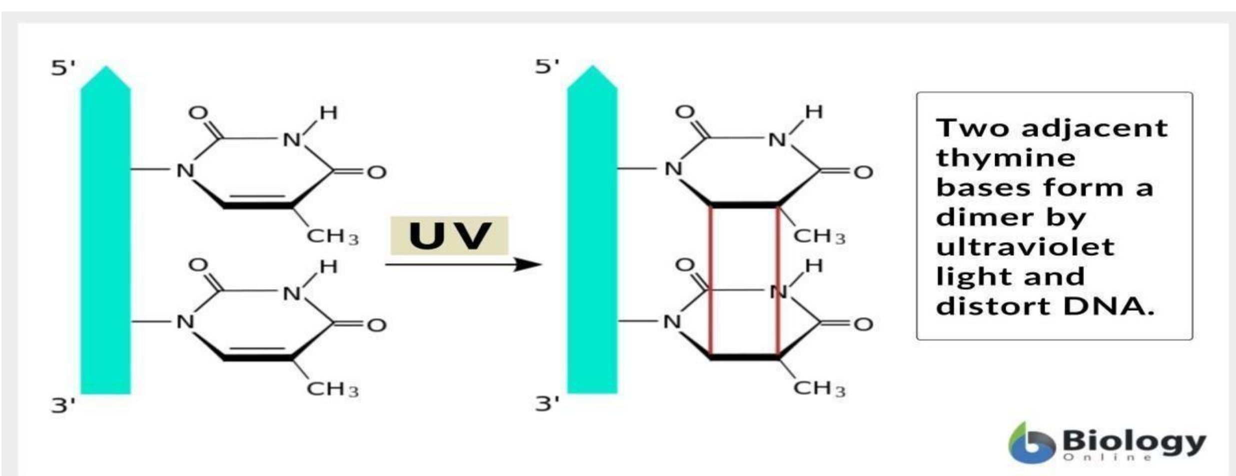

Figure 2: Effect of UV light resulting in the formation of thymine dimers.

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1- **Heat.** DNA is sensitive to temperatures above 95◦C. Above 95◦C, the phosphodiester bonds break in DNA resulting in breakage of DNA strand. Thus, heat results in DNA breakage.

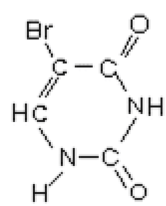
Chemical Mutagens

Chemical mutagens are standard tools for mutagenesis in a variety of organisms, and they are a primary means of creating mutations in phenotype-based screens in most genetic systems.

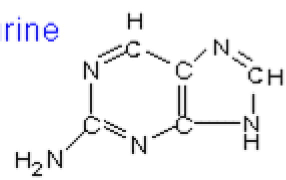
Chemical agents

a) **Base analogs.** These agents possess structural similarities to the bases i.e., purines and pyrimidines. The most common base analogs which are considered as a chemical mutagen are – 5-Bromouracil and aminopurine. Due to structural similarities these agents with the DNA bases, base analogs get incorporated in the DNA structure during the process of replication. Aminopurine is similar to adenine and can form a base pair with C or T (though base pairing with C is rare).

5-Bromouracil



2-Aminopurine



b) **Intercalating agents** are molecules with a ring structure that is similar to the base pairs in DNA. These agents insert themselves into the DNA helix, which disrupts processes like replication, translation, and transcription. This interference often leads to mutations, especially frameshift mutations. Ethidium bromide, proflavine, etc are some of the common intercalating agents.

c. **Metal ions** like nickel, chromium, cobalt, cadmium, and iron produce reactive oxygen species (ROS) that can damage DNA and interfere with its repair by causing DNA hypermethylation.
d. **Alkylating agents** add alkyl groups to DNA, (CH_3)causing damage. This increases ionization, leading to base-pairing errors and gaps in the DNA strand. Examples include mustard gas, vinyl chloride. These agents can be removed from DNA during the repair process through depurination.
e. **Deaminating agents**, like nitrous acid, can cause mutations by converting cytosine into uracil, leading to transition mutations.
f. **Polycyclic aromatic hydrocarbons (PAH)**, when activated, can bind to DNA and form harmful adducts.
g. **Nitrosamines**, found in tobacco and smoked meats or fish, can form when food amines react with nitrites used as preservatives. They are important mutagens.
h. **Alkaloids** from plants, such as those from Vinca species, can be metabolized into active mutagens or carcinogens.
i. **Benzene**, an industrial solvent, is used in producing drugs, plastics, synthetic rubber, and dyes, and can also be a mutagen.

