UNIT 16 MUTATIONS AND MUTAGENESIS

Structure

16.1 INTRODUCTION

Natural selection, as Darwin recognised more than a century ago, favours individuals and populations that inherit characlcrs conducive to their survival and reproduction. [For a detailed discussion on Natural Selection refer to Units 11 and 12 of LSE 07 course.] We must understand therefore, that the generation of biological variation is a central requirement for evolution of species in diverse and changing environment. You have already learnt in the previous blocks that the occurrence of phenotypic variability amongst the living organisms is an absolute requirement also for understanding the inheritance of the genetic characters. One of the basic mechanisms that creates genotypic as well as the phenotypic variation is the mutation or the alteration of DNA within the gene. In recent years, the terms mutation has generally been restricted to processes that result in a direct alteration of gene contents generating the new alleles of a gene that end up coding for a different sequence of amino acids.

The natural occurrence of mutations is very slow. In order to make significant progress on genetice studies in any living system it becomes imperative that the new mutations must be isolated and accumulated at a faster rate, This necessity has led to an active field of study on experimental mutations called mutagenesis. Ever since the time of M.J. Muller (1927) who reported that X-ray could induce mutations in *Drosophila* followed by L.J. Stadler's finding that the same is true in barley, a large number of agents called mutagenes have become available to induce mutations.

In this unit we will discuss the concept, types and molecular basis of mutations and detection of mutations. You will also read about various mutagens, their effecls and repair mechanisms to rectify these effects. With the availabity of whole range of mutagens it has become possible to exploit these for advancemenl of genetic studies and improve the agricultural crops. The study of mutations has alsq enhanced our understanding of the cancer process as well as abnormal development in detail.

Objectives

After studying this unit you will be able to:

- explain what are mutations, how they arise and how they can be detected,
- differentiate the types of mutations and explain their origin on molecular basis,
- discuss the role of mutagens in inducing mutations and the cellular repair mechanism to correct the DNA damage, and
- discuss how these mutations can be exploited for advancement of genetic studies, and betterment of agricultural crops.

16.2 WHAT IS MUTATION?

In the year 1791, a New England farmer, Seth Wright, noticed a peculiar male lamb in his small flock of sheep. This lamb had unusually short legs which were somewhat deformed. Mr. Wright recognised the unique advantage of sheeps like this one, as they would not be able to jump the low stone fences and therefore pot damage the crops. He carefully bred his sheep and was able to raise a short legged flock. This breed was named ancon (Greek--elbow) as the crooked legs resembled the hunian elbow. The same mutation appeared in a flock of sheep in Norway in 1925 and a separate breed of ancon sheep was established from it.

A similiar event occurred during the latter part of 19th century when a worker in South America spotted a peculiar type of orange. At one end of the fruit there was a shrivelled indented portion which resembled a hunian navel, but pulp of this orange fruit contained no seeds. You should be able to recognise tbe potential value of having the seedless orange. By careful budding and grafting this new characler could be propagated. An American tourist brought a twig back to California, and thus the great navel orange industry of America was established. What do you get from these examples? Probably that some changes have suddenly arisen in these organisms which became beneficial lo mankind.

When such changes occur in natural populations, mutation is said to have taken place. Mutation, therefore, is a sudden, heritable change in genotype that involves qualitative change in the genetic material. The change may lead to a corresponding change in the phenotype. Mutations are an extremely important source of genetic variability in living populations. They are the deviations from normal genotypic and phenotypic conditions, The normal conditions are referred to as wild-type conditions.

Mutations include changes occumng at chromosomal level as well as at gene level. At chromosomal level, the change in the organisation and structure of chroniosorne (s) is called chromosomal aberration or chromosomal mutations. You have already read about chromosomal aberration in previous block. In this unit you will study about the mutations occumngat gene level. When we say mutation we refer to the changes occurring at gene level, i.e. gene mutation.

The possibility thal new types of inherited characters may appear suddenly was first suggested by Hugo De Vries in 1901 as a result of his experiments on the plant evening primrose, Oenothera *lamarckiana*. He coined tbe term mutation to explain the variations he observed in crosses involving this plant. Most of the variations observed by De Vries, however, were later found to be chromosomal aberrations rather than mutations. Neverthless, he deserves credit for the forniulation of the concept of mutation and its importance from the point of view of evolution.

In addition to their contributions to the genetic variation, mutations are working tools for the geneticist in order to understand the structure and functioning of the gene. Mutations provide insights into basic biochemical processes such as gene expression and development (see Fig. 16.1). Certain mutations that can be easily detected and studied are induced in organisms like bacteria, fungi, fruit flies, certain plants, mice etc. These organisms have short life cycles and therefore are normally used for studying mutations and mutagenesis.

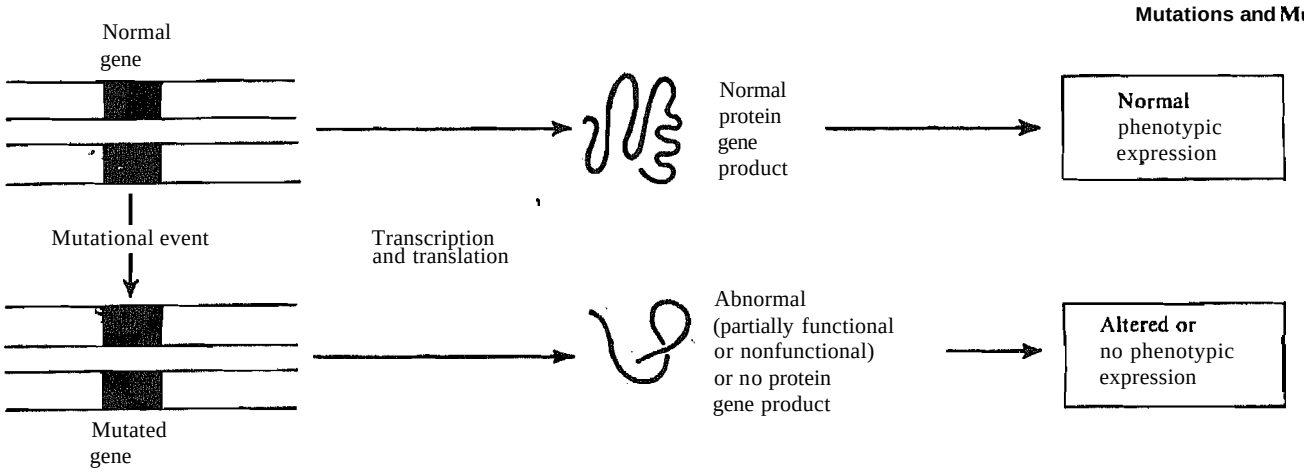

Fig. 16.1: Illustration to show the effect of mutation on gene expression.

After having understood the meaning of the word mutation and its importance let us now discuss various classes of mutations.

Mutations can be classified on the basis of several criteria. None of these are mutually exclusive. Instead they depend on simply which aspect of mutations are being discussed. In the following subsections we will discuss three ways of classifying mutations. But first do the following SAQ.

SAQ 1

Explain what do you understand by mutation ? Give any four examples of mutations.

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.....

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16.2.1 Somatic and Gametic Mutations

Mutations may occur in somatic cells as well as in germ cells. Mutations arising in somatic cells, i.e. body cells are not transmitted to future generations and die with the death of the individual. These arc called somatic mutations. Let us see how mutations in somatic cells affect the organisms.

In the tissues of adult organisms many cells perform similar function. So mutation in a single cell of a tissue may not impair the organism even if the mutation is detrimental. This has two aspects: first, mutation might occur in a gene that are not active: in other words it may occur in genes that are not essential to the functions of that cell. Second, even if the critical gene in a cell or a group of cells is affected there are still thousands of normal, unaffected cells to perform the same function in that tissue. However, mutations in somatic cells may sometimes cause damage, including cancer, to the parts of the body 'that arise from the mutated cells. As you have read earlier, somatic mutations are not significant from the stand point of heredity. However, if these mutations arise early enough during embryonic development, they may express themselves in the somatic cells. Some of such somatic mutations can be highly beneficial to mankind. You may remember the earlier examples of navel orange. Navel orange arose due to mutation in the -

meristematic cells of a bud. Such mutations can be propagated vegetatively and retain a constant phenotype. You can see an example of somatic mutation in Fig. 16.2.

Fig. 16.2 : Mutant flower heads of Zinnia. The somatic mutation was from splotched colour (peppermint) to solid colour (a).

Gametic mutations are of greater concern because they have the potential of being expressed in all cells of an offspring. Such mutations perferably occur in **germinal cells** i.e., reproductive cells of an organism. The germinal cells give rise to gametes which are the carriers of genetic information from generation to generation. So you see that mutations in germinal cells are bound to be heritable. It is possible that mutations in germ cells may cause no noticeable abnormality in the individual in which they occur, but will be passed on to its offspring and may be expressed in the offspring's phenotype. Gametic mutations may occur on autosomes or sex chromosomes of the germ cells or gametes. These are called **autosomal** and **sex-linked mutations** respectively.

