CHROMOSOME AND DNA

Chapter 22

Major Concept

In this Unit you will learn:

- Chromosomal Theory of Inheritance
- DNA as the hereditary material
- DNA Replication
- Gene Expression
- Regulation of Gene Expression
- Mutation

As we have studied in o ur previous classes that the nucleus of a cell contain a network of chromatin material. When it is placed in a dye this material became darkly stained to made it prominent. This chromatin material during cell-division condenses to form specific type of threads called **chromosome**. We have also studied about Mendelian imaginary unit of inheritance which he named **factors**. In this chapter we will study about the reality of Mendelian factors and its relation with chromosome

22.1 CHROMOSOMAL THEORY OF INHERITANCE

In 1860s Mendel presented his law of inheritance but unfortunately at that time no one was there to recognize his valueable work. He was unaware about the concept of chromosome. In 1900s and late 1890s so many cytologist work on cellular structure and chromosome so in 1900 Mendel's work got recognized by three European scientists **Hugo de varies**, **carl Corren** and **Erich Von Tschermark**. With these other scientists like **Walter Fleming**, **Waldeyer Walter Sutton**, **T. H. Morgan** and **Theodar Boven** also worked on chromosome structures, numbers and behavior during inheritance and sexual reproduction.

Carl Correns

22.1.1 History of chromosomal theory

The German embryologist Walter Fleming (1882) was the first scientist who put foundation stone for chromosomal theory by discovery of chromosome. He observed the dividing cell of salamander larvae where he found there thread like highly stained bodies and termed as coloured bodies i.e. Chromosome. The other two scientists who made major contribution for this theory, they were Walter Sutton an American graduate student of E. B. Willson's at Columbia University and Theodar a German biologist, both independently observed the behavior of chromosome distribution in sperms and eggs during meiosis. They observed that in somatic cell each chromosomes are found in pair but during meiosis the

members of each pair segregate so the sperm and egg receives only one from there W. Sutton observed the cells of Grass hopper and found that the segregation pattern of chromosomes during meiosis matched the segregation pattern of Mendel's genes, so 1902 he published his finding in a paper with the title "**The chromosome in Hereditary**". The same findings were observed by T. Boven that chromosomes number are reduced in half as egg cell matures and concluded that sperm and egg nucleus have one set of chromosomes rather than as found in all body cell.

In 1890 a German geneticist **Carl Correns**. He rediscovered and independently verified Mendel's work in a separate model organism and published his first paper on 25 January 1900 with the title "**Mendel's law concerning the behavior of progeny of Racial Hybrids**", where first time he developed the relationship of hereditary units with chromosomes.

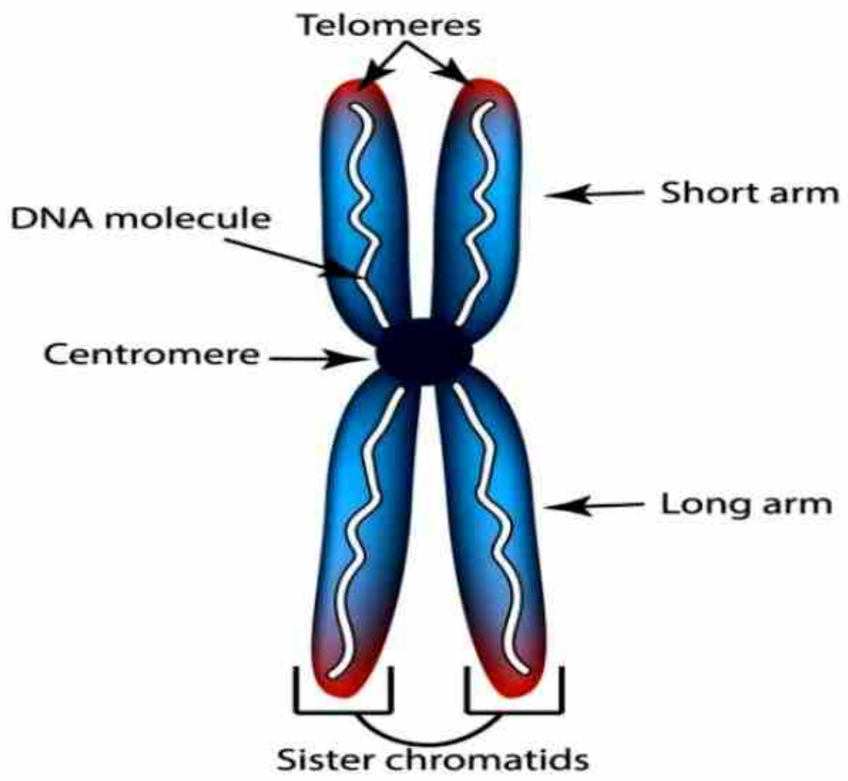


Fig. 22.1 *Chromosome*

Statement and evidences of chromosomal theory of inheritance

The research of many biologists which is discussed above led to the chromosomal theory of inheritance first formulated by W. Sutton in 1902. It states that the genes are located at chromosomes, which inherit through chromosomes of gametes cells, so chromosomes act as carriers of hereditary, the theory was supported by following evidences based on the research of different biologist.

Walter Sutton

1) Sexual reproduction involves the initial union of only two cells i.e. egg and sperm. If Mendel's model is correct then these two gametes must make equal hereditary contributions, sperm however contains little cytoplasm, therefore, considered that the hereditary material must reside within the nucleus of gametes.
2) Chromosomes segregate during meiosis in a manner similar to the Mendelian "factors" segregate according to law of segregation.
3) Gametes have one copy of each pair of homologous chromosomes, diploid individual has two copies. In Mendelian model gametes have one copy of the factor while diploid individuals have two copies.
4) During meiosis, each pair of homologous chromosomes orients on the metaphase plate, independent of any other pair. Thus, independent assortments of chromosomes are like factors of assorted trait as explained by Mendels law of independent assortment.

There was one problem with this theory as many investigators soon pointed out. If Mendelian traits are determined by factors located on the chromosomes and if the independent assortment of Mandelian traits reflects the independent assortment of these chromosomes in meiosis, why is it that the number of factors that assort independently of one another in a given type of organisms is often greater in number of chromosomes pairs that the organism possess? This seemed a fatal objection and it led many early researchers have serious reservations about Sutton's theory.

22.1.2 Experimental Verification By T.H Morgan To Chromosomal Theory Of Inheritance

Thomas Hunt Morgan in 1910 performed various breeding experiments with wild type red-eyed *Drosophila melanogaster* flies. He noticed a white eyed male mutant, crossed this white eyed male with true red-eyed female. The F_1 and F_2 population followed the simple Mendelian ratios but when white-eyed female was crossed with red-eyed male, the results were different.

All F_1 progeny had red eyes when members of F_1 generation crossed with each other. He found 18% white eyed and remaining were red-eyed. Although the ratio of red eyes to white eyes in F_2

generation was greater than 3 : 1, the result of cross was clearly showed the segregation of eye colour factors but a strange and unpredicted result was also there that in F_2 generation all white eyed Drosophita were male.

The above result left many questions unanswered. Do it was impossible to have white eyed in female? Do white eyed female are unable to survive? To get the answers of the above questions Morgan made original test cross between female of F_1 generation and the original white eyed male. He obtained both white eyed and red eyed males and females in a ratio of 1 : 1 : 1 : 1 now it is clear that a female could have white eyes. Only question was left behind that why there were no white eyed female among the progeny of original cross?

T.H Morgan

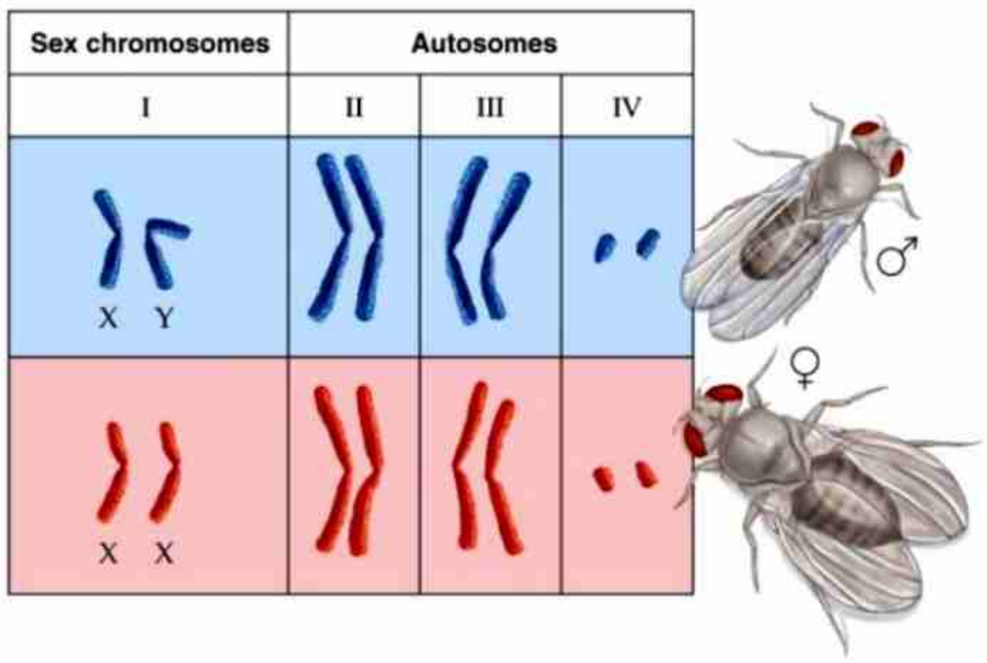


Fig.22.2. ***Drosophila and its Karyotype***

22.1.3 Chromosomes (Chroma = Colour, Soma = Body)

The literal meaning of chromosomes is coloured body but the chromosomes are not coloured bodies therefore this term is called misnomer. They were first observed by a German embryologist **Walter Fleming** in 1882 when he stained Salamander larval cell with a dye called **Perkin's Aniline**. He found darkly stained threads which he named chromosome. **Chromosomes** are thread like structure made up of highly condensed chromatin material, appear during cell-division in specific numbers according to species, and carry gene on it. In the beginning of cell-division each chromosome is consist of two identical threads which are attached with each other and called

sister chromatids. Each chromatid contains a **primary constriction** which is called **centromere** and sometime another constriction is also present called **secondary constriction**. Each chromatid consists of one or two arms. On the basis of centromere position the chromosomes are classified into 4 types i.e. **Metacentric**, equal arms where centromere is located exact in the center. If the centromere is located slightly away from center the slightly unequal arms develop these chromosome called **Sub-metacentric**, if centromere located away from center so the two arms become unique chromosome called **Sub-telocentric** or **Acrocentric,** if it is located at end called **Telocentric**.

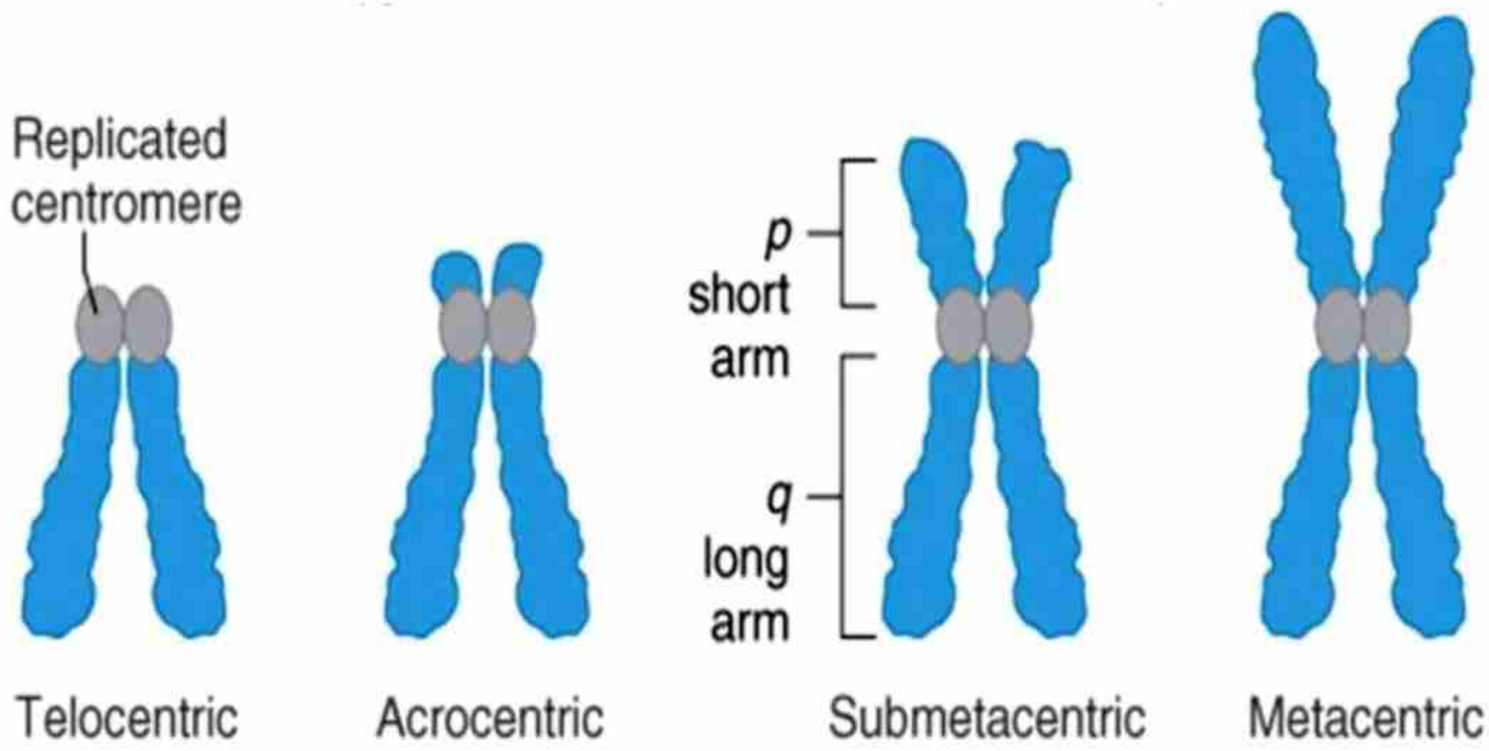


Fig.22.3. Types of Chromosomes

The secondary constriction may present which is also called **nuclear organizer**, develop from nucleolus during interphase. Due to secondary constriction, the end of chromosomes become knob like called **Satellite** which contain useless DNA i.e junk DNA called the terminated end of chromosome called **Telomeres**, require to prevent attachment of two chromosomes.

22.1.3.1 Chemical composition of chromosomes

Chromosomes are nucleoprotein made up of 40% DNA and 60% protein, a significant amount of RNA is also present due to site of RNA synthesis but RNA is not the constituent part of chromosome.

