Gene mutations

Contents: Definition; Discovery and background information; Some common examples of mutations; Classification of mutations; Gene mutations; Classification of gene mutations; An example of gene mutation; Mutagens; Mechanisms of mutations; Detection of mutations; Practical applications of mutations; Role of mutations in organic evolution and speciation; Suggested reading.

Definition

Mutation (L. *Mutare*- a sudden change) is a permanent heritable change in the genetic materials (RNA/DNA, chromosomes) of an organism**.**

- The term mutation was coined by the Dutch botanist Hugo de Vries (1901), who proposed the mutation theory of evolution.
- His observations were based on the evening primrose, *Oenothera lamarckiana.*
- Later, it was found that the altered evening primrose had chromosomal aberrations, not gene mutations.
- Though introduced in 1901, the explanations of mutation were established after the work of H. J. Muller (1927) on artificial induction of mutations by X-rays.

Fig. 9.1 Left- Hugo de Vries (1848-1935); Righy- H. J. Muller (1890-1967), who won the Nobel Prize in 1946

Some common examples of mutations in organisms

- Wild-type, normal-legged sheep mutated to ancon (short-legged) breed of sheep;
- Wild-type, red-eyed *Drosophila* turned into white-eyed recessive mutant;
- Coloured conidia in *Neurospora* became colourless white conidia;
- Sensitive strain of T1 phage (a bacteriophage of *E. coli*) turned into resistant strain; and
- Seeded grapes and oranges become seedless grapes or oranges etc.

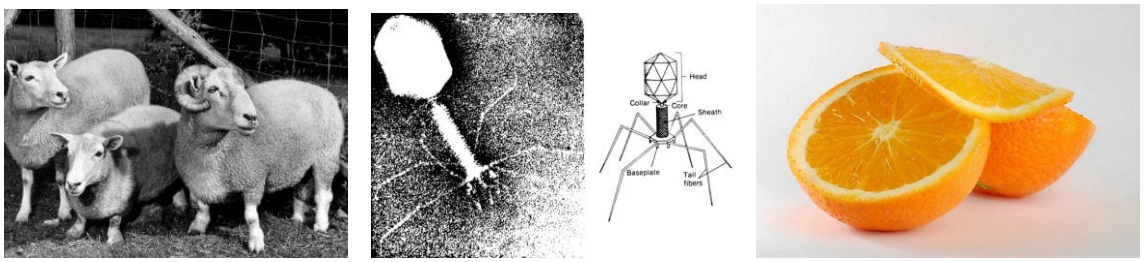

Fig. 9.2 Some common examples of mutations: Ancon breed of sheep (left), T1 phage (middle) and seedless grape (right)

Classification of mutations

A. Depending on the origin of mutations:

(a) Natural or spontaneous mutations; and

(b) Artificial or induced mutations.

B. Depending on the nature of mutations:

(a) Gene mutations (mutations proper or point mutations); and

(b) Chromosomal mutations (chromosomal aberrations/abnormalities).

Natural or spontaneous mutations

Examples include white eye in *Drosophila*, colourless conidia in *Neurospora*

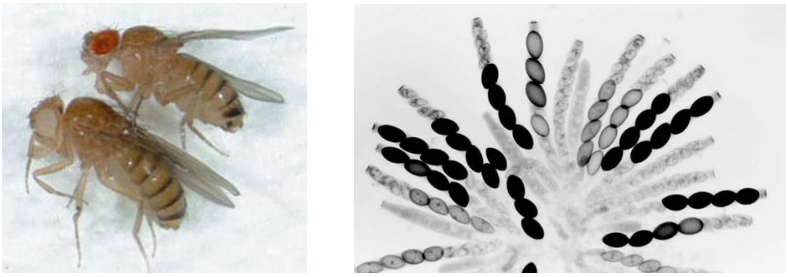

Fig. 9.3 Left: wild-type (red-eyed, top) and white-eyed (bottom) *Drosophila*, right: coloured and colourless conidia in *Neurospora*