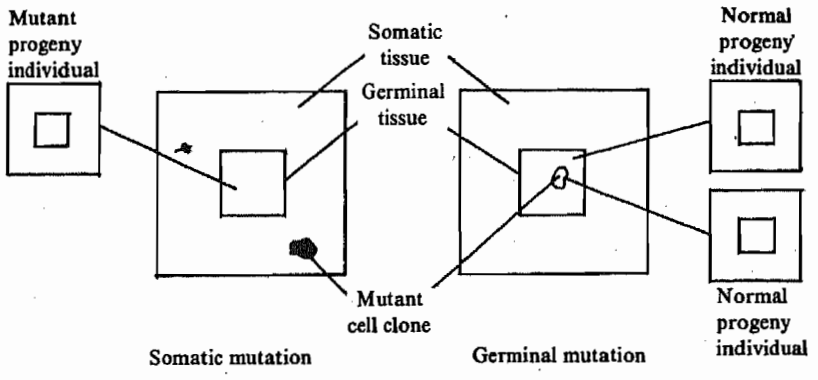

Fig. 16.3: Diagrammatic representations of the consequences of somatic and germinal mutations.

16.2.2 Spontaneous and Induced Mutations

All the mutations are categorised as either spontaneous or induced, on the basis of the way they arise in the organism.

Spontaneous mutations are those mutations that arise randomly in nature, strictly by chance. No specific agent may be required for their origin. They essentially arise due to inherent errors in DNA replication and transmission processes. The internal environment of the cell also plays a significant role in inducing mutational events. Each organism has a characteristic spontaneous mutation rate. The mutation rate is the probability that a gene undergoes mutation in a single generation. Some examples of which are shown in Table 16.1. You can infer by studying the table that spontaneous mutation rates are relatively low, most occurring one in a million genes or more. Also the spontaneous rate for different genes of the same organism may vary greatly. Measurement of mutation rates is important in population genetics, studies of evolution and in analysing the effects of environmental mutagen.

Table 16.1: Some examples of spontaneous mutations rates for various organisms.

Organism	Trait	Mutation Rate
E. coil	histidine auxotrophy	2×10^{-6}
(various sources)	streptomycin sensitivity	1×10^{-8}
	phage T_1 resistance	2.3×10^{-8}
Drosophila males	brown eyes	3×10^{-5}
	eyeless	6×10^{-5}
	yellow body	12×10^{-5}
	colourless kernel	2×10^{-6}
	shrunken kernel	1.2×10^{-6}
Human	achondroplasia	1×10^{-5}
	aniridia	2.9×10^{-6}
	retinoblastoma	6.7×10^{-6}
	muscular dystrophy (Duchenne type)	9.2×10^{-5}

Mutation rate for bacteria expressed as the number of mutations per cell per generation; and for eukaryotes as the number of mutations per gamete per generation.

Induced mutations are the mutations that occur in response to obvious externally applied agents. We referred to earlier H.J. Muller's findings that x-rays could induce mutations in *Drosophila*. Muller later received a Nobel Prize for his contribution. The agents that induce mutations are called mutagenic agents. Various forms of radiation sources and many chemicals are the known as mutagenic agents. We will discuss about mutagenic agents later in this unit. It should however, be clarified that induced mutations are not new types of mutations. Instead mutagenic agents accelerate the spontaneous mutation rates several folds, thus enhancing the chance of occurrence of a mutation.

16.2.3 Categories of Mutations

Mutations are also classified on the basis of their effects on the organism. In this subsection we will discuss these categories of mutations.

Morphological mutations, the most obvious mutations are those which affect the morphological traits of the organism. These are **visible mutations** which result in the phenotypic change that alters the morophology, i.e. visible characters of an organism. These are usually outward characters such as shape, colour or size. Curl wings in **Drosophila** and dwarfism in peas are some examples of morphological mutations (see Fig. 16.4).

Fig 16.4: A rare morphological mutation in *Rubus parviflorus* (thimble berry). The mutation arose spontaneously in nature. Flowers 1,2 and 3 are normal wild type and flower 4 is a mutant. The mutation causes increase in the number of petals. Such mutants are use in horticulture to increase the showiness of the flowers.

Nutritional mutations may not always be observed visually, but can be identified only by biochemical analysis. The inability to synthesise an amino acid or a vitamin in bacteria and fungi is a typical nutritional mutation. Nutritional mutants are called **auxotrophs** and they require a specific substance to grow as against the wild types which are self-sufficient and called **prototrophs.**

Behaviour mutations affect the behaviour pattern of an organism. For example, mating behaviour of a fruit fly may be imparied if it cannot beat its wings. Behaviour mutations have greatly helped the study of behavioural pattern in various organisms.

Regulatory mutations are the mutations which affect the regulation of gene activities. Such mutations may permanently activate or inactivate the gene by affecting the regulatory gene. You have already read about the regulation of genes earlier in this course.

Lethal mutation means that the organism carrying the mutation cannot survive. **Biochemical mutations** may also fall in this category. For example a mutant bacterium that cannot synthesise a specific amino acid needed for its growth will die if grown on a medium lacking that amino acid.

Detrimental mutations influence the viability of the organisms. **Conditional mutations** are those which are expressed under certain conditions. The conditions may be **restrictive** when the expression is inhibited and **permissive** when they allow the normal expression of a phenotype. The best examples are the **temperature-sensitive mutations** found in various organisms. In such organisms a mutant gene product functions normally at certain temperatures but loses its functional capability at other temperatures. For example, a certain class of mutations in *Drosophila* is known as dominant heat-sensitive lethal. Heterozygotes in this class (say H^+/H) are normal at 20°C (permissive condition) but die if the temperature is raised to 30°C (restrictive condition). The study of conditional mutations are extremely important for experimental genetics. You can also classify mutations as **dominant** or **recessive**. They are dominant if they are expressed in a heterozygous condition, i.e., in the presence of wild type allele. If they are not expressed, it means they are recessive in nature. Mutations could also be calssified by the direction in which the mutations occur. Accordingly they are known as **forward mutations** if wild type allele mutates to a mutant allele and **reverse mutations** if a mutant allele mutates back into wild type allele. The process of regaining the original phenotype is called **reversion** and the organism that has reverted is called **revertant.**

A **supressor** or **second site mutation** occurs at a second site that completely or partially restores a function lost at another site because of earlier or primary mutation. Supressor mutation does not reverse the original mutation, instead compensates for its effects and in fact the organism becomes a double mutant. It can occur within the same gene in which primary mutation occurs. After studying the various categories of mutations let us now discuss detection of mutation in various organisms. But before that try the following SAQ to check that you have understood the concept of mutation, its classes and basis for its classification.

SAQ 2

a) Fill in the blanks with appropriate words from the text.

i) Mutations are ..... changes in the genetic material that are ..... .

ii) Mutations are the primary source of ..... , and therefore, are essential for .....

b) Match the items given in column II with those given in column I. Write your answers in the box provided.

Column I		Column II
i) Somatic mutations	☐	a) Sources of spontaneous mutations.
ii) Errors in DNA replication	☐	b) Mutants requiring a nutrient in their medium to grow.
iii) Deformed legs of ancon sheep.	☐	c) The mutations in the meristematic cells of navel orange were vegetatively propogated.
iv) Auxotrophs	☐	d) This is the example of visible mutation.

16.3 DETECTION OF MUTATIONS

Mutations are usually detected by a change in the phenotype. For different systems different methods of detection of mutations have been designed. The detection methods are also based on the fact that most mutations are recessive in nature and their existence can be confirmed depending upon whether they are studied in diploid or haploid organisms or whether they are located on autosomes or sex chromosomes. The detections become

more significant as more and more methods of induction of mutations are becoming available resulting into the accumulation of a large variety of mutants. We shall now discuss some of the methods which are used in humans, fruit-fly, *Drosophila melanogaster* and haploid organisms.

16.3.1 Detection in Humans

In humans beings, the detection of mutation depends upon pedigree analysis and birth statistics. It is because designed matings are not possible or desirable in human beings.

For the **pedigree analysis** one has to prepare a family tree. Once any trait has been shown to be inherited, it is possible to predict whether the mutant allele is behaving as a dominant or a recessive and whether it is sex-linked or autosomal.

The detection of **recessive mutations** by this method is sometimes difficult because one cannot determine with certainity whether a recessive trait has arisen because of the mating of the two heterozygous parents or through the mutation in one of them.

In case of **recessive autosomal alleles,** mutation is hidden in heterozygous condition. An affected individual and a homozygous normal individual will produce unaffected carrier children. Mating between two carriers will produce on an average, one-fourth affected offspring. Because of the presence of a single x-chromosome in human males, **recessive sex-linked** mutations can be easily detected by pedigree analysis. The woman, who is **carrier** of the mutant trait, is not affected by the mutation because of the presence of dominant allele. However, she passes it to half of her male offspring which will show up the affected trait. The most famous case of sex-linked mutation in humans is that of hemophilia. The classical case of hemophilia in the royal family descendants of Queen Victoria can be cited here. The pedigree analysis of seven generations has shown how the gene for this lethal genetic disease for which Queen Victoria was the carrier has been transmitted to the offspring.

The **dominant mutants** are however easy to detect as they exert their effect immediately. If they are present on x-chromosomes, affected fathers pass the phenotypic trait to all their daughters. If the mutation is located on one of the x-chromosomes of female it will be passed on to 50% of her male offspring. If the condition is homozygous in female all her male offsprings will be affected. If dominant mutations are autosomol, approximately 50 per cent of the offspring of an affected heterozygous individual are expected to show the trait.