The highly condensed, double stranded, very long DNA is present in chromosome which is unbroken through the entire length of a chromosome, If the strands of DNA from a single set of human chromosome were laid out in a straight line it would be more than 7 feet (2 meter) long, this is too long to fit into a cell.

Now the question arises here how is the coiling of this long DNA fiber achieved, On examination of eukaryotic chromosome under electron microscope it was found like a string of beads. Where 200 nucleotide containing DNA duplex is coiled around an octamer of histone protein, which are small in size with high amount of basic amino acid i.e Arginine and Lysine. The octamer of histone form core which is highly positive in charge due to basic amino acids attracted by negatively charged DNA due to phosphate. The DNA wrapped around octamer and forms a unit called **nucleosome**. The nucleosome or histone core thus acts as magnetic forms that promote and guide the coiling of DNA. Further coiling occurs when the string of nucleosome wraps up into higher order called **Super coil**.

The organization of chromosome occurs in three stages.

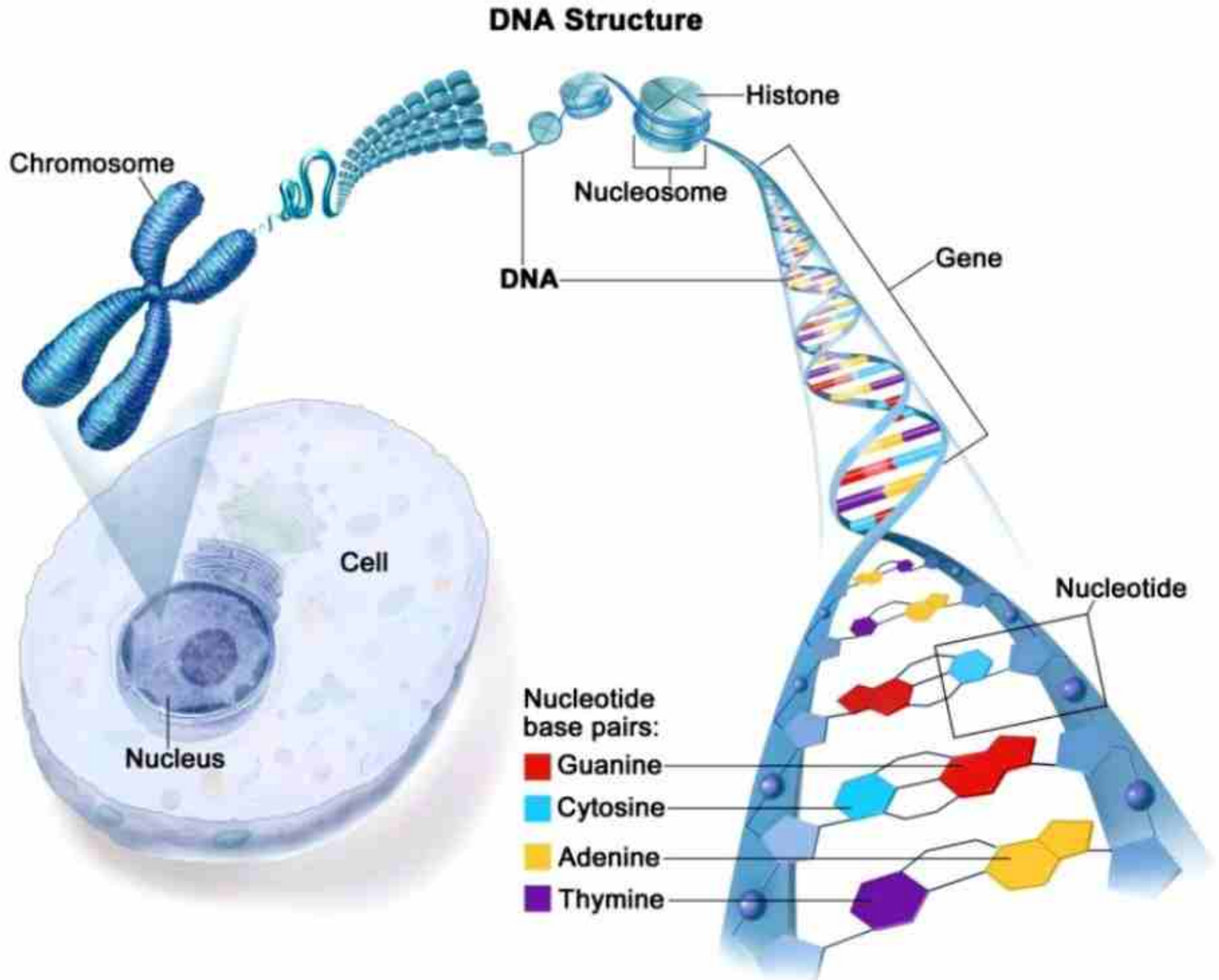


Fig.22.4. Ultra structure of Chromosome

i) Nucleosome string formation

During S-phase of cell-cycle, just after replication of DNA, negatively charged DNA coiled around a positively charge histone core which result in the formation of a complex called **nucleosome**. Each nucleosome is linked by a small segment of DNA called linker DNA 2nm thick. In this way a chain of bead appearance is formed called **Nucleosome string (10nm thick)**

ii) Chromatin fiber

Nucleosome string begins to coil again at its axis. In this way another thick fiber of 30nm is formed called **Chromatin fiber**. During G_2 phase of interphase chromatin fiber shows two regions i.e. **Heterochromatin** and **Euchromatin**. Heterochromatin is highly condensed and unexpressed while euchromatin in non-condensed it becomes condensed only during cell-division. The genes of euchromatin expressed and establish uniform chromatin fiber.

iii) Super coil formation to form chromatids

During prophase of cell-division chromatin fiber starts higher order of coiling from a super coiled structure of 300 nm. Immediately super coil developed into chromatids of 700 nm.

22.1.4 GENE AND GENE LOCUS

In 19th century Gregor John Mendel first time introduce the concept of gene which controls the expression of a character. He introduced it as "**factor**" and represented it by letter. In Biology a **gene** (Gr: genos meaning generation of birth or gender) is a basic unit of hereditary. Twenty years later in 1909, William Johansen introduced the term "**gene**" and 1906 geneticist **William Bateson** and **Eduard Strasburger** used the term "**Pangene**" for fundamental physical and functional unit of hereditary.

Now a day the gene is a small part of DNA which has information to synthesize specific polypeptide chain which work as enzyme to metabolize a specific reaction in a living organism. It means physically a gene is made up of nucleotide sequences.

Previously we have discussed chromosomal theory of inheritance according to it the genes are located at chromosomes. Each gene is located at its fixed position at particular chromosome.

This position of gene on chromosome is called **"gene locus"** (Pl: loci) we already know that both parents of an organism donated one set of chromosome so each cell usually contain two sets of chromosomes (Diploid cells). In this way each cell contain pairs of chromosomes, each pair contain maternal and paternal chromosomes if these chromosomes are morphologically similar and have same gene loci called **homologous chromosome**, if they are morphologically different chromosome and have different gene loci called **heterologous chromosome**. At homologous chromosome the gene of a trait at particular locus may be similar or different e.g. the gene of skin colour is located at same gene locus on both chromosomes. It may be of black colour on both or it may be of different colour i.e. black or white, this alternative form of a gene for a trait located at same gene locus called **alleles**. Mendel found two alleles for each traits. Mendel observed seven traits in *Pisum* plants and found two alternative forms in each trait. For example his length of *Pisum* plant trait had two alternative forms i.e. tall and dwarf both are controlled by different genes. These alternative forms located at same gene locus on homologous chromosomes are called allele. Now it is found that many traits have number of alternative forms, not only two like Mendelian traits.

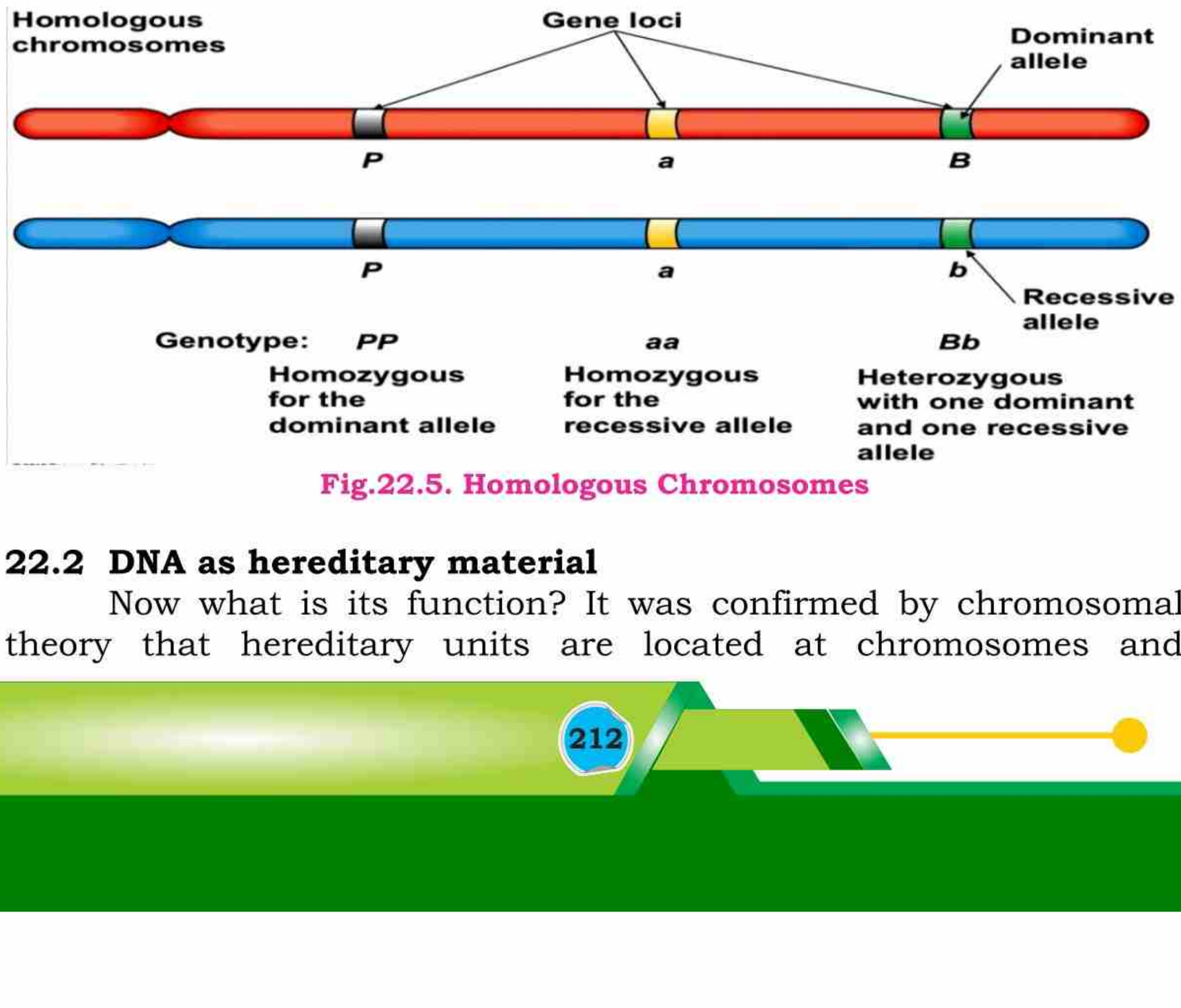


Fig.22.5. Homologous Chromosomes

22.2 DNA as hereditary material

Now what is its function? It was confirmed by chromosomal theory that hereditary units are located at chromosomes and

transformed through chromosomes from one generation to other. Whereas chemically chromosomes are made up of only DNA and protein. So question arises here which of the molecules work as heredity material or both combinely works as hereditary units. A series of experimental work had conducted by different scientists to reveal this mystery. In the beginning Fredrick Griffith had some success.

22.2.1 Evidence of DNA as hereditary material

Streptococcus pneumonia, a bacterium cause pneumonia found in two strands i.e. capsulated smooth form (S-type) and non-capsulate (R-type) S-type virulent while R-type are non-virulent both are genetically variable.

Fredrick Griffith designed some experiment, during the course of experiments. He injected R-type in laboratory mice and observed no ill effect on them whereas the injection of S-type proved fatal for mice. It was also observed that if both strains are heated, both killed at high temperature.

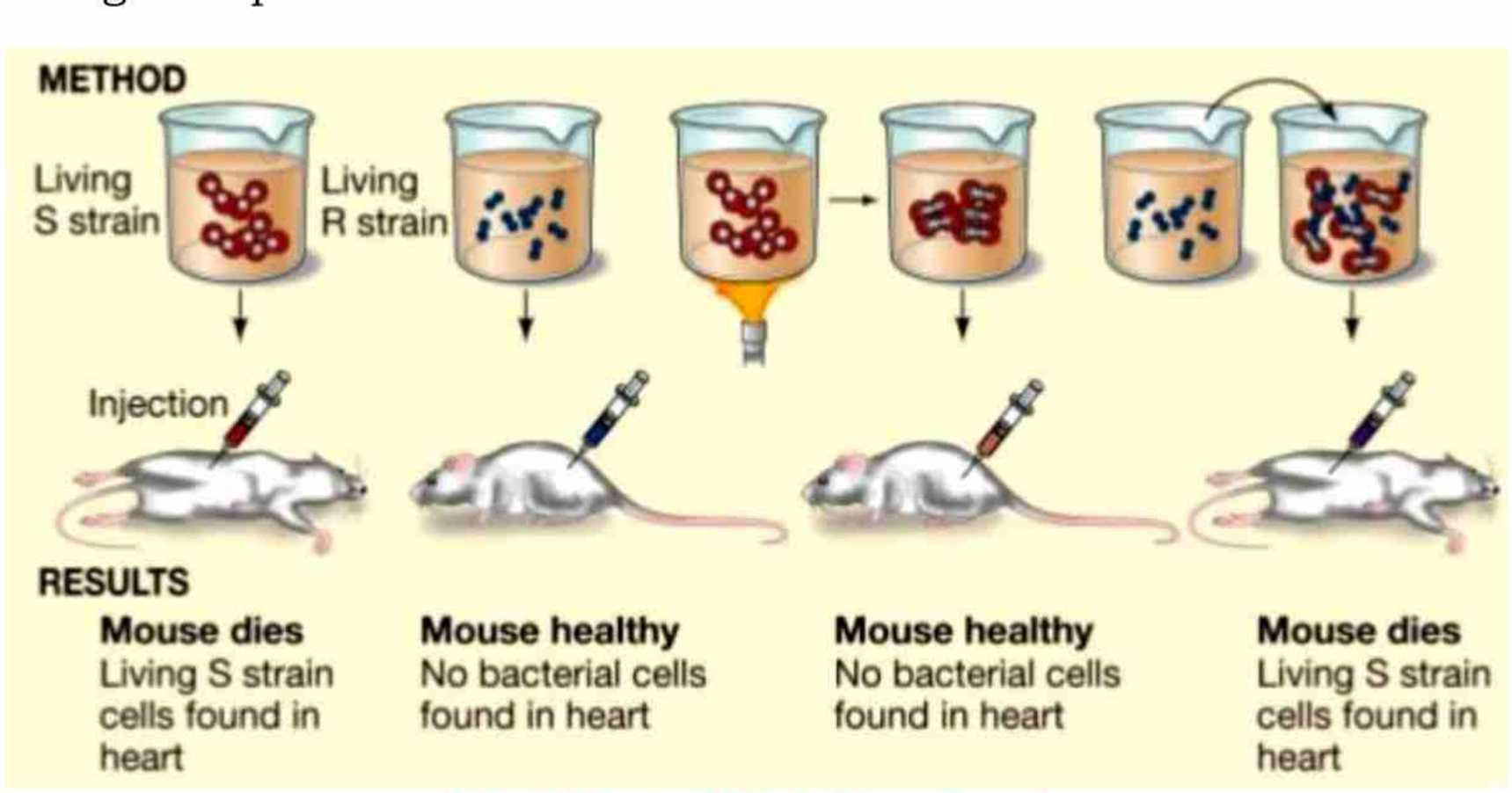


Fig.22.6. Griffith's Experiment

When heat killed S-type injected to nice no ill effect were observed on mice so it was concluded that alive R-type and heat

killed S-type had no ill effects on mice. He designed some more experiments and found unexpected results. He found when live R-type were injected to mice and heat killed S-type injected to same mice, high mortality of mice were observed. These experiment, were conducted in 1928, at that time he has no satisfactory explanation of these results. It was thought that heat killed S-type somehow become alive in the mice, but it was unacceptable. It was concluded that R-type become S-type when they come in contact with heat killed S-type. The phenomenon in which heat killed S-type could have hereditary effect on R-type is called **Transformation**.