Artificial or induced mutations

Examples include ClB and attached-X females in *Drosophila*

Fig. 9.4 A ClB female *Drosophila* showing the bar-eye dominant mutation

Classification of gene mutations

According to gene functions, H. J. Muller (1932) classified gene mutations into the following six sub-types:

1. Amorph: Mutation that causes a complete loss of gene function; phenotypes are mostly recessives;
2. Antimorph: Mutation that antagonizes the normal gene function; phenotypes are mostly dominants;
3. Neomorph: Mutation that causes a new and novel gene function;
4. Hypermorph: Mutation that increases in normal gene function;
5. Hypomorph: Mutation that causes a partial loss of gene function; and
6. Pseudomorph: Mutation that causes replacement of existing mutant but the new mutant has the appearance of the original phenotype.

Other types of gene mutations

i. Recessive: White eye in *Drosophila*, albinism in man and rabbits;
ii. Dominant: Bar eye in *Drosophila*, polydactyly and dimple in man;
iii. Lethal: Hb^S and h (haemophilia) genes in man, Cr (creeper) gene in fowl;
iv. Visible: White eye (w) and curly wing (Cy) in *Drosophila;*
v. Harmful (detrimental or deleterious): Genetic diseases like phenyl ketonuria (PKU) and alkaptonuria in man;
vi. Beneficial: CCR5-32 gene, which is resistant to HIV and bubonic plague in man;
vii. Reversible: White eye (w, mutation rate= 4×10^{-5}) to red eye (+, mutation rate= 1×10^{-6}) in *Drosophila;*
viii. Somatic: Mutations that take place in body cells like tumours which could be benign (harmless) or malignant (cancerous); and
ix. Germinal: Mutations that take place in gonads or germ cells.

An example of gene mutation

- In human adults, the normal haemoglobin is HbA, which can be mutated to haemoglobin HbS, causing the lethal disease called sickle-cell anaemia.
- In HbA molecule, there are two polypeptide chains, α and β; the α chain has 141 amino acids whereas the β chain has 146 amino acids.
- In the β chain of HbA molecule, the 6th amino acid is **glutamic acid**, for which DNA trinucleotide is **CTC** and mRNA triplet codon is GAG
- In the β chain of HbS molecule, the 6th amino acid is **valine**, for which DNA trinucleotide is **CAC** and mRNA triplet codon is GUG
- In other words, the DNA trinucleotide **CTC** is replaced by **CAC**
- That is, **T** (thymine, which is a pyrimidine) is replaced by **A** (adenine, which is a purine). This mechanism is known as **transversion**.