Another method to detect mutations in humans and other organisms is to screen various proteins and enzymes for minor biochemical changes. The technique used for this purpose is known as electrophoresis and is based on the differential migration of variant proteins in an eletric field. It is very useful as many of the variants or mutants may not produce obvious visible morphological behavioural effects but indicate the altered amino acid sequence of a portein, caused by mutation. For example, the mutant sickle cell haemoglobin has an altered electrophoretic mobility as compared to normal haemoglobin (Fig.16.5).

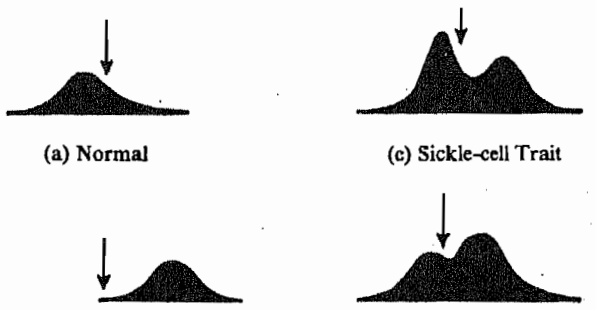

Fig.16.5: Differences in the electrophoretic mobility of normal and sickle cell haemoglobin.

16.3.2 Detection in Drosophila

Muller developed a number of systems for the detection in *Drosophila melanogaster.* We will in this subsection discuss two techniques to detect recessive sex-linked mutations devised by Muller; **the CIB** and the **attached-x-procedures.**

CIB test system detects the rate of induction of sex-linked recessive lethal mutations. The stock of CIB involves C an inversion that suppresses the crossing over, I a recessive lethal mutation and B a dominant gene duplicate causing bar shape of the eye. Genes for all these traits are present on x-chromosome.

In this technique, wild-type (P) males are treated with a mutagenic agent (X-ray in this case) and are crossed with nontreated heterozygous female having one x-chromosome with **CIB** markers, i.e. genes. As you can see in Fig. 16.6, the F_1 generation consists of four types of offspring. One type of offspring i.e. CIB male dies becasue it contains recessive lethal l gene which is expressed in hemizygous conditions showing its fatal effect. The remaining type of male offspring is wild type. This wild type male is crossed with bar eyed female of F_1 generation. These bar eyed females receive CIB chromosome from their mother and irradiated x-chromosome from their fater. F_2 generation, as a result of crossing over, will consist of bar eyed and wild-type females and two types of males. One of which will be CIB type, and will die because of the reason we have discussed above. In the other class of male offspring we might find a mutant, if induced at P_1 level due to x-ray irradiation. A lethal mutation means no males will survive in F_2. However, if morphological mutation is induced it will show up in this class of males. So we can detect the sex-linked morphological or lethal mutation by this method.

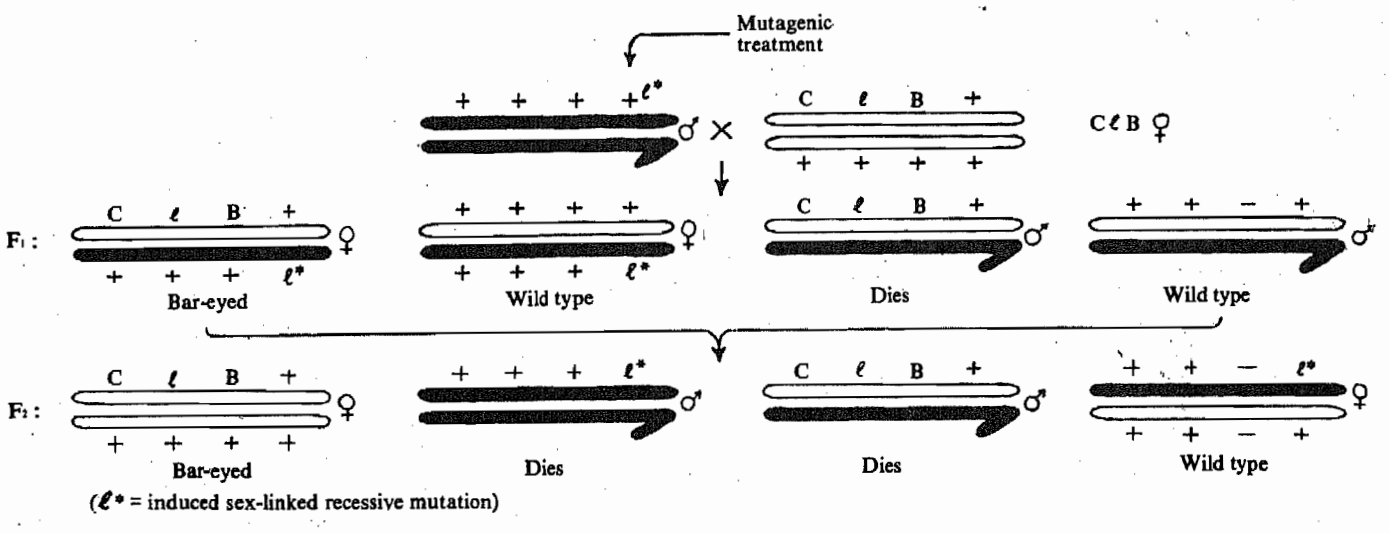

Fig. 16.6: Muller's CIB technique for detection of induced sex-linked mutation in *Drosophila*. In this case mutation is recessive and lethal.

Attached x-chromosome technique is comparatively a simpler technique as mutation can be detected in first generation itself. You must have learnt earlier that many times the two x-chromosomes fail to separate at anaphase and go to the same pole. This condition is known as attached -x and if this type of gamete is fertilised by Y sperm, a female fly of XXY composition is produced. Now look at the Fig. 16.7, you will see that when such XXY or attached -X female is crossed with a wild-type or a normal XY male P_1, which has been exposed to a mutagen, four types of progenies are produced in F_1 generation. These are as follows:

- Triplo-X (XXX) females which die
- Attached - XY (XXY) females which are viable.
- YY males that also die
- Normal XY males that are viable.

The induced sex-linked morphological mutations of P male will be expressed in both viable progenies. Lethal mutation will once again wipe out the males.

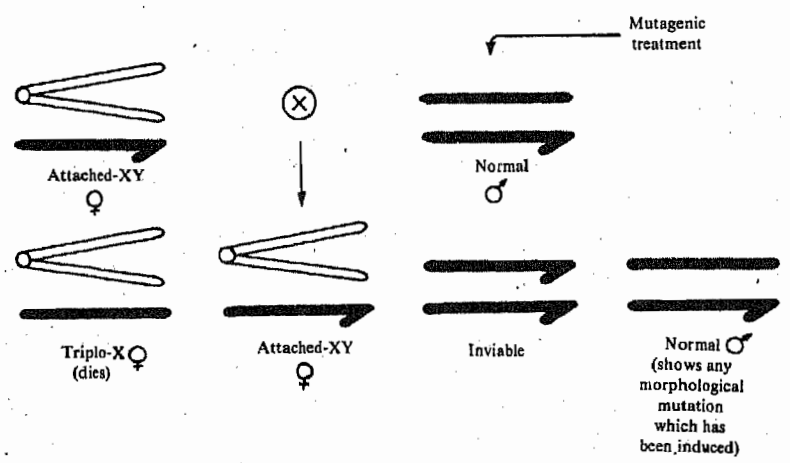

Fig. 16.7 : The attached -X method for detection of induced mutations in *Drosophila*.

16.3.3 Detection in Haploid Organisms

The detection methods in haploid organisms are much more simpler and straight forward. This is based on the fact that they contain only one set of chromosome (n) and thus also one set of alleles. The mutations, if generated, whether recessive or dominant will express themselves in the very next generation. Detection depends on selection system where mutant cells are isolated easily from non-mutant cells. For example, the microorganisms that are nutritional wild type i.e., prototrophs will grow on **minimal culture medium** which consists of glucose, a few inorganic acids and salts, a nitrogen source such as ammonium nitrate and vitamin biotin. But in comparison the induced nutritional mutants of the same microorganism, i.e. auxotrophs will not grow on minimal medium. These will grow only on **complete culture medium** which apart from contents of minimal medium also contains aminoacids, vitamins and nucleic acid derivatives. However, these mutants also grow on minimal medium supplemented with the compound, which as a result of mutations, they are not able to synthesise. So when all of their nutritional requirements are complete, in complete medium or suppplemented minimal medium, the mutants grow well. For instance a *bio*$^-$ mutant (an auxotroph which cannot synthesise biotin) will grow in a minimal medium supplemented with biotin. You can now understand that how the nutritional mutants can be detected and isolated by their failure to grow on minimal medium and their ability to grow on complete medium. You may read more about such techniques in detail in the books enlisted in further reading.

With this we end our discussion on detection of mutations in various organisms. Before we proceed further try the following SAQ to check your progress.