Nearby 16 years later in 1944, Avery, MacLeod, and McCarty discovered and identify the transforming material of Griffith. They tested reaction of heat killed bacteria for their transforming ability and found out that it was not RNA or various proteins but only DNA that possessed transforming property. If the enzyme deoxyribonuclease that hydrolyses DNA was added to the heat killed S-type bacteria, the transforming property was lost. Therefore it has become clear beyond any doubt that DNA must be the genetic material.

22.2.2 Hershey and Chase

Alfred Hershey and **Martha Chase** in 1952 performed experiments on bacteriophage after findings of Avery and co-workers. They chose bacteriophage as experimental material because the composition of chromosome and bacteriophage are similar both are made up of DNA and proteins. During lytic life cycle bacteriophage produce so many new phages but at that time no one knew that which of the molecule of phage work as hereditary material so Hershey and Chase developed experiments to find out the hereditary material of Bacteriophage.

During their experiment they radio labeled DNA of bacteriophage with $\mathbf{P^{32}}$ and its protein coat with $\mathbf{S^{35}}$. The labeled viruses were permitted to attack the bacteria. The new phages which were coming out from host contain only P^{32} not S^{35}, the S^{35} was found in medium on the basis of these result it was cleared that only

P^{32} containing DNA entered in host are directed to produce new phages. It showed that the DNA worked as hereditary material.

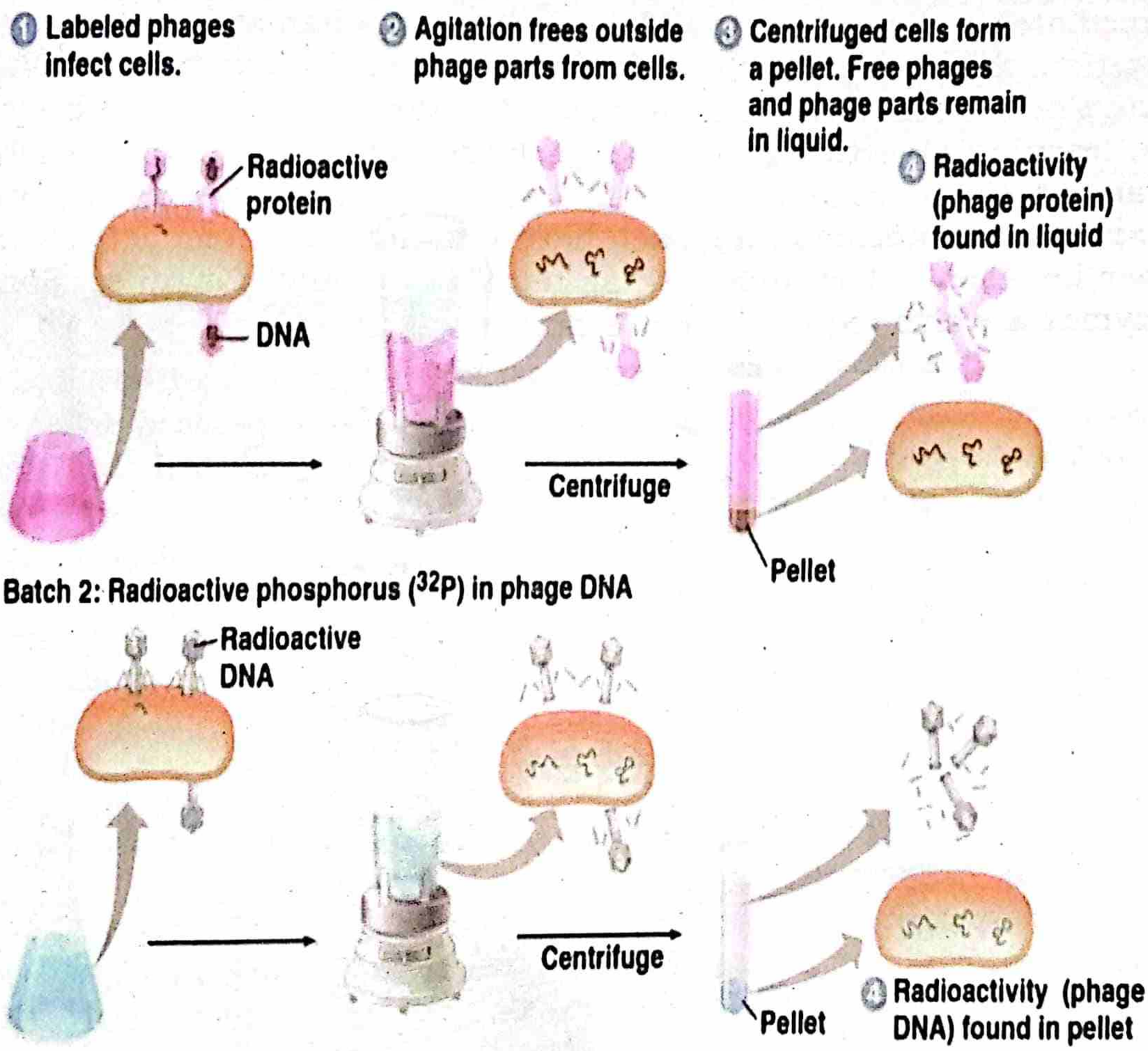


Fig.22.7. Hershey and Chase experiment

22.3 DNA REPLICAITON

The Watson and Crick Model of DNA suggest that DNA is double helix where specific pairing of nitrogenous bases occurs. They also understood the functional significance of base-pairing rules. They ended their classic paper with this statement "It has not escaped our notice that the specific pairing we have postulated immediately suggests possible copying mechanism for genetic material, this exact copying of DNA is called duplication of DNA, occurs before cell-division in S-Phase of interphase during cell-cycle. The learning objective here is to visualize how a cell copies a DNA strands to form another DNA by following base-pairing rules. The two strands are complementary, each have information to reconstruct the other i.e. each old strand work as template (mould) for other. Some enzymes are also required for this process.

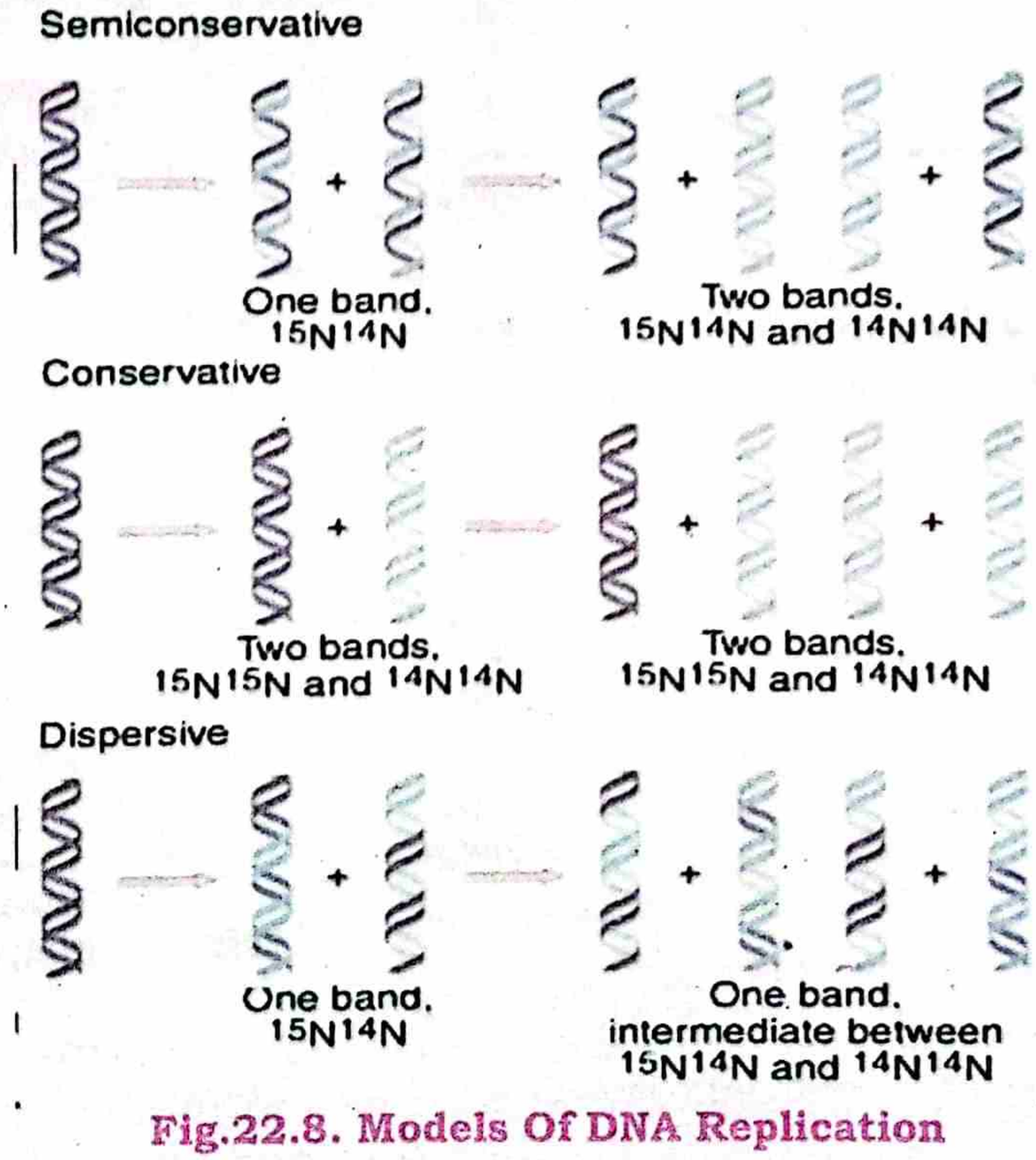


Fig.22.8. Models Of DNA Replication

22.3.1 Models of DNA Replication

The Mechanism of DNA replication was not clear. To understand this mechanism three models were proposed, these were (i) Conservative, (ii) Semi conservative, (iii) Disperssive model.

(i) Conservative Model: According to this model, the parental double helix remains intact i.e. conserved and the new molecule is formed entirely from scratch (all new copy).

(ii) Semi Conservative Model: According to this model, the two strands of parential DNA molecule separate, and each function as template for the synthesis of new complementary strands. It means the two daughter molecules formed as a result of replication, each contains one parental (old) and one newly formed DNA strand. It means some part of parental DNA is conserved.

(iii) Disperssive Model: In this model, all four strands of DNA after replication have mixture of old and new DNA.

22.3.2 Replication of DNA is Semi Conservative

The process of DNA replication suggested by Watson and Crick model is called semi conservative process because after one round of replication, the original duplex is not conserved, instead, each strand of the duplex become part of the other duplex. This prediction of Watson – Crick model was tested in 1958 by Mathew Meselson and Frank Stahl of the California Institute of Technology.

They grew bacteria for several generations in a medium containing heavy isotopes of Nitrogen (N^{15}). In this way the DNA of bacteria were, eventually denser than. Normal (N^{14}). They then transfered the growing cells to a new medium containing lighter isotope of Nitrogen (N^{14}) and harvested the DNA at various intervals.

At first, the bacteria grow in N^{15} produce all DNA contained N^{15}, but the bacteria grow in N^{14} manufactured DNA with only N^{14} in their DNA. After one round of DNA replication this bacteria which transferred from N^{15} to N^{14}, the density of the bacterial DNA has decreased to value intermediate between all light isotope and all heavy isotopes DNA. After another round of replication, two density classes were observed, one intermediate and other light isotopes, corresponding to DNA that include none of the heavy isotope. These results indicated that after one round of replication each daughter DNA duplex possessed one of the labeled heavy strand of parent molecule. When this hybrid duplex replicated, it contributed one heavy strand to form another hybrid duplex and one light strand to

form a lighter duplex, Meselson and Stahl's experiment thus clearly confirmed production of the Watson and Crick model that DNA replicate in a semi conservative manner.