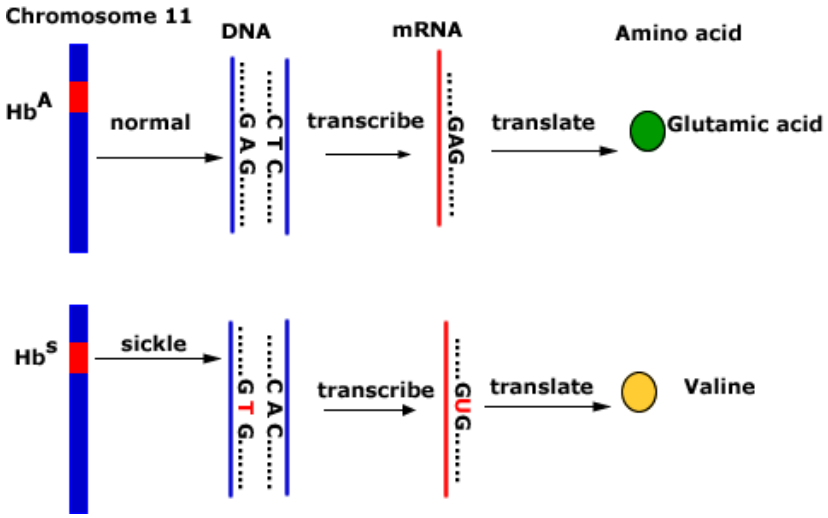

Fig. 9.5 Diagram showing the mechanism of gene mutation from Hb^A to Hb^S gene

Shape of the HbA *versus* HbS haemoglobins

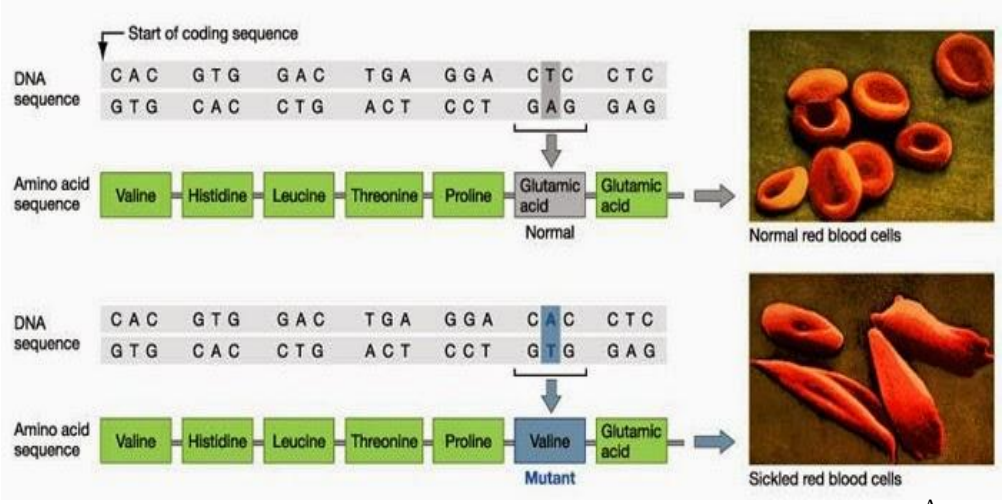

Fig. 9.6 Diagram showing the molecular mechanism of gene mutation from Hb^A to Hb^S gene and its consequence on the shape of haemoglobins in man

Mutagens

Mutagens are physical or chemical agents that cause mutations in organisms.

There are two main categories of mutagens as follows:

1. **Physical mutagens**

(a) Temperature such as heat or cold shock;

(b) Radiation: Non-ionizing radiation such as UV-rays, laser beam, microwave etc. and ionizing radiation such as X-rays, γ-rays etc.

2. **Chemical mutagens**

(a) Alkylating agents: *e.g.* Ethyl-N-nitroso urea (ENU)

(b) Methylating agent: *e.g.* ethyl ethane sulfonate (EES), ethyl methane sulfonate (EMS)

(c) Various chemicals: *e.g.* H_2O_2, HNO_2, mustard gas, colchicin, 5-bromouracil, 2-amino purine, ethidium bromide (EtBr), nitroso guanidine (NTG), hydroxyamine (NH_3OH) etc.

Effects of mutagens on *Drosophila*: Various physical or chemical mutagens can increase 3-4 times autosomal or X-linked mutations in *D. melanogaster*.

Mechanisms of gene mutations

1. Tautomerism: Replacement of a nitrogen base by repositioning of a H atom
2. Frame shift: Addition or deletion of a nucleotide in the reading frame of mRNA (*i.e.* triplet codon)
3. Depurination: Loss of a purine (A/G)
4. Depyrimidination: Loss of a pyrimidine [C/T(U)]
5. Deamination: Replacement of a normal base to an atypical base; *e.g.* C is replaced by U instead of T, A is replaced by HX (hypoxanthine) instead of G
6. Transition: A purine is replaced by another purine (A↔G), or a pyrimidine is replaced by another pyrimidine (T↔C)
7. Transversion: A purine is replaced by a pyrimidine or *vice-versa* [A/G↔C/T(U)]