SAQ 3

Tick mark (✓) the correct option in the following statements.

i) Method for detection of mutation depends/does not depend upon whether it is located on autosome or sex chromosome.

ii) Pedigree analysis is helpful in analysing mutations in humans/microorganisms.

iii) It is necessary/not necessary to irradiate the P_1 male with mutagenic agent to detect mutations in Drosophila.

iv) Mutations are detected in F_1/F_2 generation in CIB technique.

v) Triplo-X females of F_1 generation in attached -X technique are viable/non viable.

vi) Mutation detection in microoganisms are simpler beacuse they contain haploid/ diploid set of chromosomes.

16.4 MOLECULAR BASIS OF MUTATIONS

As we all know, genes are made up of stretches of DNA having a specific base sequences. Mutations involve alterations of the DNA sequence including substitutions or addition or deletion of one or more bases. All such mutations can be collectively called **point mutations.** The technical advances in the last two decades have made possible the determination of base sequence of the large segments of DNA so that any change in the sequence can be detected. In this section we will deal with some of exciting aspects of molecular basis of mutations which are so central to any genetic analysis.

16.4.1 Base Pair Substitution

It is a change in a gene in which one base pair is replaced by another base pair e.g., an AT may be replaced by a GC pair. This change can be of two types:

* **Transition** is a change when a purine replaces a purine (A ⇔ G) or a pyrimidine replaces a pyrimidine (C ⇔ T)
* **Transversion** involves change where a purine base is replaced by a pyrimidine base or vice versa

$$\begin{bmatrix} A \Leftrightarrow T & \text{or} & A \Leftrightarrow C \\ G \Leftrightarrow C & & G \Leftrightarrow T \end{bmatrix}$$

These two types of substitutions may change the composition of a triplet codon, so that it may code for a different amino acid, which in turn may change the property of the protein.

16.4.2 Frame Shift Mutation

This type of mutation arises by the addition or deletion of a base pair in the gene causing changes in the reading frame of DNA. You may recall that DNA's base sequence is read in

the form of a string composed of units of three bases, i.e triplet codon. Any addition or deletion of base pair will shift the entire reading frame of that sequence from that point, therefore, disturbing the amino acid sequence. In Fig. 16.8 we have used a sentence composed of three letter words as analogy for triple codon sequence. You can see how, the replacements, additions and deletions change the sense of the sequence.

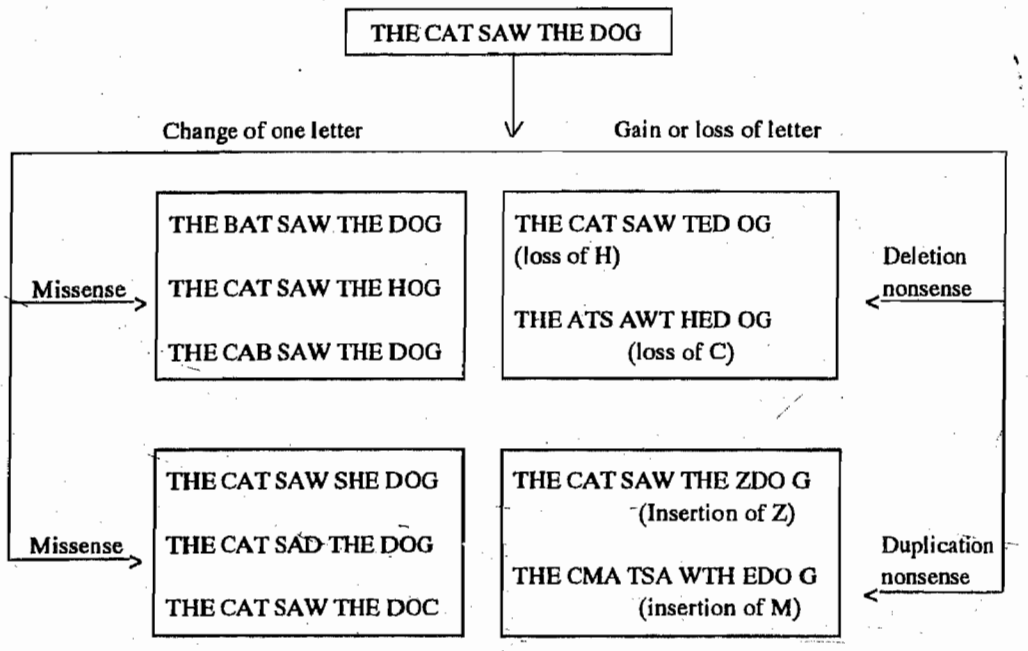

Fig. 16.8: The impact of the replacements, additions and deletions in a sentence composed of three letter words used as the analogy for triple codon sequence.

In the following subsections we are going to discuss various pathways by which single base pair changes take place.

16.4.3 Tautomerization

The purines and pyrimidines in DNA and RNA may exist in several alternate forms called tautomers. Tautomerism, i.e. change in chemical forms occurs through rearrangement of electrons and protons in the molecule. As a result some single bonds become double bonds and vice versa. Such change in chemical forms of the base is called **tautomeric shift.** An example of a tautomer of a purine and a pyrimidine is shown in Fig. 16.9. Although the normal bases posses potentially unstable bonds, they remain chemically stable in one tautomeric form most of the times. This stability is a significant genetic attribute.

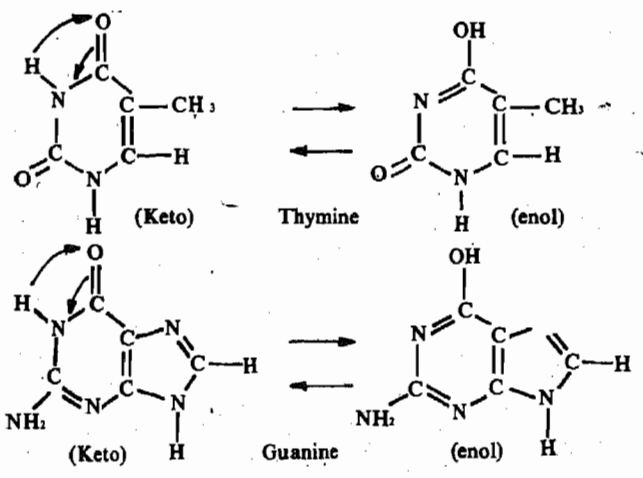

Fig. 16.9: Tautomers of thymine and guanine

16.4.4 Deamination and Depurination

Deamination and depurination of particular bases are the two common chemical events that produce spontaneous chemical mutations. Let us now discuss these processes. Removal of an amino group from a base is called **deamination**. For example, deamination of cytosine produces uracil (see Fig. 16.10). In case uracil is not repaired back, it will direct the incorporation of adenine in the new DNA strand during replication. This ultimately results in conversion of CG base pair to a TA base pair i.e., a transition mutation. Deamination is also caused by certain chemical mutagens about which you will read later in this unit.

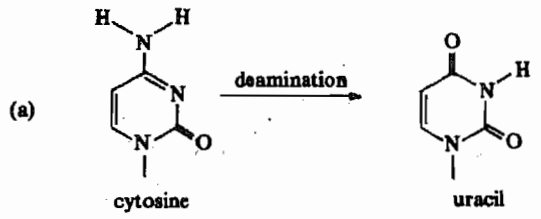

Fig. 16.10: Deamination of cytosine into uracil.

Depurination, as you can guess from the name, involves removal of a purine, either guanine or adenine, from the DNA. This removal occurs due to the breakage of bond between purine and the deoxyribose (see Fig. 16.11). If this fault is not repaired, there will be no base to specify a complementary base during DNA replication. In case a randomly chosen base is inserted a mismatched base pair will be produced resulting into genetic **mutation.** So in both cases mutation will occur.

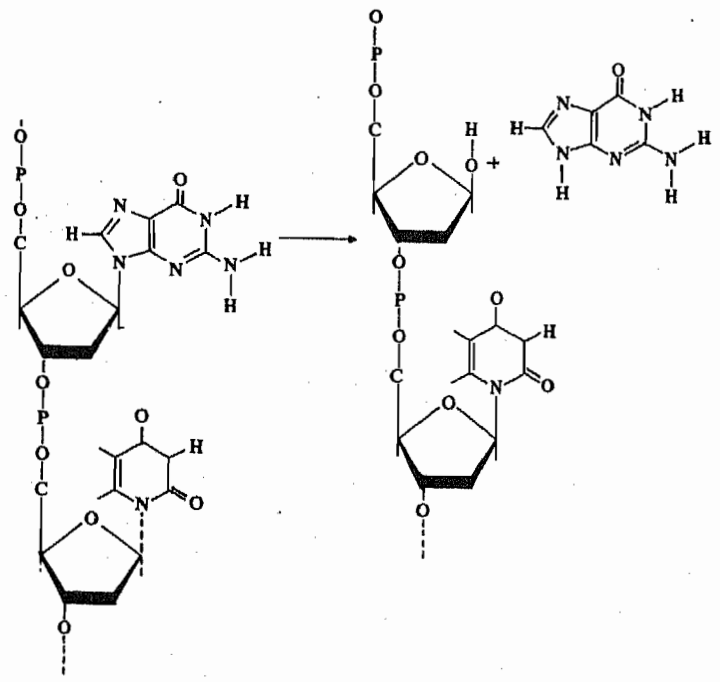

Fig. 16.11: Depurination from a single strand of DNA. You can see that sugar phosphate backbone is not broken. In this case purine adenine is lost.