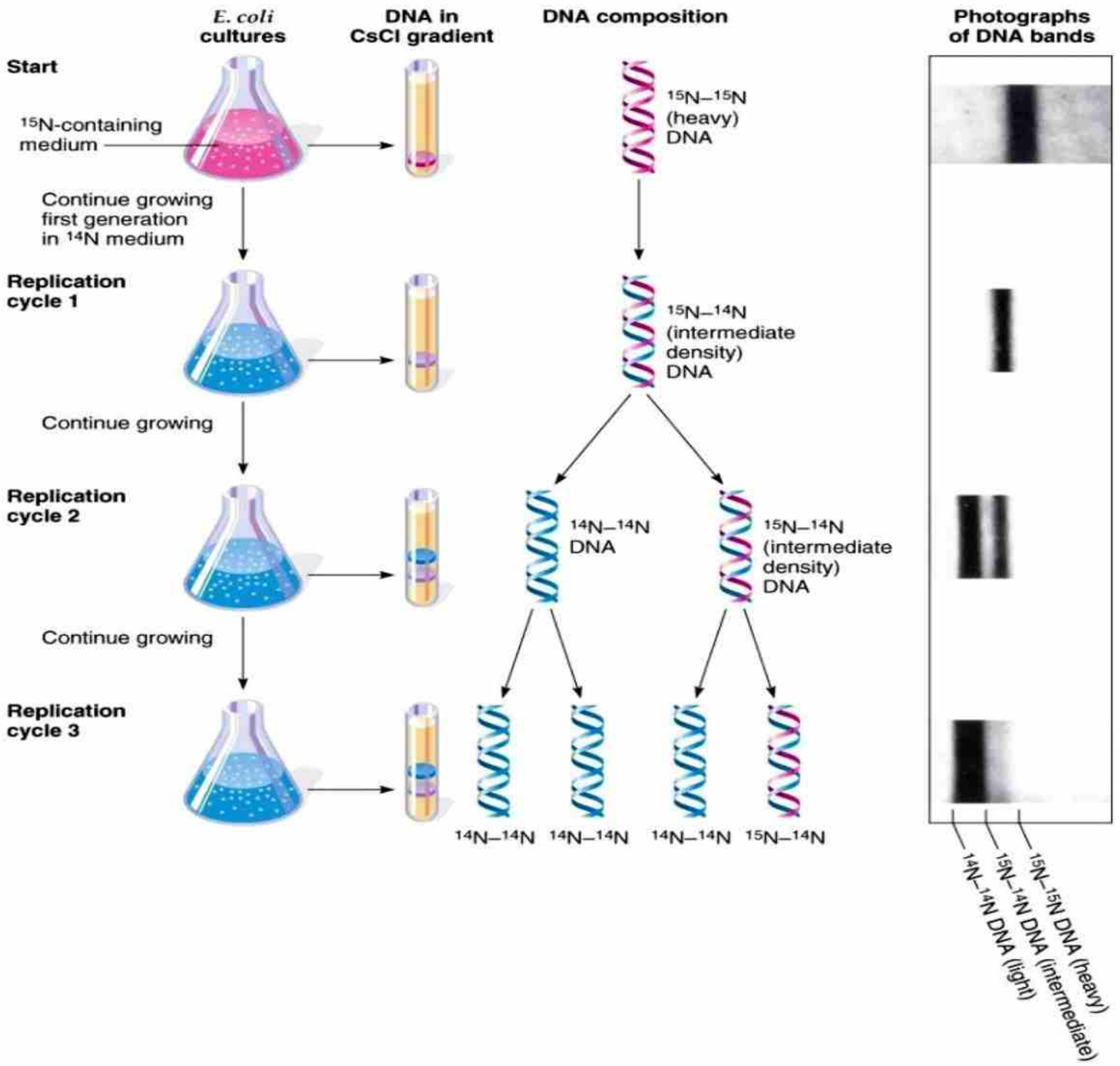


Fig.22.9. Meselson and Sthal Experiment

22.3.3 Process Of DNA Replication

The copying of DNA is remarkable in its speed and accuracy, more than a dozen enzymes and protein participate in DNA replication with number of nucleotides. The basic step of replication in prokaryote and eukaryote seems to be similar with minor

differences. We can divide this mechanism in following steps for our understanding.

(a) Origin of Replication:

The replication of DNA molecules starts at specific site called **origin of replication**. In prokaryotes a single origin site having a specific sequence of nucleotides. In eukaryotes each chromosomal DNA has hundreds and thousands of Origin of replications".

The enzyme **helicase** recognize these origin sites and open the turn of DNA duplex by breaking H-bonds present between complementary base pairs. In this way two strands of DNA are separated. Another enzyme **DNA gyrase** also works little ahead the DNA helicase to facilitate in unwinding of DNA duplex by reducing the tension created during unwinding process. As a result the complementary strands of DNA duplex gradually separate from each other which form a bubble like structure called **replication bubble**. A protein also work to prevent the re-binding of complementary strand of replication bubble, this protein is called **single stranded binding proteins (SSB)**. Both of these stranded DNA work as template for new strand of DNA. The fork like shape is formed by two separated strands of DNA called **replication fork**.

(b) Elongation of New Strands:

The phase of replication where daughter strands are formed, this elongation of new DNA strands at replication fork is catalyzed by enzymes called **DNA polymerases**. Three types of DNA polymerases are found with the name of DNA polymerase I, II and III. They perform different functions during this elongation phase. The elongation only takes place from 3' end of replication fork strand. Thus a new DNA strand can elongate only in the direction of 5' $\rightarrow$ 3'. Along one template strand, DNA polymerase synthesizes a continuous DNA strand by elongating the DNA in 5' $\rightarrow$ 3' direction called **leading strand**. To elongate other new strand of DNA polymerase work along the template away from the replication fork, and synthesize a short segment of DNA. As the bubble widen another short segment of this strand is formed this strand is synthesized in small segments these segments are called **Okazaki fragments**. Each

segment contains 100 to 200 nucleotides in eukaryotic cell. These segments are joined together by an enzyme called **DNA ligase** to form a simple DNA strand. This strand called **lagging strand**.

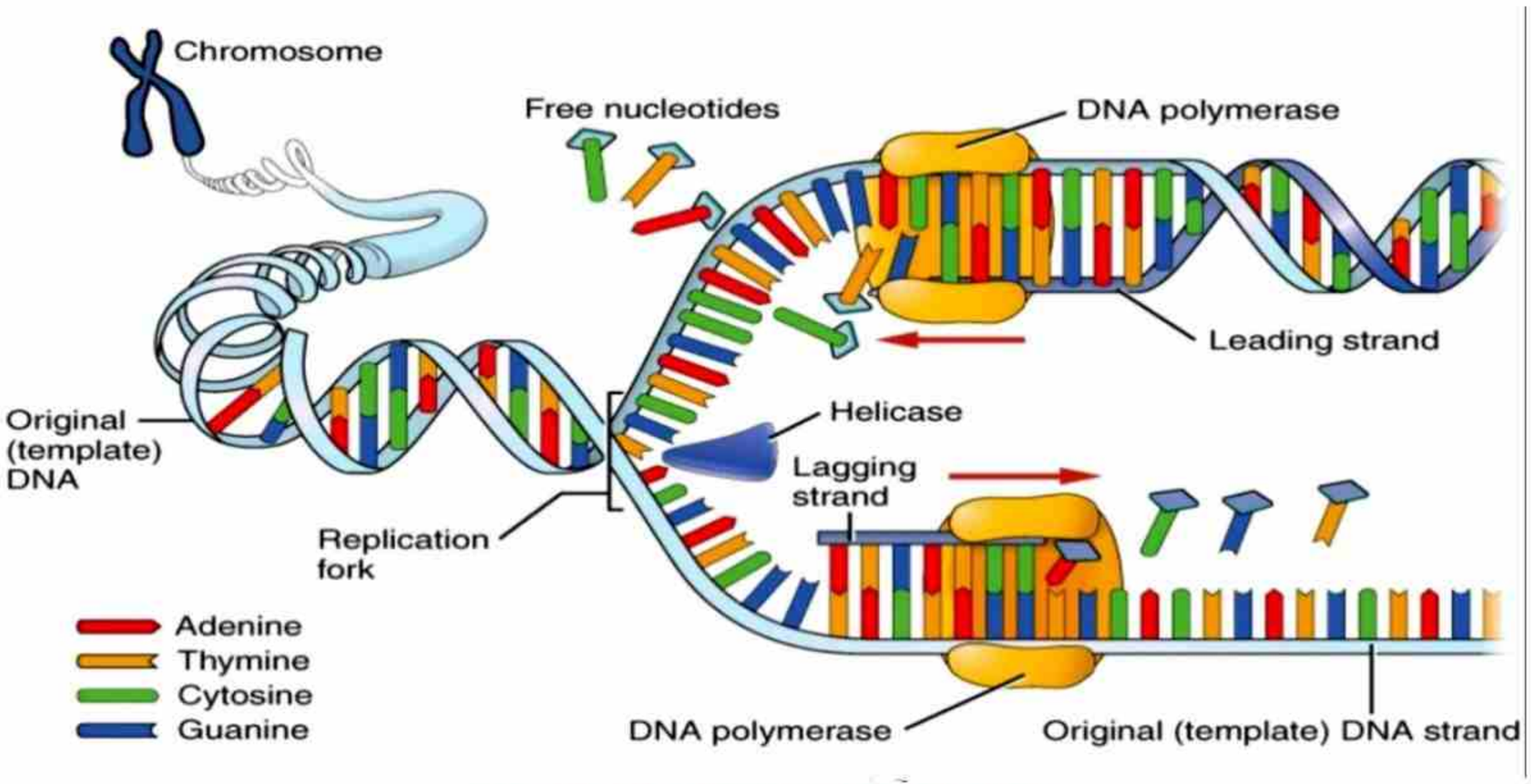


Fig.22.10. Replication of DNA

(c) Priming DNA Synthesis:

The formation of new strands is called **elongation**, takes place by an enzyme called DNA polymerase. The DNA polymerase cannot work in the absence of nucleotide already present on template strand. So the nucleotide must be added to the end of already existing chain called **primer**. The primer is a short piece of RNA, which is about 10 nucleotide long in eukaryotes only one primer, is required for polymerase to begin synthesis of new DNA. The enzyme is also required to join RNA nucleotide to make primer called **primase**.

(d) Types of DNA Polymerase and their Functions:

As we discussed earlier that there are 3 types of DNA polymerase, they play different roles during replication of DNA.

(i) DNA Polymerase-I: It performs the function of replacement of RNA primer by DNA nucleotide during termination phase.

(ii) DNA Polymerase-II: It performs the function of proof-reading, also perform the repairing of DNA damages throughout the lifetime.

(iii) DNA Polymerase-III: Main enzyme of replication which perform elongation and formation of new daughter strand.

(e) Termination:

Before termination one of the type of DNA polymerase performs proof reading during this process, it removes wrong nucleotide if it is added mistakenly. During termination phase replacement of primer by DNA nucleotide and joining of Okazaki fragment in lagging strand occur.

The primer nucleotides are removed and DNA nucleotides are replaced by DNA polymerase-I. It performs dual function i.e. exonuclease and polymerase. The joining of Okazaki fragment takes place by DNA ligase enzyme so a continuous strand DNA in synthesized.

STEPS AND ENZYMES INVOLVE IN REPLICATION

DNA Helicase & single strand binding protein

↓

Replication Fork (Double helix unwind provide single strand DNA template)

Synthesis of leading strand primase	Synthesis of lagging strand (primase)
↓	↓
Priming DNA polymerase-III	Priming for okazaki fragments (DNA polymeras III)
↓	↓
Elongation DNA polymerase-I	Elogation of fragments DNA (polymerase-III)
↓	↓
Removal of primer and replacement of DNA nucleotide (polymerase-I)	Removal of RNA primer and replacement of DNA nuclear (polymerase-I)
	↓
	Joining of Okazaki fragment (Ligase)

22.3.4. Replication of DNA as a Process of Stability and Variability

Replication of DNA is a process where stability and consistency of genetic information is maintained generation after generation or parents to off spring. This stability and high degree of accuracy is provided by hydrogen bonding between base pairs of old and newly formed DNA strands. Although DNA replication is not perfect at 1st step, it is due to speed of replication i.e. 50 to 500 nucleotides per second due to spontaneous chemical flip-flop in the base, DNA polymerase III occasionally incorporate incorrectly matched bases i.e. one mistake for every 10,000 bases pairs.

In mammalian cells, the completed DNA strand contains only about one mistake for every billion base pairs. For this rear inaccuracy the DNA, replication has a proof reading system which we have discussed earlier. This proof reading takes place by another DNA polymerase-II. The one-way directionality of DNA, each daughter strand as it structure allows the polymerase-II enzyme to recognize the parental strand, running in one direction as the right-stuff and to correct any mismatches by changing the daughter strand, which run in the other direction.

During prophase each chromosomes contain two chromatids, each chromatid contain double helix of DNA, which is consist of one original (parental) and one new strand (daughter), this new strand of DNA is an exact copy of parental strand, when these sister chromatids separate at anaphase and reach to daughter cells, each received an exact copy of parental chromosomes. Thus, if there is no spontaneous mistake in whole process, the constancy and stability of genetic information will be maintain from cell to cell and from parents to off spring.

Genetic variability can also occur due to change in DNA sequences which is termed as **mutation**. A mutation is a permanent alteration to a DNA sequence. *Denovo* change occur where there is an error occur during replication that is not corrected by DNA repair enzyme during proof reading, when this error is copied by DNA replication fixed in the DNA and transferred to next generation. DNA replication timings is also associated with variation in genome. The late replicating DNA is one of the factors which is generally more prone to mutation.

Another cause of mistake in replication is the presence of "Tautomeric forms" (interconvertable structural isomers) of nitrogenous bases. After publishing of Watson and Crick model of DNA, biologists thought that most replication errors were caused by shifting of H-group from one atom to another in nitrogenous bases, the changed form of nitrogenous base is called **tautomeric form** or **shift**. Both purine and pyrimidine bases in DNA exist in different chemical forms or tautomers, where protons occupy different position as shown in Fig.22.11 Biologist believed that if and when a nucleotide base into its rare tautomeric form it result in base-pair mismatching as shown in Fig. 22.12.