Tautomerism: Replacement of a nitrogen base by repositioning of a H atom
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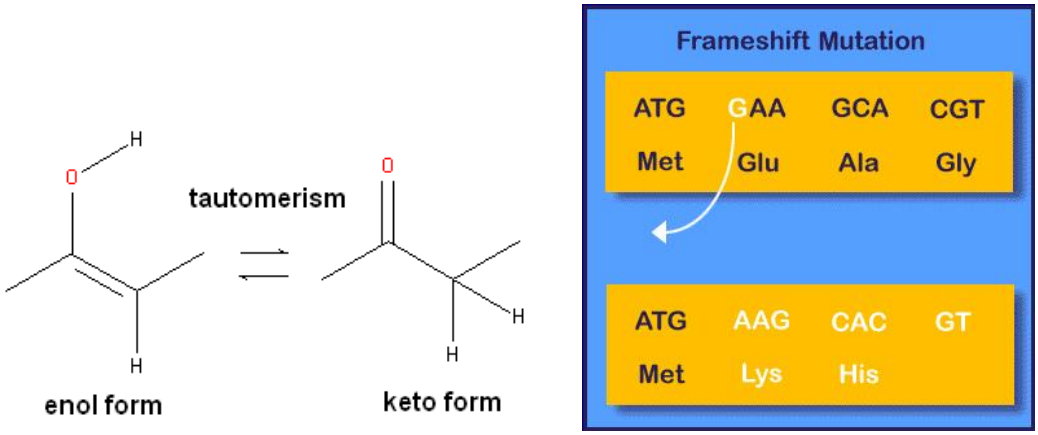

Fig. 9.7 Diagrams showing the mechanisms of tautomerism (left) and frame shift mutation (right)

Depurination: Loss of a purine (A/G)

Transition: A purine is replaced by another purine (A↔G), or a pyrimidine is replaced by another pyrimidine (T↔C)

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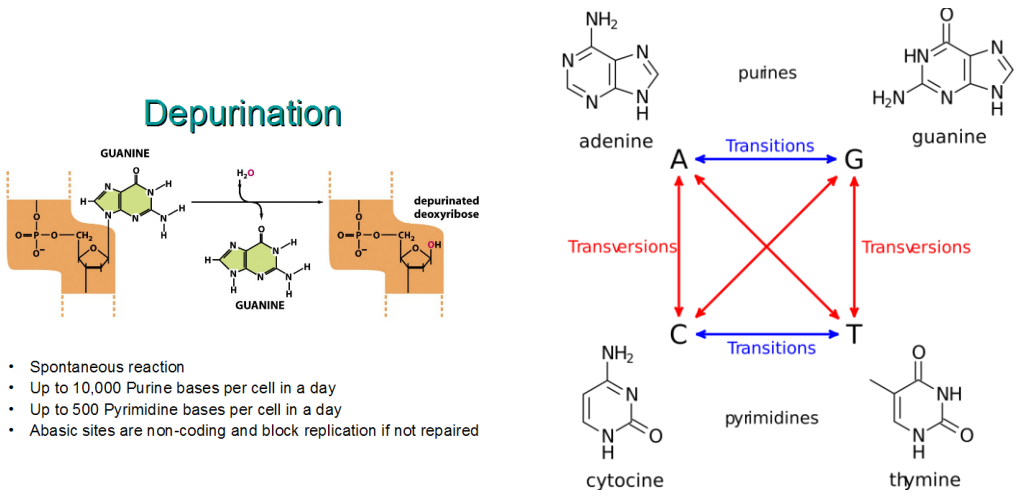

Fig. 9.8 Diagrams showing the mechanisms of depurination (left) and transitions and transversions (right)

Detection of mutations

There are several methods for detecting mutations in *Drosophila*. The common ones are:

1. ClB method: This method is used for detecting X-linked lethal mutations;
2. Muller-5 method: This method is used for detecting X-linked visible mutations;
3. Balanced-lethal method: This method is used for detecting autosomal lethal or visible mutations; and
4. Attached-X method: This method is used for detecting X-linked recessive or dominant visible mutations

1. ClB method

This method was developed by H. J. Muller (1927) for detecting X-linked lethal mutations in *D. melanogaster*. Here a special type of female (ClB female) is used, which has one normal X chromosome and the other X chromosome carries an inversion at the centre. Inversion suppresses crossing-over with the normal X chromosome, so the phenomenon is designated as 'cross-over suppressor' (C). The inverted chromosome also carries a dominant lethal gene for bar eye (B), which acts as a marker and makes it possible to recognize flies having this particular type of X chromosome. Moreover, this unusual X chromosome carries a recessive lethal gene (l). Therefore, female flies of this stock are called ClB females, where C stands for cross-over suppressor, l for lethal and B for bar eye.