16.4.5 Base Analogues

Base analogues are the chemicals that have molecular structure that are extremely similar to bases of DNA. These chemicals act as mutagens and during DNA replication get incorporated so as to form base pairs with usual bases. One such chemical is 5-bromouracil (5 BU). 5 BU is a base analogue of thymine and usually pairs with adenine. The bromine atom in 5 BUdR so alters the charge distribution of the molecule that it may tautomerise to a 5 BUdR* form quite frequently. After tautomerisation it possesses the base pairing properties of cytosine, that is, it behaves like cytosine. Fig.16.12 shows how the shift generates G → A transition.

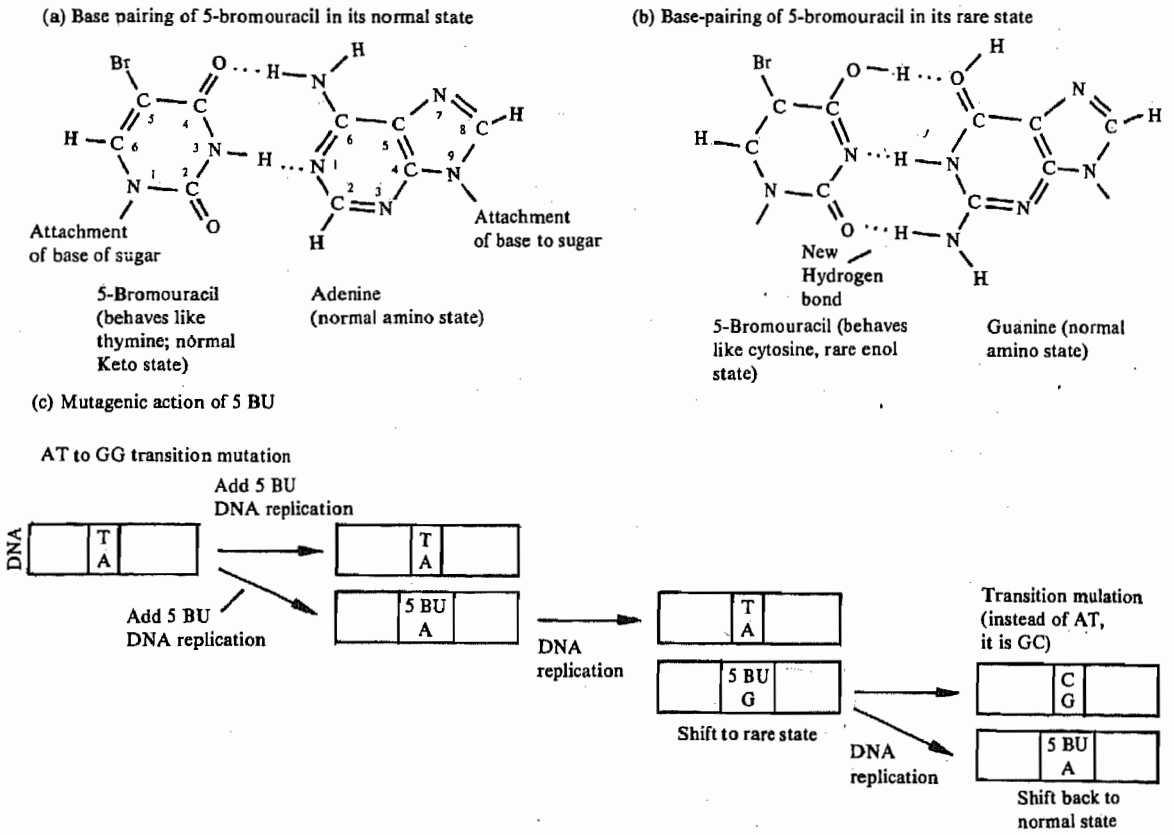

Fig. 16.12: Mutagenic effects of base analogue 5-bromouracil (5BU). (a) In normal state 5BU pairs with adenine; (b) in rare state it pairs with guanine; (c) mutations are induced when 5 BU gets incorporated into DNA in one form and then shifts to its alternate form during next replication stage.

The changes we have discussesd in the preceeding subsections can bring out mutational effect in various ways. When a base pair change causes the change in mRNA codon resulting into a modified protein in place of one specified by wild-type, a **missense mutation** occurs. **Nonsense mutation** occurs when base pair changes result in the change in mRNA that generate a chain terminating codon which will lead to premature termination of protein synthesis. **Neutral Mutation** may go unnoticed as it is a base pair change that changes a codon in mRNA such that the resulting amino acid substitution does not alter the function of the protein. For example, change from codon AGG to AAG which substitutes aminoacid lysine for arginine. Both amino acids are similar in properties, so function of protein is not altered significantly. When base pair change alters a codon in mRNA which may still code for same amino acid, **silent mutation** occurs. For example, change from mRNA codon AGG to AGA both of which specify arginine.

It is time now that you should do another SAQ to see whether you have understood the molecular basis of mutations.

SAQ 4

a) Tick mark (✓) the correct statements and (✗) the incorrect statements in the space provided:

i) When base A is replaced by base T, transition mutation occurs ( ).

ii) The rearrangements of electrons and protons in the bases is called frameshift mutation ( ).

iii) When an amino group is removed from a base, the process is deamination ( ).

iv) Base analogs are chemicals that cause mutations ( ).

16.5 TRANSPOSABLE GENETIC ELEMENTS

Studies have shown that mutations are also caused by addition of long stretches of DNA to the genome. These genetic elements have the capacity to move from one location to another and insert themselves at one or more sites in the genome. This leads to the breaking down of the reading frame and thus produces the mutational effect. The mobile

genetic elements are known by many names such as controlling elements, jumping genes, insertion sequences and transposons. However, these are generally called as **transposable genetic elements** (TGE), a widely accepted name. As you can see in Fig. 16.13 the copies of transposable elements can also be inserted at other points in the same chromosome causing disruption of the gene into which these are inserted. This often produces multiple physiological effects.

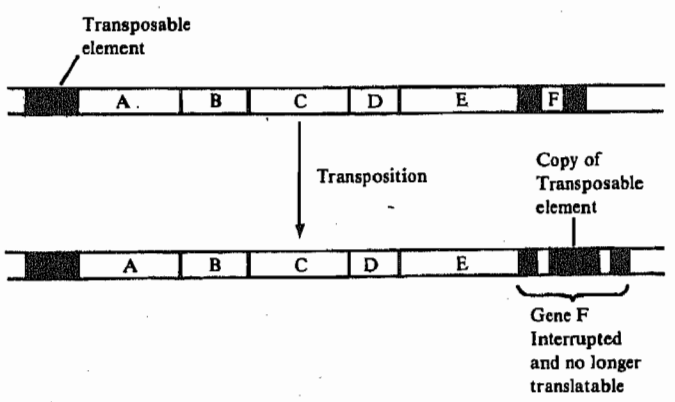

Fig. 16.13: When a transposable element is inserted in the middle of a gene, as in case of gene F in this figure the gene is disrupted. Such genes cannot be transcribed appropriately and thus do not function.

TGEs were first discovered by Barbara McClintock in 1940s. From her study of pigment patterns on kernels of the maize (*Zea mays*), McClintock inferred the existence of mobile genetic elements that influenced gene expression in the corn. She described these elements as "controlling elements". McClintock was awarded Nobel Prize in 1983 for this discovery.

Some examples of eucaryotic transposons are **Ty elements** in Yeast, **copia elements** in *Drosophila* and **retroviruses** in birds and mammals.

One of the more interesting discoveries to emerge regarding transposable elements is that in the process of moving from site to site, they influence the expression and organization of neighbouring genes. Since TGEs can migrate with considerable frequency, the process has the potential for causing rather rapid and dramatic genetic changes. Such changes are now belived to be a major contributing factors to an organism's ability to undergo evolutionary change.

16.6 MUTAGENESIS

In the above sections you have been familiarised with the concept of mutation, a concept which is so central to any genetic or evolutionary studies. The natural occurrence of mutation is very slow. In order to make significant progress in genetics studies, in any living system it becomes imperative that new mutations must be isolated and accumulated at a faster rate. This necessity has led to an active field of study on experimental mutations called **mutagenesis**. Eversince the time of H.J. Muller (1927) who reported that x-ray could induce mutations in ***Drosophila*** followed by L.J. Stadler's finding that same is true in the plant barley, a large number of agents have become available, to induce mutations. This infact has been responsible for the rapid strides that the field of genetics has taken in this century. The agents that can cause mutations are known as mutagens. All mutagenic agents induce mutations in any of the following pathways:

- They may replace a base in the DNA.
- They may after the base in such a way that it specifically mispairs with another base.
- They may damage the base so much that it can no longer pair with any base.
- They may intercalate themselves in the DNA paving way for addition or deletion of bases.

With the initial discovery of X-rays as mutagenic agents a large number of other radiations and chemicals have been identified to have the capacity to induce mutations. In fact this list is growing as more and more agents are being studied. We will discuss various types of mutagens in the following subsections.

16.6.1 Physical Mutagens

These consist of high energy radiations which could penetrate living cells and affect the genetic material. The effect of radiations on living cells and tissues is directly

proportional to the degree of penetration of the radiation. Radiations are of two types: electromagnetic radiations and particulate radiations.