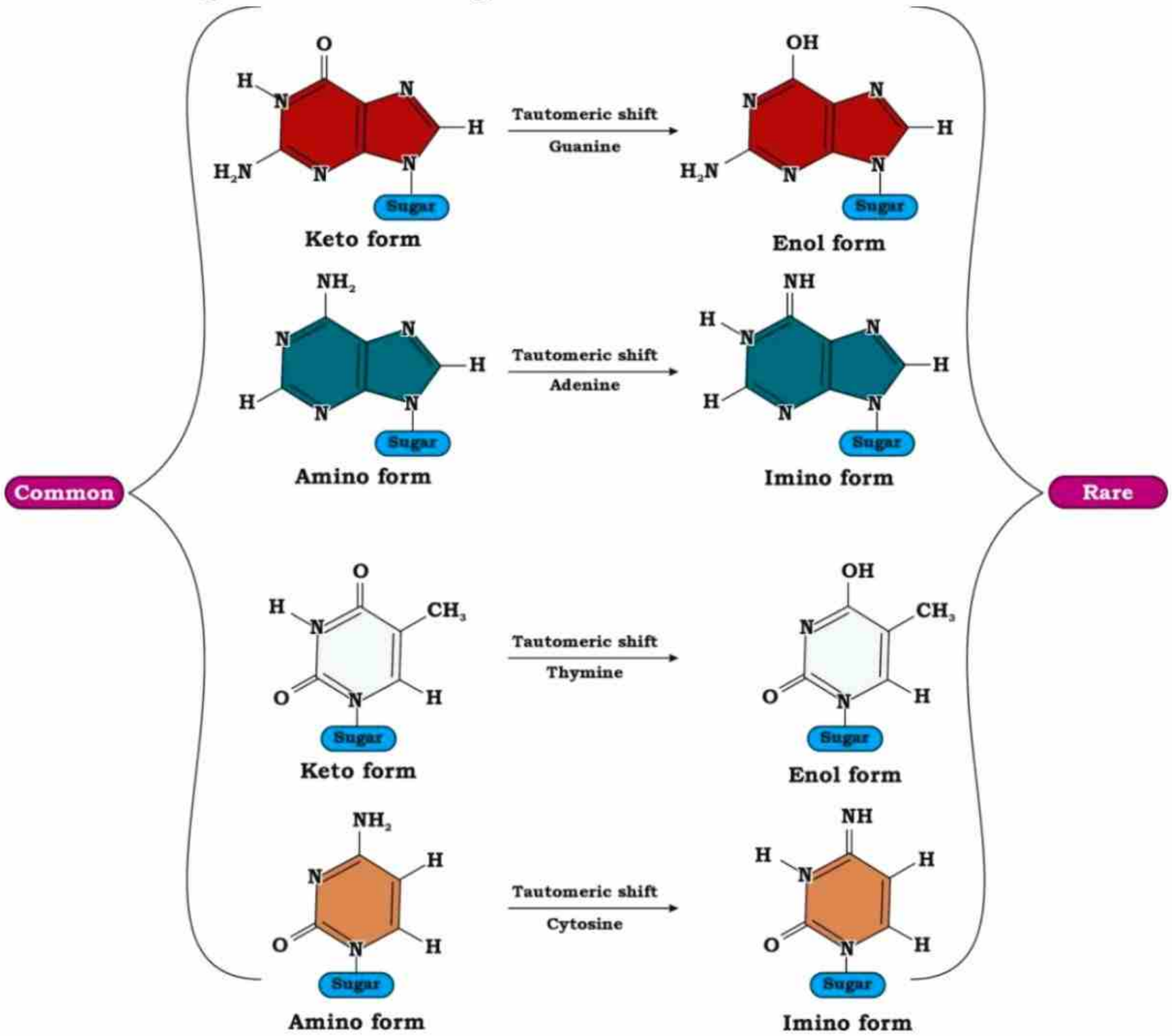


Fig. 22.11 Common and Rare Nucleotide forms

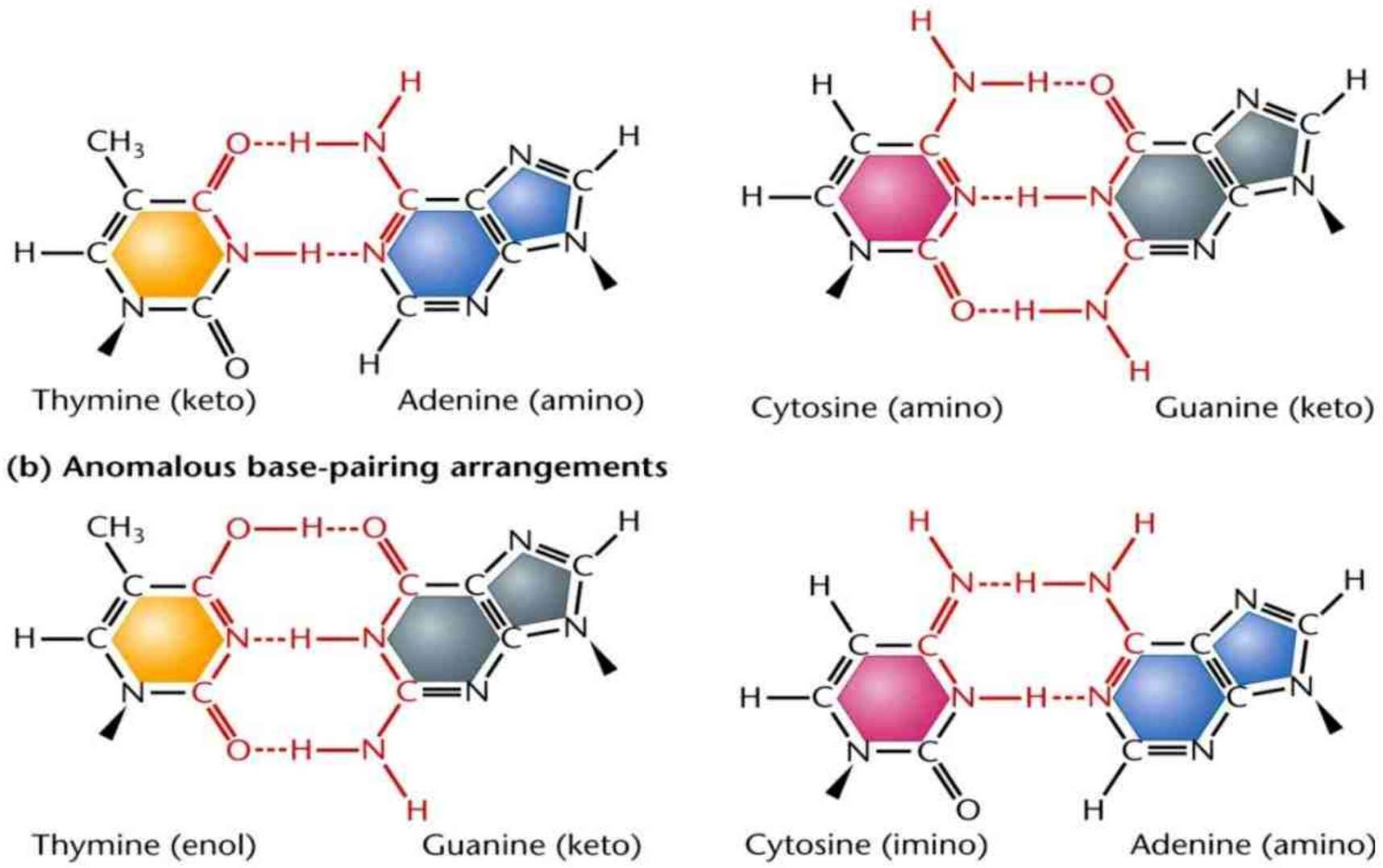


Fig. 22.12 Standard and Anomalous Base-pairing

22.4 GENE EXPRESSION

It is a process where information present on gene is used to produce a functional product required by living organism for their existence called gene expression.

22.4.1 Central Dogma of Gene Expressions

In English central dogma means basic principle but in biology especially in molecular biology it means that how genetic information flows from DNA to RNA for synthesizing a polypeptide chain or protein which works as an enzyme. This genetic information flows from DNA to proteins, in two steps.

(i) Transcription:

It is the process where information present on a specific part of DNA is copied in a complementary form to form mRNA. This mRNA carries information of DNA (gene) in coded form from nucleus to the ribosomes present in the cytoplasm to synthesize a particular

polypeptide chain. Although all three types of RNA are transcribed from DNA.

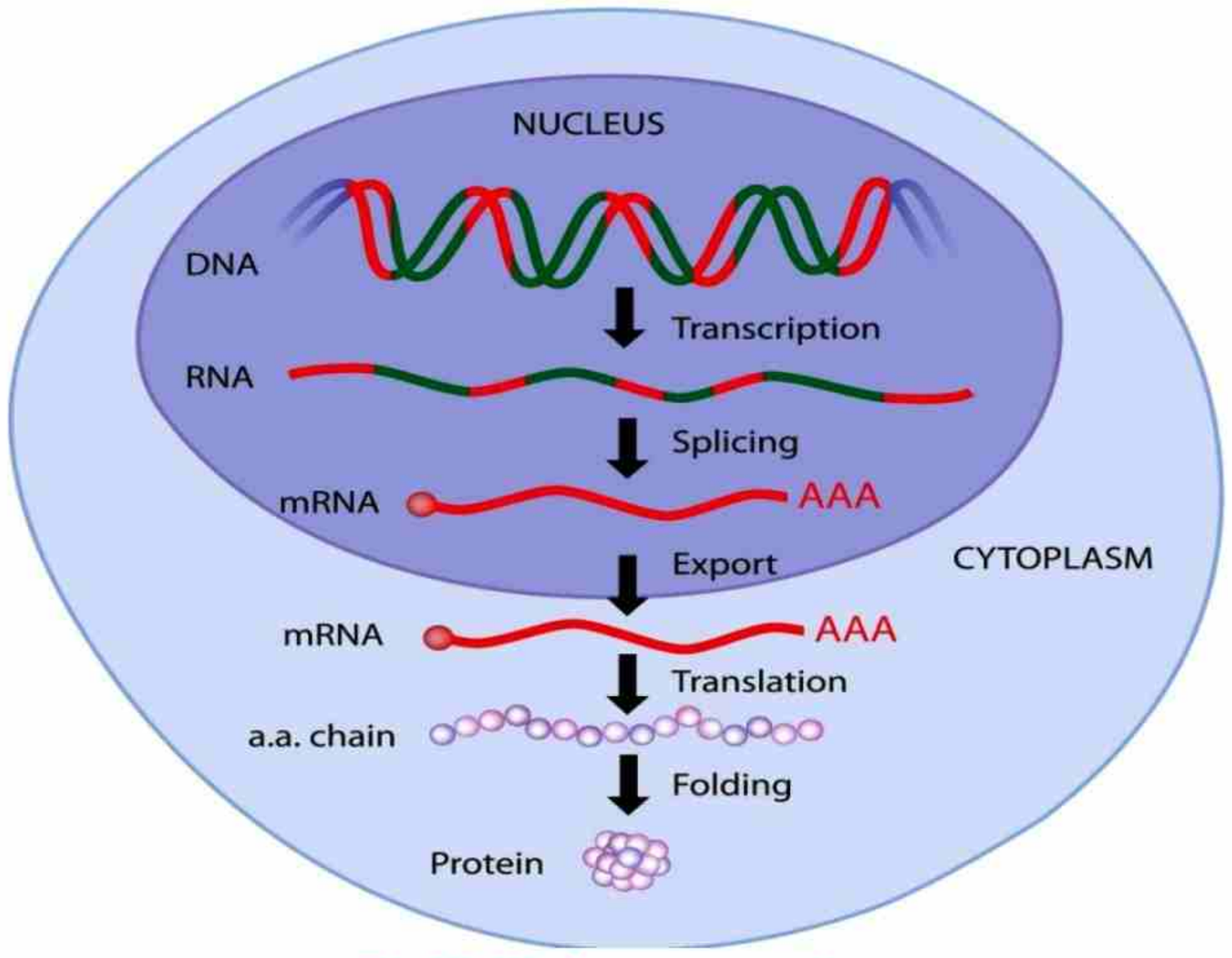
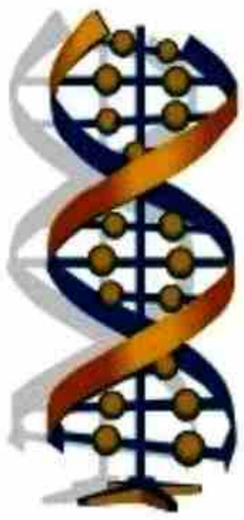


Fig.22.13. Gene expression

(ii) Translation:

The process of converting information on mRNA (messenger RNA) into correct sequences of amino acids to synthesize a protein with the help of tRNA (transfer RNA) and rRNA (ribosomal RNA)



Transcription

DNA
Protein (Enzyme)

mRNA — Translation
tRNA — Amino Acids
rRNA — Peptide Linkage

Transcription
Translation

22.4.2 Gene and Genetic Code

According to work of Archibald Garrod, William Batson, George Beadle and Edward Tatum which they concluded from their experimental work that Gene is a segment of DNA that contains the information needed to synthesize a protein. In other words gene is the basic functional unit of hereditary material. It is also observed that different genes have different base sequences and different proteins have different amino acid sequences. Therefore the sequences of nitrogenous bases in a gene work as the codes for the sequence of amino acids in proteins. Now questions arises how these bases work as codes for amino acids?

Genetic Codes

In the above discussion we have repeatedly used the word **genetic codes**. Now question arises what is genetic code? The genetic code is the set of rules used to store the genetic information within DNA for a particular protein synthesis. We know that when we want to send a secrete message or want to load pre-paid amount in our cell phone. This mobile card strip has combination of numbers on it. When we send correct sequence to the company they load specific amount which is asked for. In the same manner information about a specific protein synthesis is stored in DNA in the form of specific sequence of their nitrogenous bases. It gives three information to cell.

i) The amino acids required for this protein.

ii) The sequence of these amino acids in this protein.

iii) The length of polypeptide chain of this protein.

When this information of **Gene** in the form of genetic codes transcribed in the form of mRNA they work for amino acids during translation. The DNA and RNA both are made up of four types of nucleotides, but there are twenty (20) different amino acids which forms protein so these bases cannot serve as one to one codes for amino acids. If these sequence will be very short i.e. just consist of only two bases codes for an amino acid then there will be 16 possible combinations of bases. This is not enough either for 20 amino acids.

If three base pairs combination will be used, gives 64 combinations which is more than enough, the biologist hypothesized that each amino acid is coded by triplet of base pairs. In 1961 Francis Crick and three co-workers demonstrated that this hypothesis is correct.

	U		C		A		G		
U	UUU	Phenylalanine (Phe)	UCU	Serine (Ser)	UAU	Tyrosine (Tyr)	UGU	Cysteine (Cys)	U
	UUC		UCC		UAC		UGC		C
	UUA	Leucine (Leu)	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG	Stop	UGG	Tryptophan (Trp)	G
C	CUU	Leucine (Leu)	CCU	Proline (Pro)	CAU	Histidine (His)	CGU	Arginine (Arg)	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	Glutamine (Gln)	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	Isoleucine (Ile)	ACU	Threonine (Thr)	AAU	Asparagine (Asn)	AGU	Serine (Ser)	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	Lysine (Lys)	AGA	Arginine (Arg)	A
	AUG	Methionine (Met)	ACG		AAG		AGG		G
G	GUU	Valine (Val)	GCU	Alanine (Ala)	GAU	Aspartic acid (Asp)	GGU	Glycine (Gly)	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	Glutamic acid (Glu)	GGA		A
	GUG		GCG		GAG		GGG		G

Fig.22.14. Genetic Codes

Further experimental work verified that the mRNA has information for amino acid in the form of their triplet base pair these triplets of bases on mRNA which encode one amino acids are called CODONS. Now there are 64 codons, some works as starts CODON and some of them work as stop CODON. Research showed that the CODON AUG signals "starts" while three codons work as stop codon i.e. UAG, UAA, UGA the genetic codes and codon does not need and does not have punctuation, between them have. It is like "**FATMANHITTHECAR**"

Table 22.1 The CODON for each amino acid

GENETIC CODES AT DNA

Gene	T	A	G	T	A	G	T	A	G	T	A	G	T	A	G	T	A	G	T	A	G
mRNA	A	U	C	A	U	C	A	U	C	A	U	C	A	U	C	A	U	C	A	U	C
	Codon			Codon			Codon			Codon			Codon			Codon			Codon		

AUC is the CODON for Isoleucine. If a polypeptide chain will be synthesized if will contain seven isoleucine amino acids in it. As we have discussed that there are 61 codons to code 20 amino acids, with these 61 codons some are stop codons. All 61 codons are used in the genetic coding for amino acid. The genetic code is thus highly redundant or degenerate. We can say that, a single amino acid may be specified by several CODONS. e.g. six different codons are present for a single amino acid i.e. Arginine. Even the code is redundant, but it is not ambiguous. Each codon specifies one and only one amino acid.