Procedure for ClB method

This method involves the use of a *ClB* female stock which carries:

(i) An inversion to work as crossover suppressor (C),
(ii) A recessive lethal gene (l), and
(iii) A dominant marker, bar eye (B)

- One of the two X chromosomes in a *ClB* female carries all the above three features and the other X chromosome is normal
- Irradiated or mutagen-treated male flies are crossed to *ClB* females
- Male progenies receiving *ClB* X chromosome will die
- Male progenies receiving mutagen-treated X chromosome will also die, if lethal mutation is induced by the treatment.

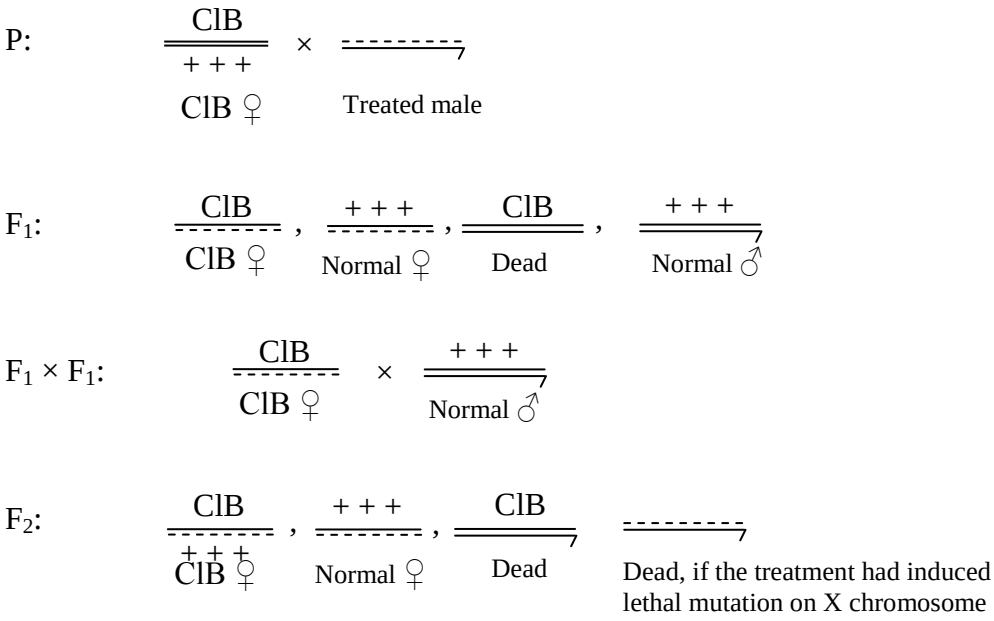

Fig. 9.9 Detection of X-linked lethal mutations in *Drosophila* by ClB method

2. Muller-5 method

Muller-5 method is an improved and advantageous method than the ClB method because of two marker genes for apricot eye colour (w^a) and bar-eye (B).

Procedure for Muller-5 method

- In parental generation, Muller-5 females are mated with treated males;
- In F_1 generation, apricot and bar-eyed females and males are produced;
- In F_2 generation, Muller-5 females, apricot and bar-eyed males and females are obtained; but no normal males are found if the treatment had induced lethal mutation on X chromosome.
- However, if no mutation was induced, normal males will be produced.