X-rays,γ-rays and UV rays are some short wave length **electromagnetic radiations** which have more penetrations in cells and tissues. As a rule the penetrating power of electromagnetic radiation is inversely proportional to their wave length.

Particulate radiations are in the form of subatomic particles emitted from the atoms with high energy. Alpha particles, beta particles and neutrons fall in their category. Alpha particles and beta particles are charged particles. However beta particles being smaller in size are more penetrating than alpha particles. Neutrons ejected from radioactive isotopes do not carry any charge and hence are not deflected when they travel through living matter. Thus they are extremely penetrant and can cause severe damage to the living tissues as well as genetic material. Cosmic radiations that pour down on us from the outer space have the properties of both particulate and electromagnetic radiations.

These physical mutagens are also divided as high energy ionizing radiations which include cosmic rays, X-rays, γ-rays and particulate radiations and low energy non-ionizing radiations which include ultraviolet light. Let us now see how these radiations tamper with the genetic material.

The **high energy radiations** create ionizations in the living cells. While passing through cells and tissues they collide with molecules such as water and cause the expulsion of electrons. This expulsion creates a positively charged ion. The ejected electron can not remain in free state and therefore, is picked up by another ion creating a negative ion. The generation of free ions by radiations is the basis of extensive damage caused by them at the somatic and gametic level. These ions may combine with oxygen producing highly reactive chemical which may act on genes, chromosomes and other parts of the cells. Peroxides which are mutagenic may be formed in the presence of oxygen following the splitting of water. Experiments have shown that sensitivity to a radiation and the rate of mutation are much lower in the organisms maintained in oxygen-free environment.

Non-ionizing radiations such as UV have more precise mode of action. One of the major effects of UV is the formation of dimers whereby adjacent pyrimidine bases become linked to one another by carbon to carbon bonds. For example, thymine-thymine, cytosine-thymine and cytosine-cytosine dimers of which the first is most common type.

Dimerization results in intrastrand or interstrand cross linking which distorts the DNA conformation, thereby affecting the normal replication. Several studies have shown that the affected cells employ a specific repair process to counteract the effects of UV. We will discuss about the repair mechanism at a later stage in this unit. UV can also cause hydroxylation of cytosine that results into weakening of bonds with guanine permitting localised strand separation thus affecting the replication.

The potential hazards that these radiations may cause to all living beings have led to several investigations working out a **dose-effect relationships**. Such studies were necessitated by the fact that many of these radiations have found use in medicine, agriculture and warfare. It is therefore important to know the effects on living matter when a range of doses of radiations are used.

The dosage of ionizing radiations is measured by the **roentgen unit (r).** It is defined by physicists as the amount of radiation that yields 2.08×10^9 ion pairs per cubic centimeter of air under standard conditions of temperature and pressure. In biological terms this amount of radiation produces two ionizatioins per cubic micron of tissue or water. Most of the research studies with ionizing radiations have been conducted with X-rays and have led to following conclusions.

Irrespective of the wave length used ($0.1A^0$ to $10.0\ A^0$) the number of lethal mutations induced by X-rays is directly proportional to the dose in r units. Thus as you see in Fig. 16.14 when lethal mutation rate is plotted against the dose a linear relationship is observed. As this relationship holds true for very low doses, it is suggested that there is no dose which may be absolutely ineffective. Each doubling of dose results into the doubling of mutations induced. The dosage of an ionizing radiation is based on the amount of ion pairs produced or the amount of energy deposited in the tissue.

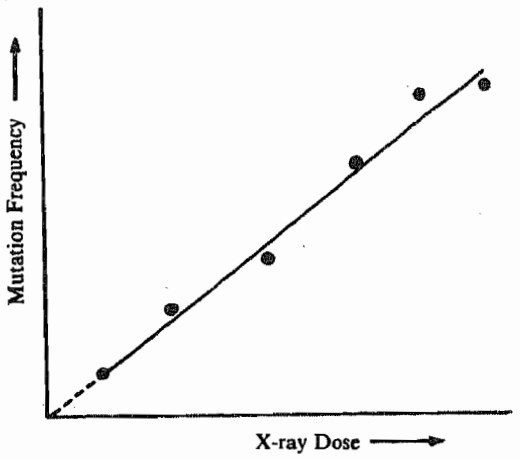

Fig. 16.14: Linear relationship between X-ray dose and sex-linked mutation in Drosophila.

Another interesting finding is that in general the effect of ionizing radiations is cumulative. This means that a given dosage administered in a single acute dose or cumulatively in the form of smaller doses given over an extended period of time will produce same mutagenic effect. However, an exception to this generalisation occurs in mice and probably all mammals. It has also been found that chromosomes are more prone to the radiation damage when they are highly condensed during mitosis. This observation formed the basis of radiations used in treating human malignancy where cells undergoing fast and uncontrolled division will provide more targets for radiations.

Before we proceed further on chemical mutagens try the following SAQ to check your progress.

SAQ 5

a) What are transposons? How are they responsible for mutations?

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b) Write answers to the following statements in the space provided along with.

i) What are the radiations that have the properties of both electromagnetic and particulate radiations? .....

ii) Which subatomic particles emitted with high energy have no charge? .....

iii) Which radiations do cause mutations by creating positive and negative ions? ....

iv) Which radiations do cause the distortion of DNA helix due to dimerization? .....

16.6.2 Chemical Mutagens

As we have discussed earlier a large number of chemicals are known to cause mutation employing different pathways. These chemical mutagens are classified into four major groups on the basis of their specific reaction with DNA. We will now discuss these groups.

Base analogues are the chemical compounds structurally very similar to the normal nitrogenous bases of DNA. The analogues can get incorporated into replicating DNA in place of normal base leading to base pair substitution mutations. Like the normal bases they also exist in two alternative forms i.e., **keto** or **enol** form or **amino** and **imino** form, and change spontaneously from one to another form (tautomeric shift). As previously discussed, 5-bromo uracil is one such mutagen.

Alkylating agents such as ethyl methane sulphonate (EMS), ethyl ethane sulphonate (EES), nitrogen and sulphur mustards and diethyl sulphate (DES) act on DNA by adding alkyl group (ethyl or methyl) to all four bases. However these agents show a strong

The nitrogen atoms attached to the purines and pyrimidines are usually in the ***amino*** (NH_2) form and only rarely assume the ***imino*** (NH) configuration. Likewise the oxygen atoms attached to the C 6 atoms of guanine and thymine normally have the **keto** (C=O) form and only rarely take up the **enol** (COOH) configuration.

Intercalation is a process in which mutagens such as acridines which are flat, aromatic molecules interact with DNA in such a way that they become wedged between the stacked bases of double helix.

preference for base guanine. This results either in mispairing of affected base or its loss entirely, creating a gap and thus causing mutations.

Acridine dyes are the chemicals that intercalate between the bases of DNA. They include proflavin, acridine orange compounds which can mimic base pairs and are able to slip themselves in between the nitrogenous bases. This results in deletion or addition of base pairs during replication.

Direct acting chemicals like nitrous acid reacts with the nitrogenous base and deaminates them by removing amino group from adenine, cytosine and guanine by oxidative deamination. This results in mispairing and base pair substitution mutations.

16.6.3 Environmental Mutagens

In addition to the above mentioned chemical and physical mutagens, there are a number of chemicals present in the environment that are potentially mutagenic. A wide variety of mutagens occur naturally. Some major sources of natural mutagenic agents include parasitic fungi of field crops, mushrooms, certain vegetables and medicinal herbs. Other environmental mutagens include air and water pollutants, food additives and preservatives, agricultural chemicals, cosmetics, drugs, pesticides, cigarettes and industrial products such as benzidine, vinyl chloride, asbestos etc. In addition many potentially mutagenic compounds may be **carcinogens** or capable of inducing cancer in humans. We will discuss carcinogenesis later in this block.

16.6.4 DNA Repair Mechanism

Both prokaryotic and eukaryotic cells have repair systems to deal with DNA damage. All the systems consist of enzymes to repair DNA. Damages are corrected directly or by excision of base pairs. Let us now see how damages are repaired by these two processes.

Direct Correction of DNA damage

We shall discuss here two systems of direct corrections of mutational lesions. One system involves repairs of UV induced pyramidine dimers. The first relevant discovery on UV repair mechanism was made in 1949 when Kelner observed that UV damage to DNA of *E.Coli* could be reversed if UV irradiated cells are exposed to visible light in the blue range (blue light has wave length range of 320-370 nm). This process known as **photoreactivation** or **light repair** was found to be temperature sensitive. Photoreactivation means that light induces an enzymatically controlled chemical reaction. The enzym was subsequently isolated from *E.Coli* cells and was named as **photoreactivation enzyme** or **photolyase**. You can see in Fig. 16.15 that the enzymes cleave the bond between thymine dimer thereby, restoring the structure. The enzyme is also known to bind to the dimers in dark but is activated only when it absorbs a photon of light. Photolyases are apparently very effective since few thymine dimers and mutations are left after photoreactivation.

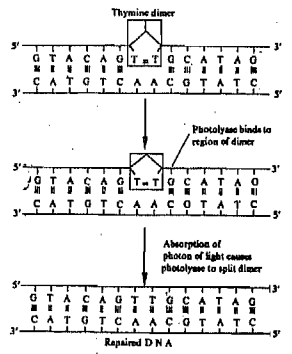

Fig. 16.15: Repair of thymine dimer induced by UV radiation by photoreactivation.

