RAMA UNIVERSITY

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FACULTY OF AGRICULTURAL SCIENCES

AND ALLIED INDUSTRIES

MUTATION

In the broad sense, the term 'mutation' refers to all the heritable changes in the genome, excluding those resulting from incorporation of genetic material from other organisms. A mutation is an abrupt qualitative or quantitative change in the genetic material of an organism.

Types of mutations:

- Intragenic or intergenic. Intragenic mutations or point mutations include alterations in the structure of the DNA molecule within a gene. In a point mutation there is a change in the normal base sequence of the DNA molecule. This change results in a modification of the structural characteristics or enzymatic capacities of the individual. The unit of gene mutation is the muton. This may consist of one or many nucleotide pairs. Intergenic mutations, of which chromosomal changes in structure are examples, involve long regions of DNA, i.e. many genes. These include deletion or addition of segments of chromosomes, resulting in deficiency and duplication, respectively. In large deletions a base sequence corresponding to an entire polypeptide chain is sometimes lost. Such mutations are very useful in genetic mapping.
- Germinal and Somatic Mutations Eukaryotic organisms have two primary cell types - germ and somatic. Mutations can occur in either cell type. If a gene is altered in a germ cell, the mutation is termed a germinal mutation. Because germ cells give rise to gametes, some gametes will carry the mutation and it will be passed on to the next generation when the individual successfully mates. Typically germinal mutations are not expressed in the individual containing the mutation. Somatic cells give rise to all non-germline tissues. Mutations in somatic cells are called somatic mutations. Because they do not occur in cells that give rise to gametes, the mutation is not passed along to the next generation by sexual means. To maintain this mutation, the individual containing the mutation must be cloned. Two example of somatic clones are navel oranges and red delicious apples.
- Spontaneous and Induced Mutations In general, the appearance of a new mutation is a rare event. Most mutations that were originally studied occurred spontaneously. This class of mutation is termed spontaneous mutations. But these mutations clearly represent only a small number of all possible mutations. To genetically dissect a biological system further, new mutations were created by scientists by treating an organism with a mutagenizing agent. These mutations are called induced mutations. The spontaneous mutation rate varies.

Large gene provides a large target and tends to mutate more frequently. A study of the five coat color loci in mice showed that the rate of mutation ranged from 2 x 10-6 to 40 x 10-6 mutations per gamete per gene. Data from several studies on eukaryotic organisms shows that in general the spontaneous mutation rate is 2-12 x 10-6 mutations per gamete per gene.

Mutations can be induced by several methods:

Three general approaches used to generate mutations are radiation, chemical and transposon insertion. The first induced mutations were created by treating Drosophila with X-rays. In addition to X-rays, other types of radiation treatments that have proven useful include gamma rays and fast neutron bombardment. These treatments can induce point mutations (changes in a single nucleotide) or deletions (loss of a chromosomal segment).

Other Types of mutations: Morphological mutants affect the outward appearance of an individual. Plant height mutations could changes a tall plant to a short one, or from having smooth to round seeds. Biochemical mutations have a lesion in one specific step of an enzymatic pathway.

For bacteria, biochemical mutants need to be grown on a media supplemented with a specific nutrient. Such mutants are called auxotrophs. Often though, morphological mutants are the direct result of a mutation in a biochemical pathway.

In humans, albinism is the result of a mutation in the pathway which converts the amino acid tyrosine to the skin pigment melanin. Similarly, cretinism results when the tyrosine to thyroxine pathway is mutated.

For some mutations to be expressed, the individual needs to be placed in a specific environment. This is called the restrictive condition. But if the individual grow in any other environment (permissive condition), the wild type phenotype is expressed. These are called conditional mutations. Mutations that only expressed at a specific temperature (temperature sensitive mutants), usually elevated, can be considered to be conditional mutations. Lethal mutations are also possible. As the term implies, the mutations lead to the death of the individual. Death does not have to occur immediately, it may take several months or even years. But if the expected longevity of an individual is significantly reduced, the mutation is considered a lethal mutation. If a mutation occurs in that allele, the function for which it encodes is also lost. The general term for these mutations is loss-of-function mutations. The degree to which the function is lost can

vary. If the function is entirely lost, the mutation is called a null mutation. If is also possible that some function may remain, but not at the level of the wild type allele. These are called leaky mutations.

Mutagens:

A variety of agents increase the frequency of mutation. Such agents are called mutagens. They include chemical mutagens, and radiations like X-rays, γ-rays and UV-light. Chemical Mutagens.

The first chemical mutagen discovered was mustard 'gas'. In the 1950s chemical mutagens with more or less specific action were developed. Chemical mutagens can be classified according to the way in which they bring about mutations: (1) Base analogues which are incorporated into DNA instead of normal bases (2) Agents modifying purines and pyridines and agents labilizing bases, and (3) agents producing distortions in DNA.

The agents in categories (1) and (3) require replication for their action, while agents in category (2) can modify even non replicating DNA. Chemical mutagens work mostly by inducing point mutations.

Two major classes of chemical mutagens are routinely used. These are alkylating agents and base analogs. Each has a specific effect on DNA. Alkylating agents [such as ethyl methane sulphonate (EMS), ethyl ethane sulphonate (EES) and musta rd gas] can mutate both replicating and nonreplicating DNA. By contrast, a base analog (5-bromouracil and 2- aminopurine) only mutate DNA when the analog is incorporated into replicating DNA. Each class of chemical mutagen has specific effects that can lead to transitions, transversions or deletions.

CIB Technique for detection of mutation:

This method was discovered by Muller. In this method, females containing one normal X-chromosome and another X-chromosome (CIB) containing extra 3 genes are used for the analysis. Out of the 3 extra genes, one gene suppresses crossover (c), the other is a recessive lethal (L) in heterozygous condition, and the last gene is semi dominant marker, Bar (B) gene. Females containing CIB chromosome are called as CIB stock drosophila. The normal males are exposed to mutagenic source for a fixed period and then mated to the CIB stock drosophila. Males containing CIB chromosome will die due to the effect of lethal genes, whereas norm ill males and females both normal and with CIB will survive. Females with CIB chromosomes and identified by barred phenotype are selected and crossed to normal males. In this next generation 50% of males (which have received the CIB gene) will die. If mutation has occurred in normal X chromosome then even the normal male (without CIB gene) will die. If no mutation has occurred all the other 50% of males will survive. The frequency of lethal mutations can be

accurately scored in large samples. This technique is simple, rapid and there is little chance of an error in scoring. However, it is suitable for the scoring of sex linked recessive lethal only.