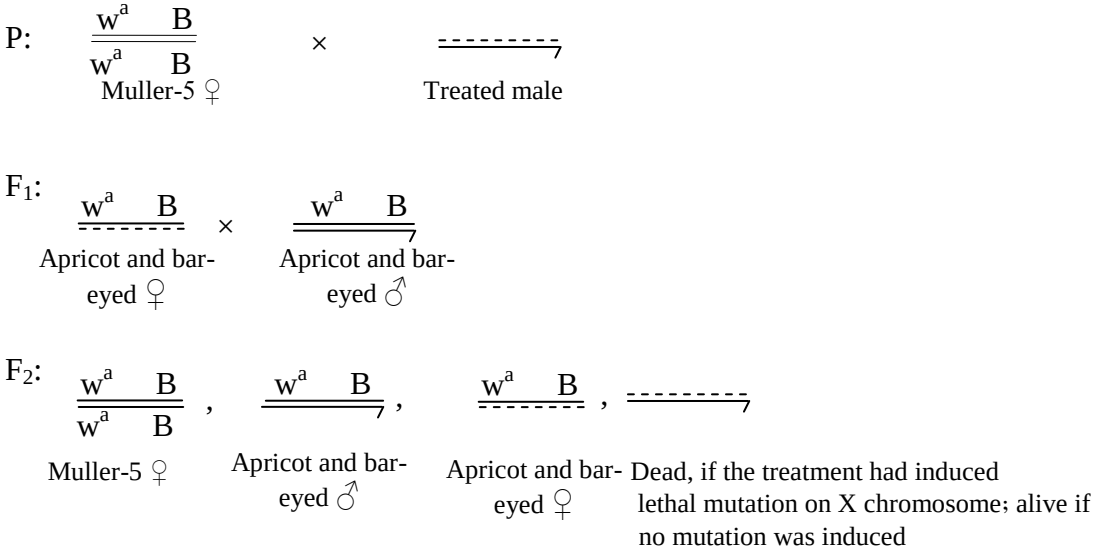

Fig. 9.10 Detection of X-linked lethal or visible mutations in *Drosophila* by Muller-5 method

3. Balanced-lethal method

By this method, any visible autosomal mutations can be detected. The balanced-lethal stock of *Drosophila* has curly-wing (Cy) and lobbed-eye (L) genes that are situated on one of the the second chromosomes. The other chromosome of the homologous pair has Pm gene for plum eye colour. Since all the three genes, Cy, L and Pm cause lethality in homozygous conditions, the stock is maintained in heterozygous (Cy+L/ +Pm+) condition.

Procedures for balanced-lethal method

The heterozygous balanced-lethal flies, charcterizd by the curly-wing (Cy), lobbed-eye (L) and plum eye colour (Pm), are mated with X-ray- or any other mutagen-treated flies. In F_1 generation, two phenotypes, *viz*., curly-lobbed (Cy+L) and plum-eyed (+Pm+), will be found. Then the curly-lobbed males are back-crossed with the curly-lobbed-plum females. The resulting F_3 progenies with only have curly-lobbed (Cy+L) females, if the treatment had resulted in lethal mutations. Otherwise, any visible autosmal mutations will be found in the surviving males in F_3. The balanced-lethal method has been shown in Fig 10.11 below.