Another system of this kind corrects bases that have become alkylated by chemical mutagens such as EMS. An enzyme called **alkyltransferase** catalyzes the removal of the alkyl group from the base. So now you know that in direct rapair system the modified base is not removed from DNA, but corrected there itself. We will now discuss the repair process involving excision of base pairs.

Repair Involving Excision of Base Pairs

As you have read earlier excision of a base pair is second way of correction of DNA damage. The repair process of UV light induced pyrimidine dimers is called **excision repair** or **dark repair** as it does not depend on visible light as an energy source.

This repair mechanism was discovered in 1964, independently R.P. Boyce and P. Howard Flanders and by R.Setlow and W.Carrier. As you can see in Fig. 16.16 this multienzyme repair process involves several steps. First, the UV induced dimers are recognised by an endonuclease enzyme which produces a single-strand break in the DNA helix backbone on either side of the distorted region. The removal or **excision** of this distorted region occurs with the help of exonuclease enzyme. The gap created is filled by **repair synthesis** of DNA. DNA polymerase, specifically DNA polymerase I in *E. Coli*, catalyses the synthesis using the opposite strand as a template. Final closure of the break to repair the gap is carried out by polynucleotide ligase.

Defects in excision repair porcess leads to genetic diseases. In humans, an inherited disease called **xeroderma pigmentosum** is caused by a recessive mutation that blocks this excision repair process. People with this disease are very sensitive to sunlight and particularly the UV wavelength in the sunlight. They demonstrate a very high incidence of skin cancer, including malignant melanomas on the areas of the skin exposed to sunlight. Cell cultures from humans with xeroderma pigmentosum are defective in excision repair and are killed at very low doses of UV light.

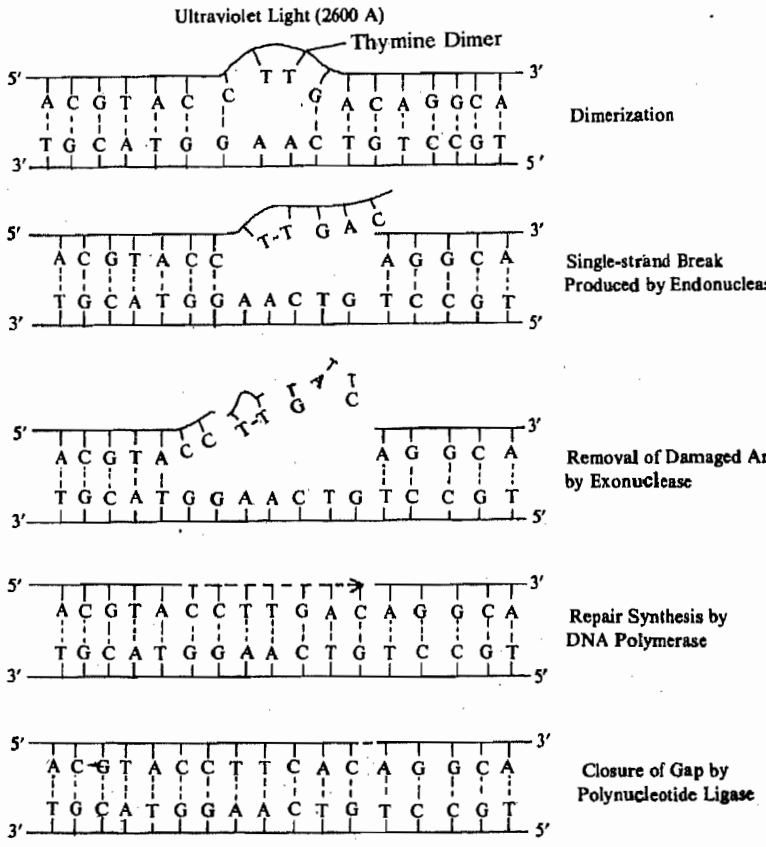

Fig. 16.16: Excision repair of a thymine dimer induced in DNA by ultraviolet radiation.

If UV induced pyrimidine dimer survives the photoreactivation and excision repair systems, another repair system acts during replication. This process is called **post replication repair.** This repair process was discovered in 1968 in an excision defective strain of *E.Coli.* During post-replication, the replicating enzyme slips over the dimers creating gaps on the newly synthesized strand opposite the site of a dimer present in the template strand. These gaps after the subsequent rounds of replication gradually disapper due to the activities of **rec loci** or genes : **rec A, rec B, rec C** and others but in particular rec A gene. You have already read about rec genes earlier in the course.

Another excision repair process to correct chemically induced DNA danage is **repair by glycosylases.** Enzyme glycosylases can detect and excise the altered base from deoxyribose sugar to which it is attached. Different glycosylases have been discovered that can remove deaminated bases, alkylated bases, ring open purines and also UV photodimers. They cleave base-sugar bond (N-glycosidic) and liberate the altered base consequently creating a hole called **AP site.** AP site can be apurinic where there is no A or G or apyrimidinic where there is no C or T.

Such AP sites, produced either by glycosylase action or by spontaneous loss of a purine or pyrimidine base are repaired by AP endonuclease. AP endonuclease breaks the chain by cleaving the phosphodiester bond at AP sites. This initiates excision repair process in

which exonuclease removes few nucleotides ahead of missing base, DNA polymerase I fills in the gap and DNA ligase seals the nucleotides. You can see various steps involved in this repair system in Fig. 16.17.

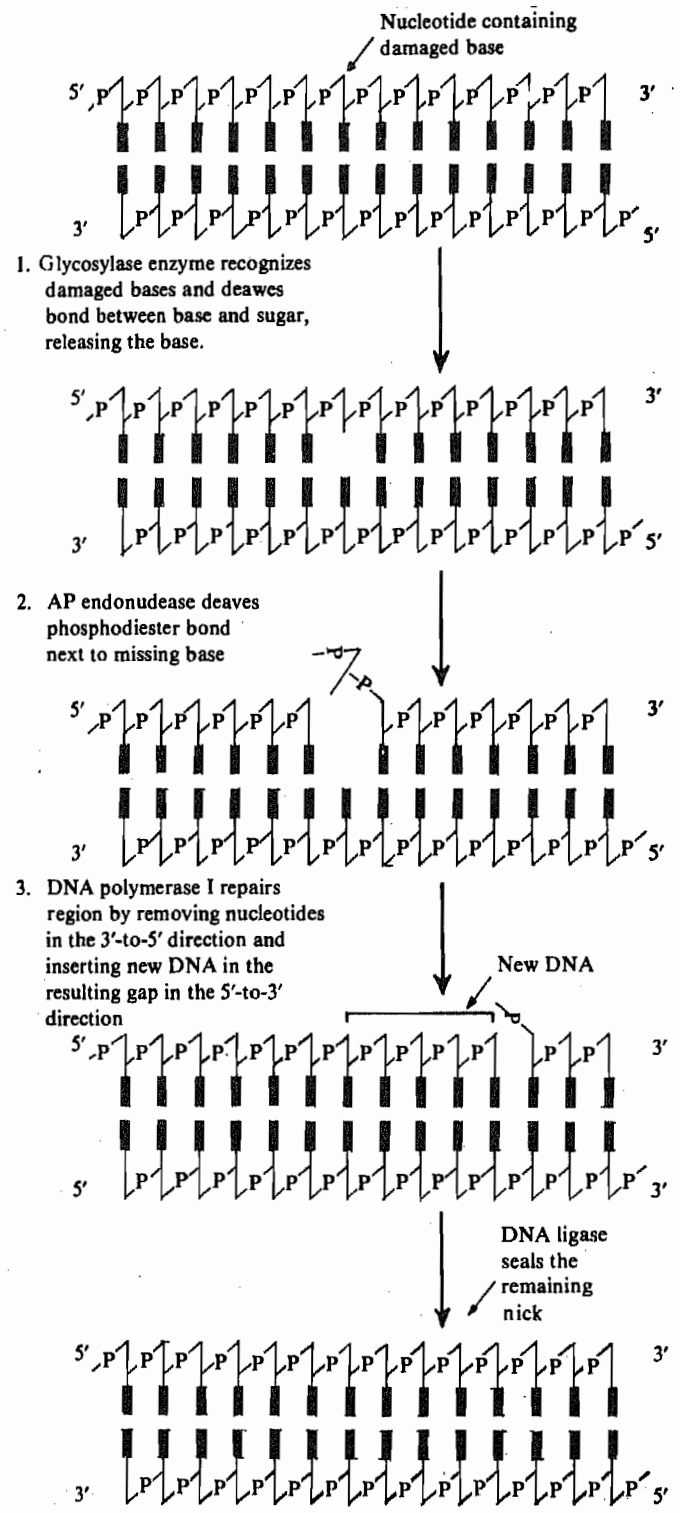

Fig. 16.17: Repair of damaged DNA bases involving the action of glycosylases.

So far you have studied how the mutagenic effects of physical and chemical mutagens can be successfully combated by repair mechanism. However, the errors introduced during the repair cause the mutation. Also not all mutational lesions are repaired and hence mutations are produced. We will now proceed to the last section of this unit which deals with the applications of mutations. But before that try the following SAQ to check your progress.

