Causative Agents of Mutation

Mutation can be caused by (*a*) viruses, (*b*) radiation, or (*c*) chemicals.

‣ Viruses

Bacterial viruses (*mutator bacteriophage*) are an example of viruses that cause a high frequency of mutation by inserting their DNA into the bacterial chromosome. Mutations can occur in various genes as viral DNA can insert bacterial chromosome at many different sites. The mutations caused by these viruses may be either frame-shift mutations or deletions.

‣ Radiations

X-rays and ultraviolet light are the examples of radiation that can cause mutation in chromosomal DNA.

■ **X-rays:** X-rays damage DNA in many ways. They cause damage by producing free radicals that can attack the bases or alter them in the strand, thereby changing their hydrogen bonding. They also damage DNA by breaking the covalent bonds that hold the ribose phosphate together.

■ **Ultraviolet light:** Ultraviolet radiation causes damage in DNA by cross-linking of the adjacent pyrimidine bases to form dimers. For example, the cross-linking of adjacent thymine to form thymine

Chemicals

Various chemicals, such as nitrous acid, alkylating agents, benzpyrene, and base analogs, such as 5-bromouracil cause mutation in several different ways:

■ **Benzpyrene:** This is commonly present in tobacco smoke that binds to existing DNA bases and causes frame-shift mutations. The benzpyrene, which is a carcinogen as well as a mutagen, intercalates between the adjacent bases, thereby distorting and offsetting the nucleotide sequence in the DNA.

■ **Nitrous acid and alkylating agents:** They act by altering the existing base in the DNA. This results in formation of a hydrogen bond with a wrong base. For example, adenine does not form bond with thymine but makes wrong pair with cytosine.

■ **Base analogs:** Base analogs, such as 5-bromouracil, have less hydrogen bonding capacity than thymine, so they bind to guanine with better frequency. This results in a mutation due to a transition from AT base pair to a GC base pair. Iododeoxyuridine, an antiviral drug, also acts as a base-pair analog.

Effects of Mutations

Mutations in the bacteria cause a lot of changes in their various properties. Mutation alter drug susceptibility, antigenic structure, and virulence of mutant bacteria. It also alter susceptibility of bacteria to bacteriophages, alter their colony morphology and pigment productions, and affect their ability to produce capsule or flagella. Development of drug resistance due to mutations in bacteria is a major health concern.

Plasmids

Plasmids are extrachromosomal DNA substances. They are replicons that are maintained as discrete, extrachromosomal genetic elements in bacteria. They are usually much smaller than the bacterial chromosome, varying from less than 5 to more than several 100 kbp. However, plasmids as large, as 2 million base pairs can occur in some bacteria. Plasmids are circular and doublestranded DNA molecules that encode traits that are not essential for bacterial viability. They are capable of replicating independently of the bacterial chromosomes. The plasmids can also be present as integrated with bacterial chromosomes, and plasmids integrated with host chromosome are known as ***episomes***. Plasmids are present in both Gram-positive and Gram-negative bacteria.

‣ **Types of plasmids**

Plasmids depending on their transmissibility and nature of the factor can be of the following types:

Transmissibility of plasmids

Plasmids, depending on transmissibility are of two types: (*a*) transmissible plasmids and (*b*) nontransmissible plasmids.

1. Transmissible plasmids: They can be transferred from cell to cell by a process of genetic transfer known as conjugation.

They are large (mol. wt. 40–100 million) plasmids.

They contain more than a dozen genes responsible for synthesis of the sex pilus and for the synthesis of enzymes required for their transfer. Usually, one to three copies of the plasmid are present in a cell.

2. Nontransmissible plasmids: These cannot be transferred from cell to cell, because they do not contain the transfer genes. They are small (mol. wt. 3–20 million), usually nonconjugative,
and have high copy numbers (typically 10–60
per chromosome). They depend on their bacterial host to provide some functions required for replication and are distributed randomly between daughter cells at division.

Nature of factors

Depending on the nature of factors, plasmids are of the following types: (*a*) the F factor, (*b*) the R factor, and (*c*) the Col factor.

1. The F factor: The F plasmid, also called F factor, is a transfer factor that contains the genetic information, essential for controlling mating process of the bacteria during conjugation.

The F plasmid of *Escherichia coli* is the prototype for fertility plasmids in Gram-negative bacteria. Strains of *E. coli* with an extrachromosomal F plasmid are called F_ and function as donors, whereas strains that lack the F plasmid are F□ and behave as recipients. The conjugative functions of the F plasmid are determined by a cluster of at least 25 transfer (tra) genes. These genes determine (*a*)expression of pili, (*b*) synthesis and transfer of DNA during mating, (*c*) interference with the ability of F_ bacteria to serve as recipients, and (*d*) other functions.

The F plasmid in *E. coli* can occur as an extrachromosomal genetic element or be integrated into the bacterial chromosome. Both the F plasmid and the bacterial chromosome are circular DNA molecules. Hence, reciprocal recombination between them produces a larger DNA circle consisting of F-plasmid DNA inserted linearly into the chromosome.

2. The R factor: Resistance factors, also called R factors, are extrachromosomal plasmids. They are circular with double-stranded DNA. R factors occur in two sizes: large plasmids (mol. wt. 60 million) and small plasmids (mol. wt. 10 million). The large plasmids are conjugative “R” factors, which contain extra DNA to code for the conjugation process. The small plasmids contain only the “r” genes and are not conjugative. R factor consists of two components: the resistance transfer factor (RTF) and resistant determinant (r). The RTF is responsible for conjugational transfer, while each r determinant carries resistance for one of the several antibiotics.