Gene Mutations at the Molecular Level.

In Principle Mutations are changes in the DNA sequences. At the DNA level, there are two main types of point mutational changes:

1. base substitutions and

2. base additions or deletions.

1.Base substitutions are those mutations in which one base pair is replaced by another. Base substitutions again can be divided into two subtypes:

a) transitions

b) transversions

A transition is the replacement of a base by the other base of the same chemical category (purine replaced by purine: either A to G or G to A; pyrimidine replaced by pyrimidine: either C to T or T to C).

A transversion is the opposite—the replacement of a base of one chemical category by a base of the other (pyrimidine replaced by purine: C to A, C to G, T to A, T to G; purine replaced by pyrimidine: A to C, A to T, G to C, G to T). In describing the same changes at the double-stranded level of DNA, we must state both members of a base pair: an example of a transition would be G·C → A·T; that of a transversion would be G·C → T·A.

I. Silent substitutions: the mutation changes one codon for an amino acid into another codon for that same amino acid.
II. Missense mutations: the codon for one amino acid is replaced by a codon for another amino acid.
III. Nonsense mutations: the codon for one amino acid is replaced by translation termination (stop) codon.

Addition or deletion mutations are actually of *nucleotide* pairs. The convention is to call them *base*-pair additions or deletions.

The addition or deletion of a single base pair of DNA will change the reading frame starting from the location of the addition or deletion and extending through to the carboxy terminal of the protein. Hence, these lesions are called **frameshift** mutations. These mutations cause the entire amino acid sequence translationally downstream of the mutant site to bear no relation to the original amino acid sequence. Thus, frameshift mutations typically exhibit complete loss of normal protein structure and function.

Mutations also occur in **regulatory and other noncoding** sequences. Those parts of a gene that are not protein coding contain a variety of crucial functional sites. At the DNA level, there are sites to which specific transcription-regulating proteins must bind. At the RNA level, there are also important functional sequences such as the ribosome-binding sites of bacterial mRNAs and the self-ligating sites for intron excision in eukaryote mRNAs. Mutations at such sites may render them non functional.