Gene (DNA)	G	C	A	G	C	G	G	C	T	G	C	C	T	C	T	T	C	C	G	C	G	T	C	T
mRNA	C	G	U	C	G	C	C	G	A	C	G	G	A	G	A	A	G	G	C	G	C	A	G	A
Polypeptide chain	Arg			Arg			Arg			Arg			Arg			Arg			Arg			Arg		

Mechanism of Transcription

'The process of copying over, 'in the form of RNA' is called Transcription, where a particular part of DNA is copying in a form of RNA.

Transcription has two limitations:

(i) Only a selected part i.e. gene part of DNA is transcribed e.g cell of hair follicle transcribe only the DNA which contain genetic information about keratin protein synthesis.

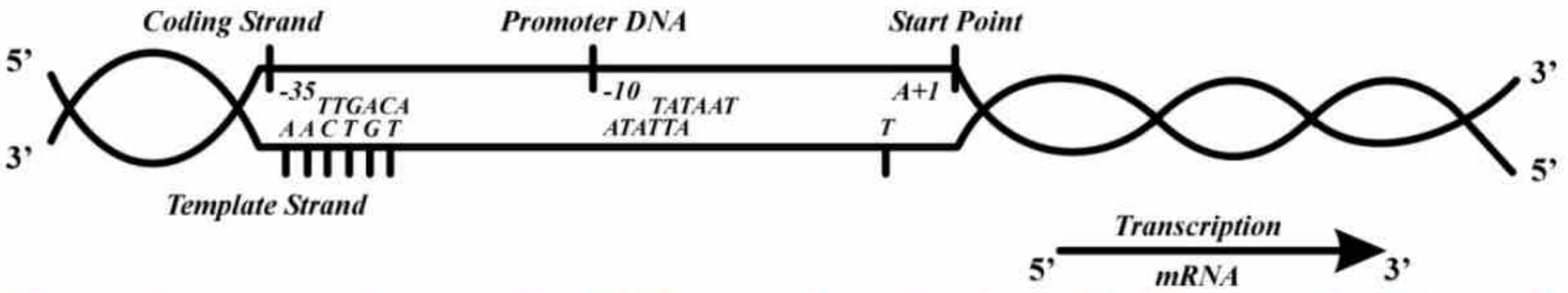
(ii) It occurs only when it is required, it copies only one strand of DNA because the two strands of DNA are complementary not identical. If the sequence of bases on the strand present at one strands that form keratin protein will not found on other strand.

The DNA strand which contains exact information about functional protein is called template strand or **anti-sense** strand. The opposite strand is called **coding strand** or the **sense strand**. The RNA polymerase enzyme synthesizes RNA from 5` → 3` direction. Keeping in view the above limitations we can divide the process of transcription in following three steps.

(i) Initiation (ii) Elongation (iii) Termination

(i) Initiation: It is the first step of transcription where attachment of RNA polymerase at the start of gene occurs. This start region of gene is called **Promoter region**. The promoter region of a gene is a

short sequence of DNA bases located just in the 3' direction. The RNA polymerase recognizes the base sequences of promoter at the beginning of gene and bind with it. In prokaryotic DNA three promoters are TATAAT or -10 sequence and TTGACA or -35 sequences. In eukaryotic DNA TATA (TATA box) or -25 sequences and CAAT (CAAT box) or -70 sequence.



Promoter region of DNA and start of Transcription in Prokaryotes

(ii) Elongation: After binding of RNA polymerase at promoter site, it forces to unzip DNA double helix from beginning of gene, moves along the template strand of the DNA in the 3` → 5` direction. The free ribonucleotides present in the nucleus now utilize to make and elongate RNA polymer. In this way during elongation a single strand of RNA which is complementary to template strand of DNA is synthesized. The same base pairing rules are used during transcription for RNA synthesis as for DNA replication except that Uracil is paired with adenine instead of thymine as follows.

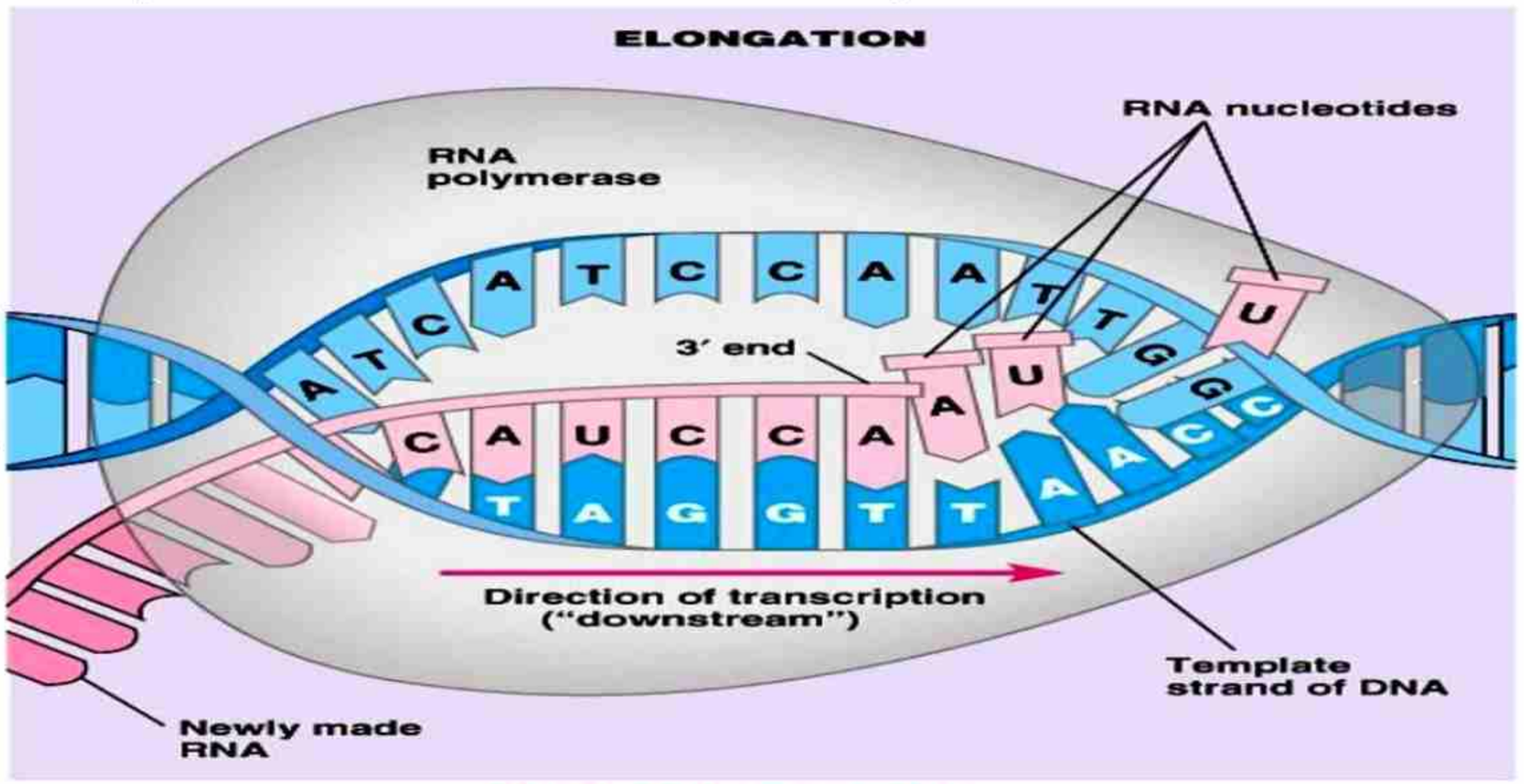


Fig.22.15.Transcription

The RNA polymerase adds RNA nucleotides to the growing RNA strand according to rule of base-pairing but this pairing does not persist. After about 10 nucleotides have been added to the growing RNA chain, the beginning of the RNA molecule separate from DNA. In this way long 'tail' drift away from DNA. The elongation remains continue till the RNA polymerase reaches the terminator region of the gene.

(iii) Termination: As we have discussed that the RNA polymerase adds RNA nucleotides when RNA polymerase continues along the template strand until it reaches the termination region (signal). Termination region is a sequence of DNA bases trigger two events. Firstly, the RNA molecule completely separate from both the DNA and the RNA polymerase. Secondly, the RNA polymerase detach from template strand of the DNA. These events terminate transcription. The terminator region consists of a series of GC base pair followed by AT base pairs. The mRNA region transcribed by this region form a loop like structure called **GC hairpin** followed by a small tail of polynucleotides. The GC hairpin causes the RNA polymerase to stop the synthesis of RNA.

Modification in mRNA before Translation

The mRNA before translation is modified in eukaryotes for next stage i.e. translation. In prokaryotic cell transcription and translation both takes place in cytoplasm therefore it does not require any modification in mRNA of prokaryotic cell. The genome of eukaryotic DNA contains coding and non-coding regions within the genes. The coding regions are called **Exons** while the non-coding regions of gene are called **Introns**. During transcription both exon and intron regions are transcribed but before translation the transcription of intron region are spliced, new mRNA contain transcripts of exon region only. The removal of introns and the conversion of long primary mRNA into short secondary RNA without intron called RNA **splicing**. It requires

a small nuclear ribonucleoprotein (sn RNPS) i.e. a RNA protein complex RNA splicing takes place in following three steps.