SAQ 6

The mutagen causes deaminations of adenine into hypoxanthine in the DNA. Name the repair mechanism to rectify this alteration and briefly write the steps involved in this process in the space given below.

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16.7 USE OF MUTATIONS

In the previous sections you have read that mutations bring about the changes in the genetic material of the organisms which may adversely affect their normal functioning. Such changes sometimes lead to serious consequences. But mutations are known to produce certain benefits as well. Let us now look into the beneficial aspects of mutations.

Genetic recombination helps in the construction of an array that indicates the position of genes on a chromosome with respect to one another. When this is done by genetic technique, the array is called a genetic map.

Mutations are raw material for evolution as they bring about variations that are inheritable. It is rather difficult to conceive any evolutionary process in the absence of mutations Secondly., they are the working materials for the geneticists. Some of our significant knowledge in microbial genetics has come from the study of mutant organisms. By noting the specific aberration in a particular mutant organism we can find about various aspects such as the functions, metabolic pathway and its regulations, site of action and interrelationship of various normal cells and systems, and genetic mapping. For example, if a mutant *E.coli* unable to synthesise lactose is found to lack a specific gene group, we can say that the particular gene group is responsible for lactose synthesis. Without mutants, we would still be in the dark as to how gene expression is regulated, and we would still be unaware of many essential features of DNA replication.

Thirdly, mutations being the principal source of variations, are very important for agriculatural purposes. Plant breeeders throughout the world rely on the genetic variability available in crop plants for their improvement.

Induced mutagenesis has been practised by plant breeder since the time of Muller and Stadler. More and more mutagens have been tried as and when they are discovered. Many mutants have been able to attain the status of a variety. The application of induced mutations can be specially rewarding under the following conditions:

- When the naturally occurring variablility is low.
- Where sexual reproduction is absent and, therefore, variability does not arise by recombinations.
- Where change in a specific trait is required in an otherwise superior cultivar.
- When a phenotypic change brings a distinct economic value.
- When generation time is very long as in plantation crops and fruit trees.
- Where a plant product is to be improved by manipulating its biosynthetic pathway.
- Where a desirable gene is tightly linked to an undesirable gene.
- Where plants can be easily propagated by vegetative means as many mutations may lead to seed sterility.

Infact, one could find many other situations where breeding mutants becomes very beneficial. Highly useful mutations have been obtained. For characters like, improved variety, increased growth, reproduction and high yield, quality of the plant product, disease and pest resistance, and stress tolerance to various agronomic factors like pH, temperature, salinity and deficiency of water and nutrients. Some of the examples where mutations have helped are crops like wheat, maize barley, mustard, sorghum, cotton and pea for increased yield and improved variety. Synchrony of flowering has been obtained through mutation in castor beans. Seedless mutation has been obtained in grapes and banana. Here you may recall the examples of navel orange and ancon sheep which after spontaneous mutations have been of advantage to human beings.

The above discussion should make it very clear that induced mutations can be exploited for advancement of genetics as well as to yield useful mutations in any type of crop plants. The applicability of this technique is dependent on the type of the organism and the type of character in question.

With this we end our discussion on mutations and mutagenesis. In case you want to know more about any aspect of mutations you can read the books enlisted under further reading. In the next unit we will discuss about carcinogenesis and teratogenesis. Before we summarise what we have learnt in the unit; do the following SAQ to check upon your progress.

SAQ7

Fill in the blanks in the following sentences with appropriate words:

(i) Mutations enable one to learn about ..... regulation.

(ii) Mutations can indicate..... between apparently unrelated systems.

iii) Induced mutations can be applied when..... is long.

(iv) The technique to induce mutation depends upon the ..... of plants.

16.8 SUMMARY

In this unit you have studied that:

- A mutation is a sudden and hertitable change in the genetic material. Mutations can be classified into several types depending upon the criteria used and therefore can be somatic, germinal or zygotic; spontaneous or induced by application of mutagen; visible, detrimental, or lethal; forward or reverse, and other categories like nutritional biochemical etc. Although all genes are mutable, they do not change with the same frequency or at the same rate.
- Mutations can be detected by simple observation or by employing a specific technique. Various detection methods have been devised keeping in mind the type of mutation and the organism under study.
- At DNA level mutations may be generated by replacing the original base by a new base, by shifting the reading frame of the codons, by base analogues or by tautomerization. These phenomena will lead to a protein which will differ in its function as compared to the original one producing the mutational change.
- Transposable genetic elelments are unique DNA segments that can insert themselves at one or more sites in the genome in both prokaryotes and eukaryotes.
- Mutations can be generated at an accelerated rate by employing various agents called mutagens. Mutagens can be physical e.g. , X-rays, γ-rays UV radiations, subatomic particles and cosmic radiations; chemical e.g. alkylating agents, base analogues, acridines and many other chemical compounds or environmental mutagens like pollutants, preservatives, pesticides etc.
- Cells can employ various repair mechanisms to correct the radiation damage caused by chemicals such as light repair, excision repair, postreplication repair and repair by glycosylases.
- Despite having their adverse effects on the normal functioning of the organisms, mutations offer certain benefits to human beings. Apart from bringing out variability in organisms they are helpful in advancement of studies in genetics and improvement of various characteristics of several crop plants that has been achieved to some extent through induction of mutations.

16.9 TERMINAL QUESTIONS

1) Mutations, the working tools of genetics are studied in a variety of organisms. Suggest any two advantages of using microorganisms for mutation studies.

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2) Explain the following terms.

i) Induced mutations

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ii)Auxotrophs

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iii)Mutagenic agents

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iv)Base analogues

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v) CIB method detecting mutation.

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(3) What are mobile genetic elements ? How can they cause mutations ?

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(4) DNA damage caused by mutagens is repaired directly or by excision of damaged DNA. Give one example of each system of repair.

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(5) How mutations can be applied to increase the agricultural yield ?

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16.10 ANSWERS

Self Assessment Questions

1) Mutations are sudden hertitable changes in the genetic material and involve a qualitative or quantitative change in them. The change results in a corresponding change in the phenotype. Some of the examples are the sickle cell anemia, haemophilia, ability to taste PTC (phenyl thiocarbomide) bitter, navel orange.
2) Student can give many other examples of such types.
   a) i) sudden, hertitable
      ii) genetic variation, evolution
   b) i) c, (ii) a, (iii) d , (iv) b.
3) i) depends, (ii) humans, (iii) necessary, (iv) F_2, (v) non-viable, (vi) haploid
4) a) (i)x, (ii) x , (iii) ✓ , (iv) ✓
5) a) Transposons are genetic elements of long stretches of DNA that have the capacity to move from one location to another. They insert themselves at one or more sites of the genomes. The mutational effect is caused when they cause a break down in the reading frame.
   b) i) cosmic radiation, ii) neutrons,
      iii) ionizing radiations, iv) UV radiations
6) Deamination of adenine will be repaired by glycosylases. In this process enzyme glycosylase detects and excises the altered base creating an AP- site. The AP- site gap is filled by the removal activity of exonuclease and gap filling activity of DNA polymerase I.
7) i) metabolic, ii) relations
   iii) generation time, iv) type

Terminal Questions

1) i) They carry only one set of allele (haploid) and therefore mutations can be easily detected.
   ii) They have a short life span and, therefore, results can be easily obtained.
2) i) Induced mutations arise as a reponse to an extremally applied agent. Various forms of radiations and many chemicals can induce mutations.
   ii) Auxotrophs can otherwise be called nutritional mutants. These mutants lose their ability to synthesise specific nutrients and such nutrients have to besupplemented in their medium for their normal growth. For instance strains of *E-coli* may not synthesise galactose or tryptophan and are respectively known as *gal* and *try* mutants.
   iii) Agents which can induce mutations are known as mutagenic agents. They include various kinds of radiations such as eletromagnetic radiations and particulate radiations. Mutagenic chemicals such as base analogues, alkylating agents acridine dyes and compounds such as nitric acid bring bring about changes in the genetic material. Environmental mutagens such as water pollutants food additives and preservatives, cosmetics, drugs and industrial products can induce mutations.
   iv) Base analogues are chemical compounds structurally similar to the normal nitrogenous bases of DNA. They tend to substitute the purines and pyrimidines in

the DNA and cause mutations. 5 Bromouracil, for instance, is one such base analogue which substitutes thymine.

v) **CIB** method is a method devised by Muller for detecting mutations in *Drosophila.* This procedure can detect the rate of induction of sex linked recessive lethal mutations. For more detailed account of **CIB** method refer to section 16.3.2.

3) These elements are able to move from one position to another. They get inserted in a gene, break its reading frame and thus cause the mutation.
4) The examples are repair of damage caused by UV radiations and any of the excision repair mechanism like dark repair or postreplication reapir. Student can explain these from the text.
5) It has been long since known that many of the present day agricultural varieties arose as a result of mutations from the wild type. Crop scientists use mutations as a tool for obtaining increased agricultural yield. Mutations can result in improved variety, increased growth and reproduction, high yield, better quality of the plant product, disease and pest resistance and stress tolerance to various physical factors. Mutations have helped crops like wheat, maize, barely, sorghum, cotton and pea for increased yield and improved variety.