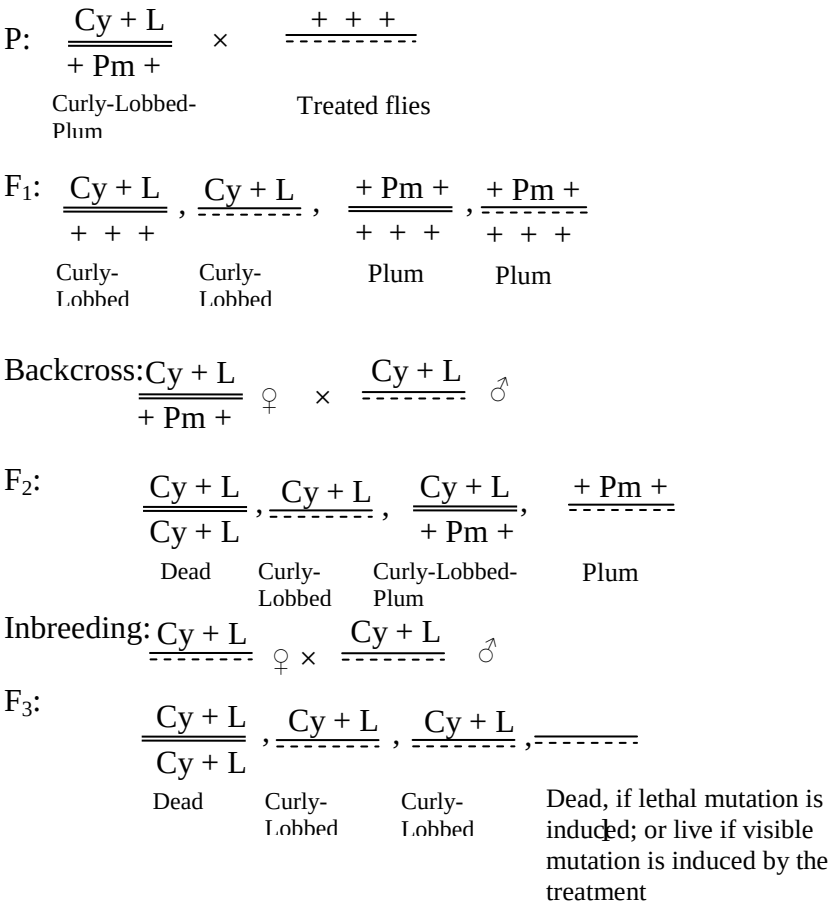

Fig. 9.11 Detection of autosomal mutations by balanced-lethal method

4. Attached-X method

L. V. Morgan (1922) discovered a special type of *Drosophila* in which females ($\hat{XX}Y$) had attached-X chromosomes. In these flies, compulsory non-disjunction takes place during meiosis. This stock of flies is important for detecting sex-linked, visible and recessive mutations.

Procedures for attached-X method

Initially Attached-X females are mated with treated males. As a result, four types of offspring found in F_1 generation are: (1) superfemales ($\hat{X}XX$), (2) attached-X females ($\hat{X}XY$), (3) normal males (XY) and (4) YY males. Of course, YY males die in the embryos. The normal males (XY) are important because they received their X chromosomes from the treated fathers (XY) and the Y chromosome from the attached-X mothers.

Now, if radiation or any other mutagen treatment had induced a visible and recessive mutation in the flies, it could be detected immediately in these F_1 males. There is an advantage of the attached-X method. For detecting mutations, there is no need for continuing the experiments up to the F_2 generation. The attached-X method is shown below.

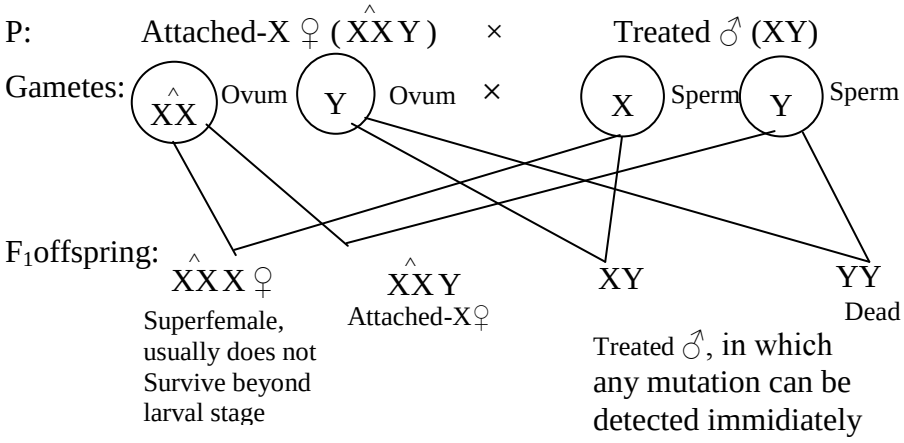

Fig. 9.12 Attached-X method by which induced, visible and recessive mutations can be detected

Practical applications of mutations

A few examples of the practical applications of both gene and chromosomal mutations are described below:

1. Mutations are utilized for the production of improved varieties of fruits like apples, oranges, strawberries and grapes;
2. Production of antibiotics like penicillin is made from the mutant strains of bacteria;
3. Improved breeds of wheat, barley, soybean, tomato, potato and other crops having increased productivity, disease resistance, increased protein and vitamins are being produced through utilizing mutations (see Fig 9.13 below);
4. Polyploidy (>2n) in agricultural and horticultural plants has increased productivity of the crops (see the table below);
5. Tetraploid (4n) plants like melon, orange, grapes, bananas, coffee, cotton, sugar-cane, ground nuts, tobacco, timber plants etc. contribute a huge improvement in the economy of a country;
6. Luxurious and valuable fur and wool from mink and sheep are produced from the mutant varieties of the animals.