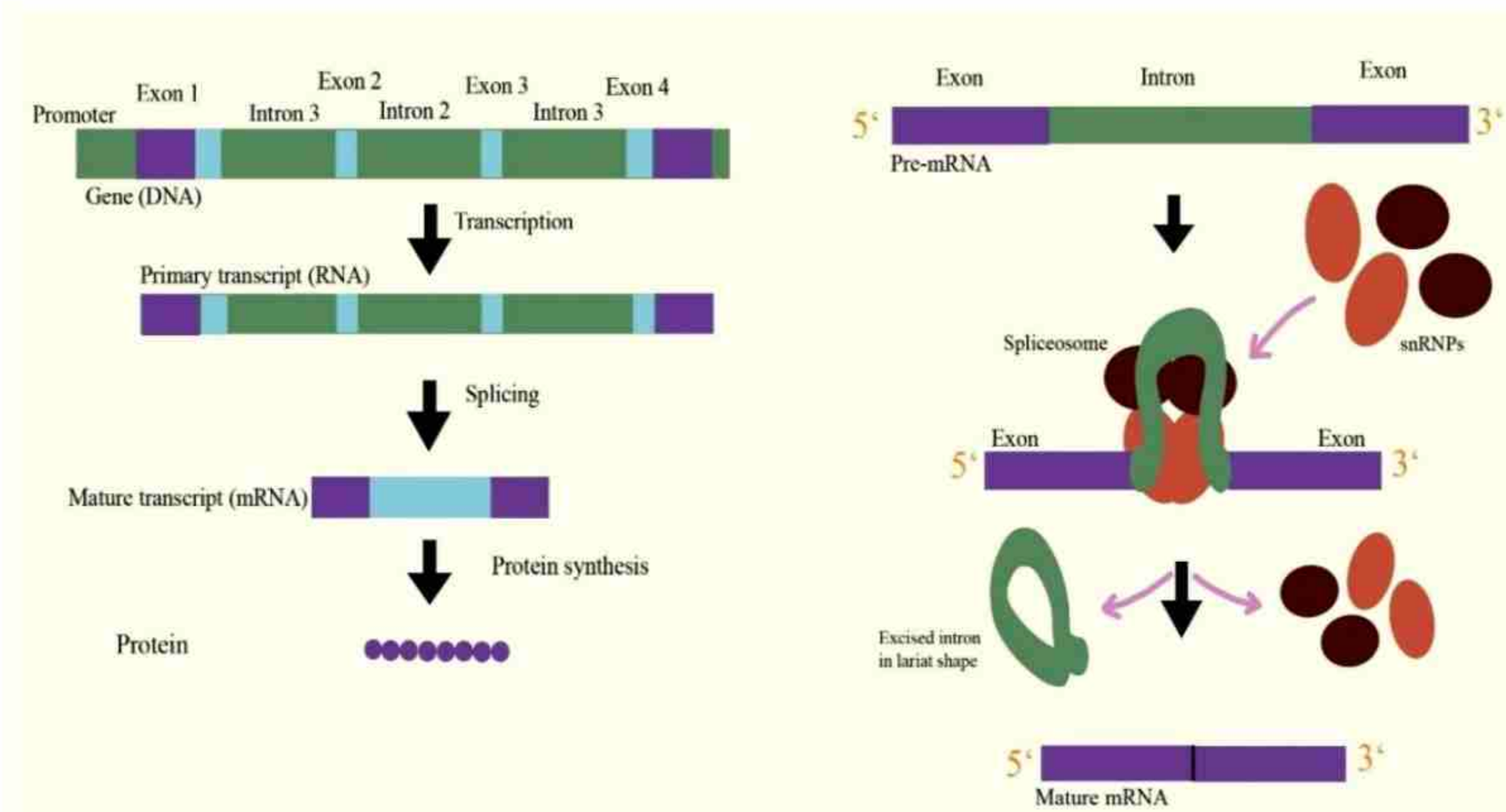


Fig.22.16.RNA splicing

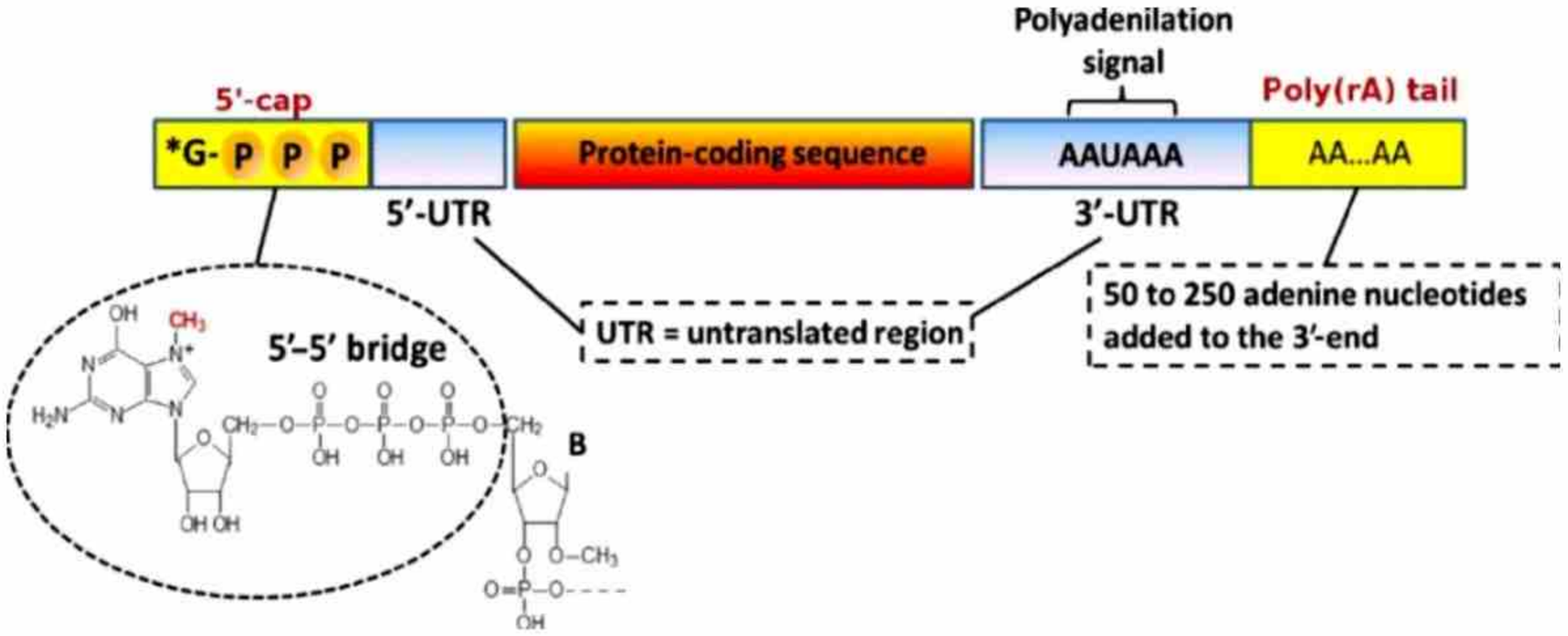
Step – I: A group of sn RNPS's bind to intron of primary mRNA.

Step – II: Binding sn RNPS's at intron, which cause folding of mRNA which bring the 5' and 3' ends of the intron closer, which make a loop in this way, the end of the exon also come closer, and ultimately join each other.

Step – III: The intron removed and splice site connect to make a mRNA, the intron are also used in other process. The sn RNA detach from the intron and reused.

Another modification occurs in primary mRNA that a cap and tail are added to it. It is to protect mRNA from degradation and remain stable. The cap is in the form of 7 – methyl GTP linked 5' → 5' with the first nucleotide. On the opposite end of mRNA a small chain of adenine nucleotide called **poly A tail** is attached i.e. at 3' end.

These changes protect secondary mRNA from degrading enzyme like nuclease and phosphate.



22.17. 7-methyl GTP and Poly A

Translation

It is the second phase of gene expression or protein synthesis. During translation the secondary mRNA attaches with ribosome and decoded its information with the help of tRNA. The tRNA contains anticodon which translates CODON of mRNA and carries related amino acid to ribosome in sequential manner where rRNA bind and form peptide linkage to form polypeptide chain. For our convenience we can divide it in four phases. i.e. activation of amino acid, formation of initiation complex, elongation and termination.

(i) Activation of Amino Acids:

The cytoplasm of cell contains amino acids which are taken from digested food or synthesized in cell. These amino acids when bind with a particular tRNA is called activation of amino acid. As we know that tRNA has 4 sites at 3' end three unpaired nucleotide site called **amino acid site** is present, opposite to it five nucleotide containing site is called **anticodon site**, whereas out of them five nucleotide the middle three nucleotides work as **anticodon**. Another loop is called **activation site** where an enzyme **aminoacyl synthase** attach to activate this tRNA. A particular amino acid attach with its specific tRNA through this activating enzyme, one of which exists for each of the 20 amino acid.

(ii) Formation of Initiation Complex:

Translation require initiation complex. This initiation complex is a complex of ribosomal subunit mRNA and first aminoacyl tRNA complex. The first aminoacyl tRNA complex contains a modified **methionine**. The initiation complex formation is metabolized by an enzyme called **Initiation factor-I**. During this process 5' end of mRNA molecule also bind to the smaller sub-unit of ribosome with the help of another enzyme called **Initiation factor-II**. In the last of this initiation complex formation process, large sub-unit is placed on smaller sub-unit.

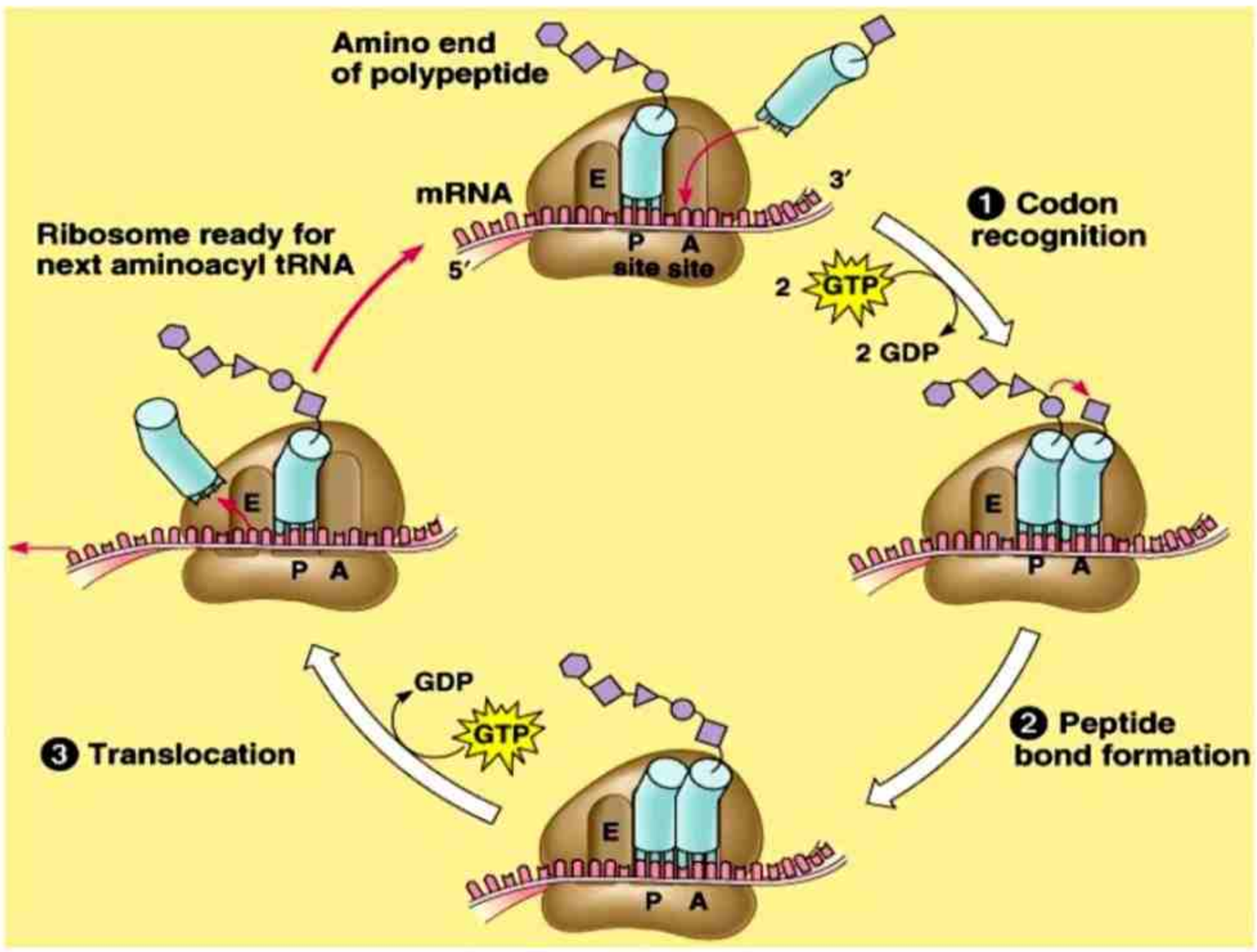


Fig.22.18.Translation

(iii) Elongation

The ribosome has 3 sites **P site**, i.e. peptidyl site, **A site** i.e. aminoacyl site and **E site** i.e. exit site, as shown in Fig. 22.18. Another tRNA with appropriate amino acid binds at next site i.e. A site. Its anticodon bearing aminoacyl tRNA complex bind with the help of an enzyme called the **elongation factor**. In the next step an enzyme peptidyl transferase released from P site, remove the amino acid from tRNA present on P site and bind to new amino acid present on A site by making peptide bond, It take place at the site on large

sub-unit called **catalytic site**. After it, ribosomal sub-unit slightly move along mRNA from 5' → 3' end so that the empty tRNA shift to E-site, while the tRNA at A site shifted to P-site and a new CODON is exposed at A site the movement of ribosome called **translocation**, another tRNA with its amino acid reached at A site to bind with its anticodon. In the same way the process is repeated again and again to form a poly peptide chain until the ribosome is reached to stop codon at A site.

(iv) Termination

When the ribosome is reached at stop codon which is also called **non-sense CODON**, this codon do not bind with any tRNA so no elongation takes place further. Now the polypeptide chain is released from ribosome by separating ribosomal sub-units from mRNA.

Difference between protein synthesis in Prokaryotic and Eukaryotic

Prokaryotes	***Eukaryotes***
➢ Prokaryotes have ribosomes in cytosol so protein synthesize completely takes place in cytosol.	➢ Ribosomes of Eukaryotes are attached with RER so it mainly occurs in R.E.R.
➢ The prokaryotic gene (DNA) found in cytosol so transcription and translation both occur in cytosol.	➢ The Eukaryotic genes are found in nucleus, so transcription occurs in nucleus and translation occurs in cytoplasm.
➢ The prokaryotic gene does not contain intron.	➢ Eukaryotic gene contain exon and intron region.
➢ In prokaryotes the gene promoter-I for transcription are TATAAT or -10. sequence and TTGACA -35 sequences.	➢ In Eukaryotes DNA gene promoters are TATA or -25 sequences and CAAT or -70 sequences.
➢ The ribosomes are 70s for translation initial amino acid is modified N-formyl methionine.	➢ The ribosomes are 80s for translation the initial amino acid is not modified i.e. methionine.
➢ In prokaryotes no cap and tail are formed with mRNA.	➢ In Eukaryotes the Cap of 7 – methyl GTP and poly-A tail is formed.

22.5 REGULATING GENE EXPRESSION

The cell requires protein in the form of enzymes for regulating its function, developing its structure and for its differentiation. Therefore all cells regulate synthesis of protein from information present on DNA. The process of turning ON or OFF a gene is called **Regulatory gene expression**. Each cell controls the gene expression according to its requirement i.e. when and how its genes are expressed. This control requires a mechanism which tells the cell when a gene is expressed and when it will be stopped i.e. this protein is no longer required by cell.

22.5.1 Importance of Regulating Gene Expression

The regulation of gene expression conserves energy and space. The process of gene expression requires enormous amount of energy so it is important to save energy. Therefore the gene only express at the time of its requirement. On the other hand DNA is present in the form of highly coiled form in the nucleus of cell. To express a gene this part of DNA should be unwind, only that part of DNA unwind where required gene is located, it save the space of cell.

In multicellular organisms, high degree of cellular differentiation occurs due to regulation of gene expression. All cells of multicellular organism contain same genome but cells do not express all genes present in them, only specific genes are expressed in particular type of cell by this regulation process.

The regulation of gene expression also regulate normal metabolism of an organisms by synthesizing proper activating and inhibiting factors at proper time. If this regulatory process of gene expression is disturbed, metabolic disorders and other genetical disorder take place. Like cancer, lysosomal disorder e.g. Liver perform a function of alcohol removal from blood stream, for this liver cells express gene of an enzyme called alcohol dehydrogenase. This enzyme breaks alcohol into non-toxic substance but the R.B.C cannot do it, so R.B.C keep this gene turned off. Similarly the liver cell cannot carry O_2 so they keep their genes turn off which synthesized hemoglobin protein.

Method of Gene Regulation

Regulation of gene expression takes place in two ways i.e. positive and negative regulation. The genes are expressed by specific protein called **activators** this type of regulation is called **positive gene regulation**. On the other hand the gene expression is suppressed by the presence of specific regulator protein, i.e. **repressor** this type of gene regulation is called **negative gene regulation**.

Unicellular living things regulate gene expression so that their metabolic and biosynthetic pathways change in response to changes in their environment. e.g. *E.coli* bacteria, growing in the presence of lactose, synthesize enzymes which allow lactose to be utilize as energy source, if lactose is replaced by another disaccharide then a different set of metabolic genes are expressed and the genes required for lactose metabolism are not regulated, so the genes of lactose are repressed.

Multicellular organisms have additional capacity to regulate gene expression so that many genes are expressed in specific tissues. The sequential activation of specific genes in different regions of the embryo drives the development of the embryo, the formation of the different tissues and cell types. In these cells DNA remains in nucleus, some of its regions (genes) transcribed into RNA which transported out of the nucleus into cytoplasm where ribosome translate it into protein.

The genes can regulate at all stages of gene expression. This regulation can be occur when DNA is uncoiled from nucleosome to bind with transcription factor i.e. epigenetic level or when RNA is transcribed i.e. transcriptional level or when it is transported to cytoplasm from nucleus i.e. Post transcriptional level or when mRNA is translated into protein i.e. translational level or after the protein has been synthesized i.e. Post translational level.

Regulatory element can operate. So that the product of one gene controls the activity of other gene. Some of which may themselves regulate other gene. Activation of one gene can initiate a cascade of regulatory event.

Role of Intron and Exon in Gene Expression

The eukaryotic genomes contain introns and exons while prokaryotic gene does not contain intron. During gene expression all introns are transcribed into RNA and replicated during replication process but introns do not participate in translation because before coming out from nucleus the introns regions are eliminated by spliceosome.