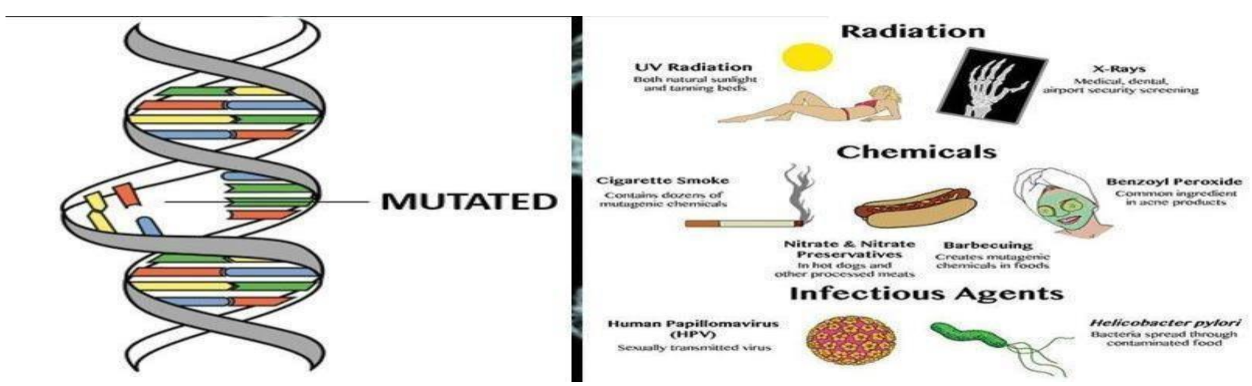


Figure 3: Mutations Caused by Chemicals

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Biological agents

1. **Transposons and Insertion sequences (IS) :** are DNA units that move or multiply in the genome. Both IS and transposons are called "jumping genes" because they move within the DNA. Insertion sequences (IS) are the simplest type, around 10-50 base pairs long. They can disrupt gene function when added to the DNA.

Three types of transposons are usually found:

1. **Replicative transposons**: Copy themselves to a new location.
2. **Conservative transposons**: Move to a new location, leaving the original behind.
3. **Retrotransposons**: Move using RNA intermediates.

2. **Viruses**: Inserting viral DNA into the genome can disrupt genetic function and cause cancer, as seen with the Rous sarcoma virus. This shows that viruses can be mutagenic.
3. **Bacteria**: Inflammation-causing bacteria like *Helicobacter pylori* produce reactive oxygen species that damage DNA and reduce its repair, increasing the chances of mutations.

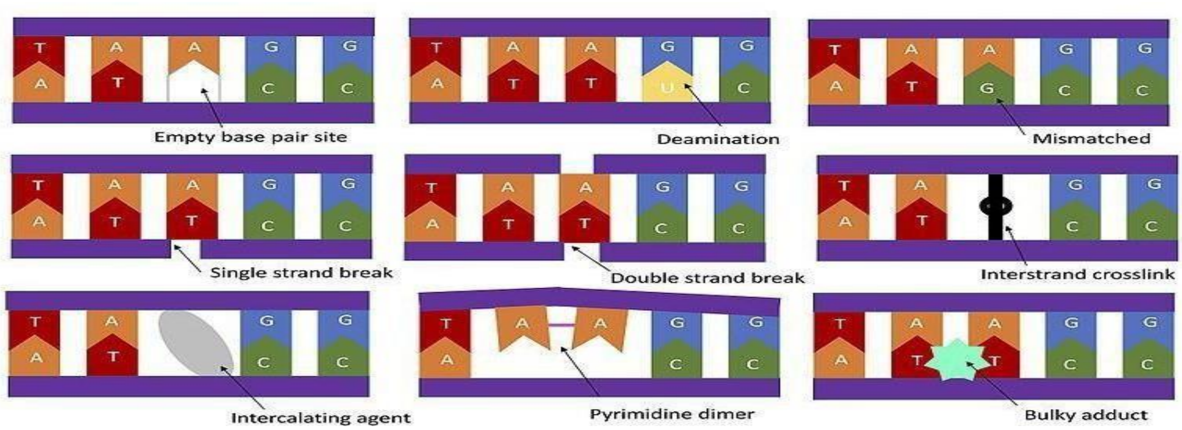

Figure 4: Different types of damage to DNA.

Single nucleotide polymorphism (SNP)
An SNP is a change in a DNA sequence where one of the four DNA bases (A, G, T, or C) is altered. It must occur in more than 1% of a population to be considered a polymorphism. Example: Changing C to G in the sequence "AACGAT" to "AACCAT."

1. SNPs occur every 100–300 nucleotides in the human genome.
2. About 90% of human genetic variation is due to SNPs.
3. Most SNPs do not affect cell function or cause noticeable changes.
4. Some SNPs can contribute to diseases like cancer or affect how the body responds to drugs.

2. **Role in Disease:**
    1. SNPs act as markers for specific DNA regions. If an SNP is near a disease-causing gene, it can help predict the risk of the disease.
    2. SNPs can be useful for diagnosing diseases and determining how a person will respond to drugs, helping to avoid harmful drug reactions.

Types of SNPs:

1. **Synonymous SNPs (Silent mutations)**
2. **Non-Synonym SNPs**