Table 5.1: A list of major crops and their ploidy

Common name	Ploidy	Name	Propagation
Maize	2x=20	Diploid	Outcrossing
Wheat	6x=42	Hexaploid	Outcrossing
Rice	2x=24	Diploid	Selfing
Potatoes	4x=48	Tetraploid	Outcrossing; Vegetative
Soybeans	2x=40	Diploid	Selfing
Barley	2x=14	Diploid	Selfing
Tomatoes	2x=24	Diploid	Selfing
Bananas	3x=33	Triploid	Vegetative
Watermelon	2x=22	Diploid	Outcrossing
Sugarcane	8x=80	Octoploid	Outcrossing; vegetative
Sugar beet	2x=18	Diploid	Outcrossing
Cassava	2x=36	Diploid	Outcrossing; Vegetative

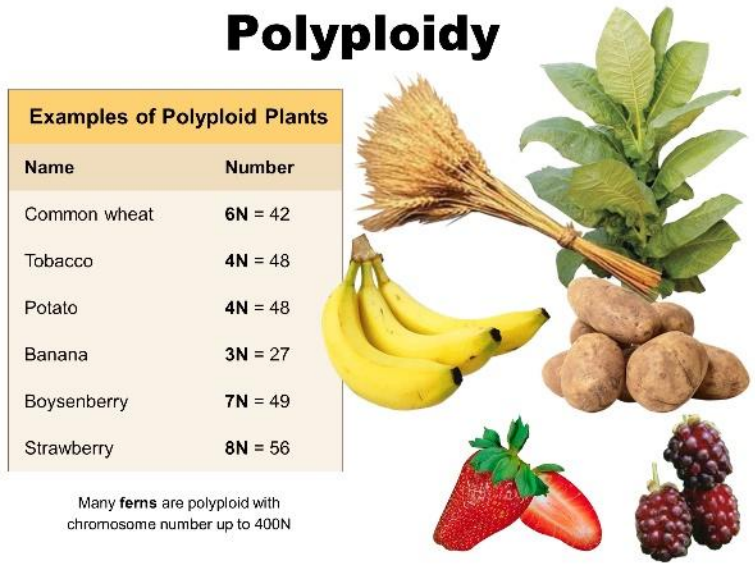

Fig 9.13 Some commonly produced mutated (polyploid) food crops

Role of mutations in organic evolution and speciation

The mutation theory of evolution was originally proposed by the Dutch botanist Hugo de Vries in 1901. Although the events in the evening primrose *Oenothera lamarckiana*, with which de Vries studied, did not actually show gene mutations, the changes which de Vries noticed were due to chromosomal aberrations, polyploidy in particular. Subsequent observations and experiments in plants and animals revealed that both gene mutations and chromosomal aberrations are capable of inducing random and unpredictable changes in the

allelic frequencies of a population, thus leading towards evolution of a species. A couple of examples are given below:

1. In an Australian grasshopper *Moraba scura*, translocation, a type of structural chromosomal aberration, brought about so drastic changes that a new species *M. viatica* evolved within a relatively short period of time.

2. In the underground rodents, *Thomomys talpoides* (2n chromosomes= 40) inhabiting the Rocky Mountains of the USA, polyploidy (numerical chromosomal aberrations) gave rise to four different species of the rodents, in which the 2n chromosome number varies between 40 and 60.

Ayala & Kiger (1980), however, designated the above cases as the rapid, quantum or saltational speciation.

Suggested reading:

Ayala & Kiger, 1980.
Gardner *et al*. 1991.
Islam, MS. 2018
Sinnott *et al*. 1973.
Winchester, AM. 1966.
Wikipedia: www.wikipedia.com
ইসলাম, ম.সা. ও অন্যান্য ২০১৭।