The total genomes contain 40% of intron on average. Now question arises here why introns are present in genome? The existence of introns in genome is a real mystery given the expensive energy cost for a cell to pay for copying the entire length of several introns in a gene and eliminates them at the exact position, controlled by big RNA and protein complex after transcription. Do introns are not totally junk? It has come to know that introns are not totally junk, these are crucial because protein variety is greatly enhanced by alternative splicing in which introns play important role. The alternate splicing is a controlled molecular mechanism for synthesizing multiple variant proteins from a single gene.

Introns also play important role in positive regulation of gene expression. It was found that without introns the protein products were significantly diminished. It was also found that some introns are designed to construct expression vectors for guaranteeing a high level of expression compared to genes without introns. Introns are involved in transcription, initiation and termination processes.

These processes require some sequence elements, in intron in correct order. Introns may be associated with mRNA transport or chromatin assembly. Intron also plays some indirect role. The first intron plays important role in transcription. It has been found that the first intron is the longest introns which work as the signal for the transcription. So many other roles of introns are going to be established day by day research in molecular biology.

22.6 MUTATION

There are so many ways to explain the terms mutation. The DNA is the genetic material which is responsible to store information of an organism and its inheritance faithfully to next generation. If it does not take place properly it is called **Mutation**. In a sense, mutation is the failure to store genetic information faithfully. In

Eukaryotes, DNA is present on chromosomes, so historically, the term mutation includes both chromosomal changes in their number and structure. The changes occur in the location of gene on chromosome and changes within a single gene also called mutation. We discussed all of these here under the title of heteroploidy, chromosomal aberration and gene mutation respectively.

22.6.1 Sources and Types of Mutation

The substances which cause mutation or responsible of mutation are called **mutagens**. The mutagens or mutagenic agents may be physical, chemical or biological.

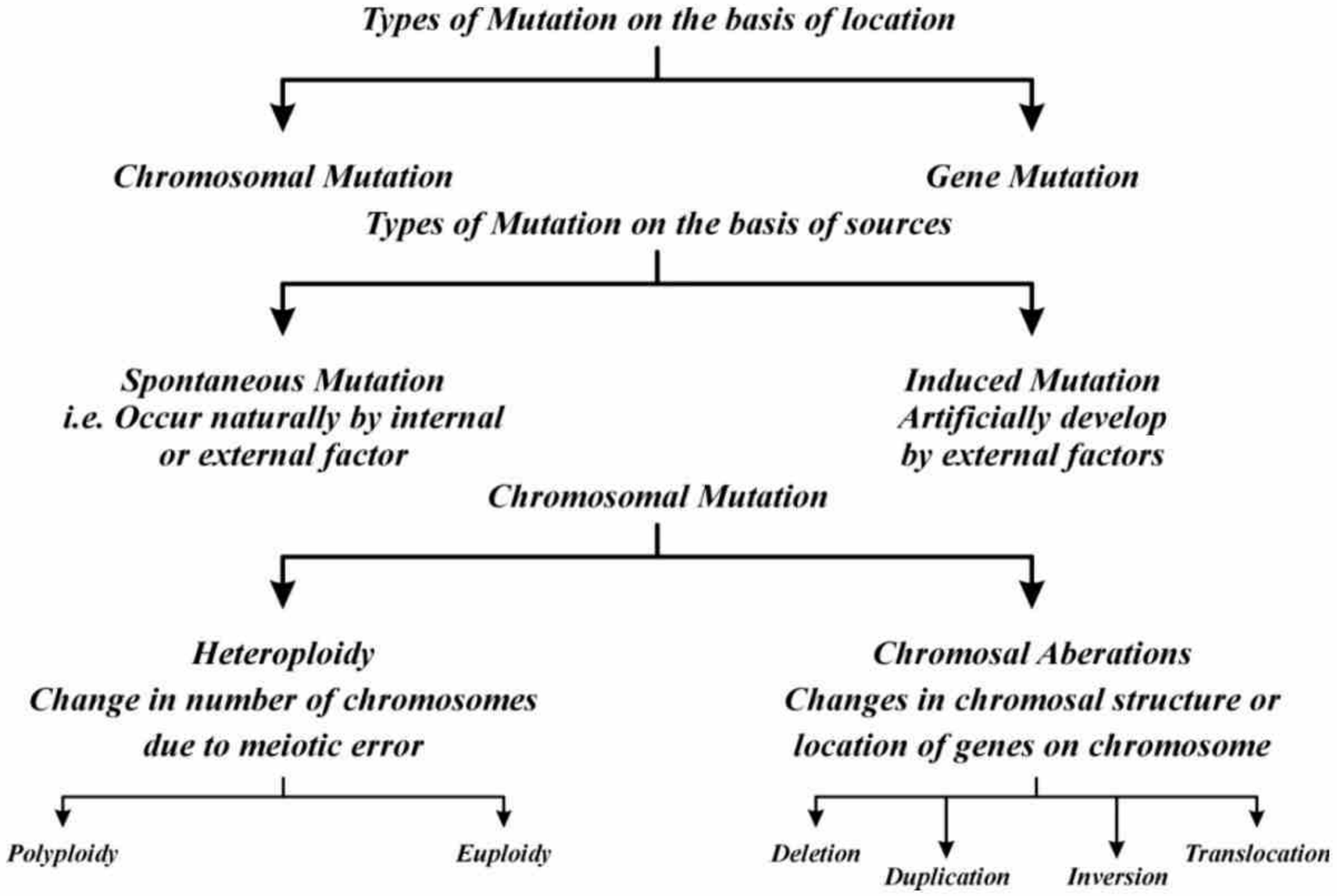
Physical Mutagens: These are the physical forces which are responsible to break any type of bond present in the DNA i.e. phosphodiester bond of DNA or bonds present in nitrogenous bases. These physical mutagen may be ionizing radiation like gamma (γ) rays, x-rays or other types of radiation like ultra violet radiation sometimes cosmic waves or ultrasonic waves, it may be high temperature.

Chemical Mutagens: A number of chemical compounds may alter the shape of DNA and its nucleotides, some of them are very similar to nitrogenous bases which can be replaced by original nitrogenous bases. The other chemicals may be environmental or industrial like Nitrous oxide, mustard gas, photochemical, or radioactive isotopes, free oxygen may work as mutagenic chemical.

Biological Mutagens: Some micro-organism and biochemical, which are produced during metabolism may work as mutagenic agent, sometime errors in normal physiological processes leads to mutation e.g. error in disjunction leads to heteroploidy or some viruses like HIV lead to skin cancer i.e. Kaposi's sarcoma.

Types of Mutations

The process of mutation is called mutagenesis, the organisms in which mutation occur called **mutant** and the organism where mutation does not occur or found in its original form called **wild type**. There are so many ways to classify the types of mutation.



22.6.3 Do Most Mutation are Harmful

It is generally considered by the people that changes in genetic material in any way is harmful for the living organisms this is not true completely, although in number of cases mutation is harmful but there are three types of mutation i.e. negative mutation, positive mutation and neutral mutation.

(i) Negative Mutation: It is the type of mutation which is harmful for living organisms and cause different types of abnormalities like, sickle cell anemia, Down's syndrome etc. These mutant genes are usually eliminated by natural selection from gene pool.

(ii) Positive Mutation: It is the type of mutation which produced better allele to produce more adaptable genes. These genes are selected repeatedly by natural selection. e.g. mutated gene of black skin colour, polyploidy, to produce different varieties within the same species of plants, genes of beaks and claws in birds etc.

(iii) Neutral Mutation: The some genes are mutated but do not leave any harmful or observable effects on phenotype. These genes inherit in normal pattern this type of mutation is called **neutral mutation**.

Mutation produces fitness to adapt in a specific environmental condition, which leads to evolution of organism. It explains the evolution of aquatic animals and plants to land habitat. The organisms which do not accumulate mutated genes became unable to survive on land. Nature only selects those which accumulate mutated genes, which were required to develop, characters for survival on land. Above discussion showed that the mutation is not only harmful process.

22.6.4 Chromosomal Mutation

As we have classified mutation in different groups, one of it is chromosomal mutation, i.e. any change in number and shape of chromosomes is called **chromosomal mutation**. It is further classified into two groups.

(i) Heteroploidy (ii) Chromosomal aberration

(i) Heteroploidy: Heteroploidy is the change in the number of chromosomes due to non-disjunction during **Diakinesis** of meiotic prophase-I. There are two types of heteroploidy (a) Polyploidy (b) Aneuploidy

Polyploidy: It is a type of heteroploidy, where a set of chromosomes may increase i.e. As a result of polyploidy triploid (3N) tetraploid (4N) etc organisms are produced. The polyploidy produce varieties within the species of on organism, especially in plants e.g. different varieties of wheat and rice are produced.

Aneuploidy: It is the type of chromosomal mutation where one or two chromosome increase or decrease in the karyotype of an organism i.e. monosomy where one chromosome decrease (2N – 1), Trisomy where are chromosome increases (2N +1). Some example of monosomy and Trisomy of human are given below.

(a) Down's Syndrome: It is a trisomic (2n+1) condition of autosomal chromosome number 21, found in both male and female of human beings.

Symptoms: Abnormal body and mental development, round face small head, skin flap at the back of neck, wide short hands with short fingers and long tongue.

Treatment: There is no treatment but continuous psychological counseling and some medicine required to reduce aggression of patient.

(b) Klinefelter's Syndrom: It is also a trisomic condition but it is a trisomy of sex-chromosome (44 + XXY).

Symptoms: It is a male disorder having feminine character i.e. less body and facial hairs, enlarged breast, long neck, wide hips, curved shoulder and thighs. The male has small testicles, voices are not deep as male and infertile male.

Treatment: Testosterone therapy is the only solution but it does not help in reducing infertility.

(c) Turner's Syndrome: It is monosomic (2n-1) condition of sex-chromosome in female i.e. (44 + X).

Symptoms: The effected individuals are infertile female with short height, webbed neck, low hairline at the back of neck, edema in the hands and feet, low IQ level.

Treatment: There is no specific treatment, only growth hormone therapy is administered in this case. Female hormonal therapy also helps in the development of puberty characters and reproductive cycle. It is started at the age of 12 or 13 years.

(ii) Chromosomal Aberration: The type of chromosomal mutation where change in chromosome structure or position of genes on chromosome occur. There are four types of chromosomal aberration

(A) DELETION OR DEFICIENCY: A chromosome breaks from one or more than one places so some of its portion is lost. The remaining part in the karyotype is left this loss in genetic material is called Deletion or deficiency. As a result the chromosomal size reduces.

(b) Duplication: Processes where a broken part of a chromosome attaches with its homologous chromosome, the genes of same characters become duplicated and the size of chromosome increases.

(c) Translocation: A process where a broken part of a chromosome attaches with its non-homologous chromosome is called **Translocation**. As a result of translocation the size of that chromosome also increases but genes do not duplicate as present in duplication.

(d) Inversion: It is a type of structural variation in chromosome where arrangement of gene loci inverted due to 180° turn of chromosome.

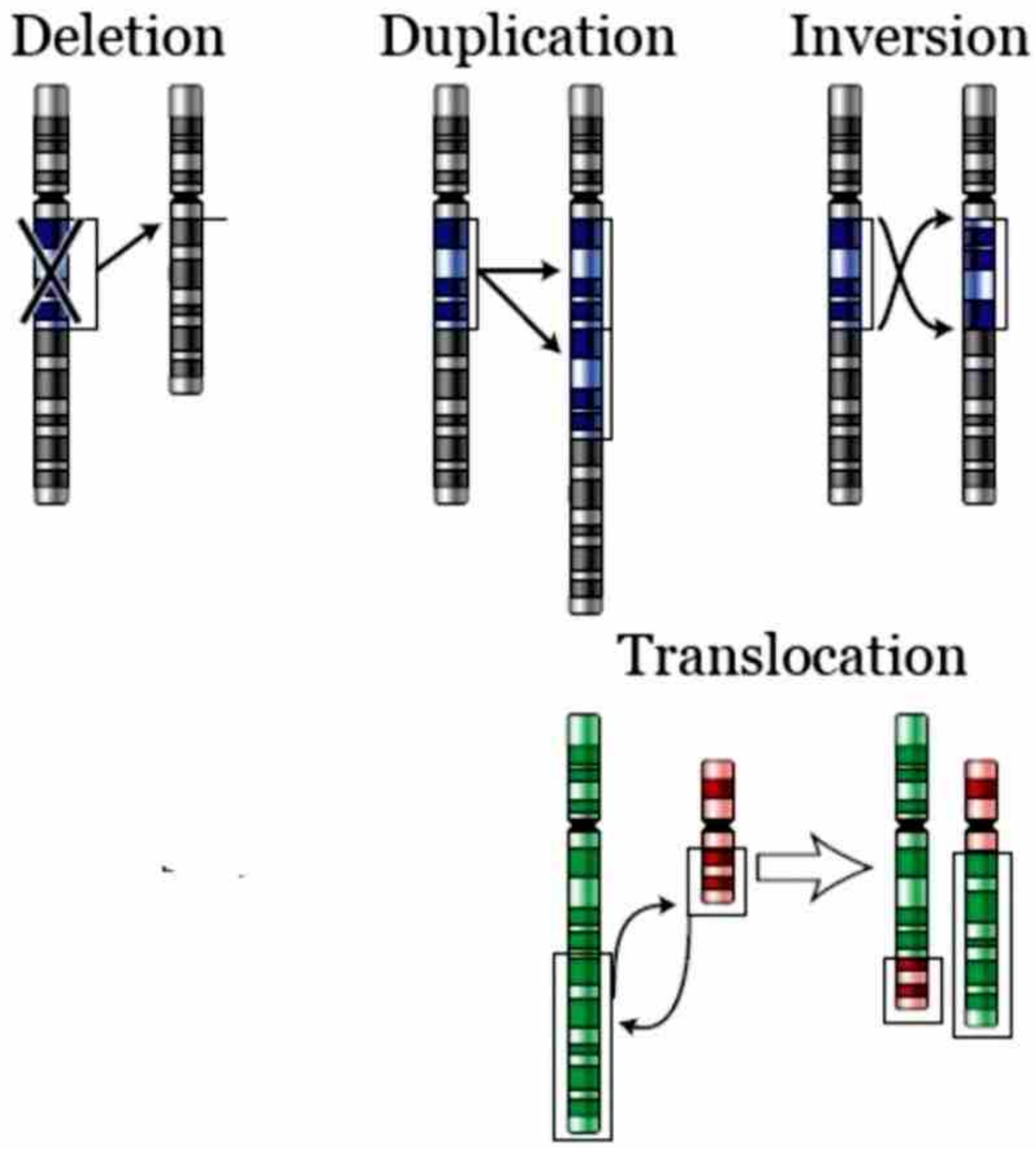


Fig.22.18. Chromosomal Aberration

22.6.5 Gene Mutation

Mutation occurs in a specific gene at specific genetic code(s) or the location of a gene change on chromosome, this type of mutation is called **Gene Mutation**.

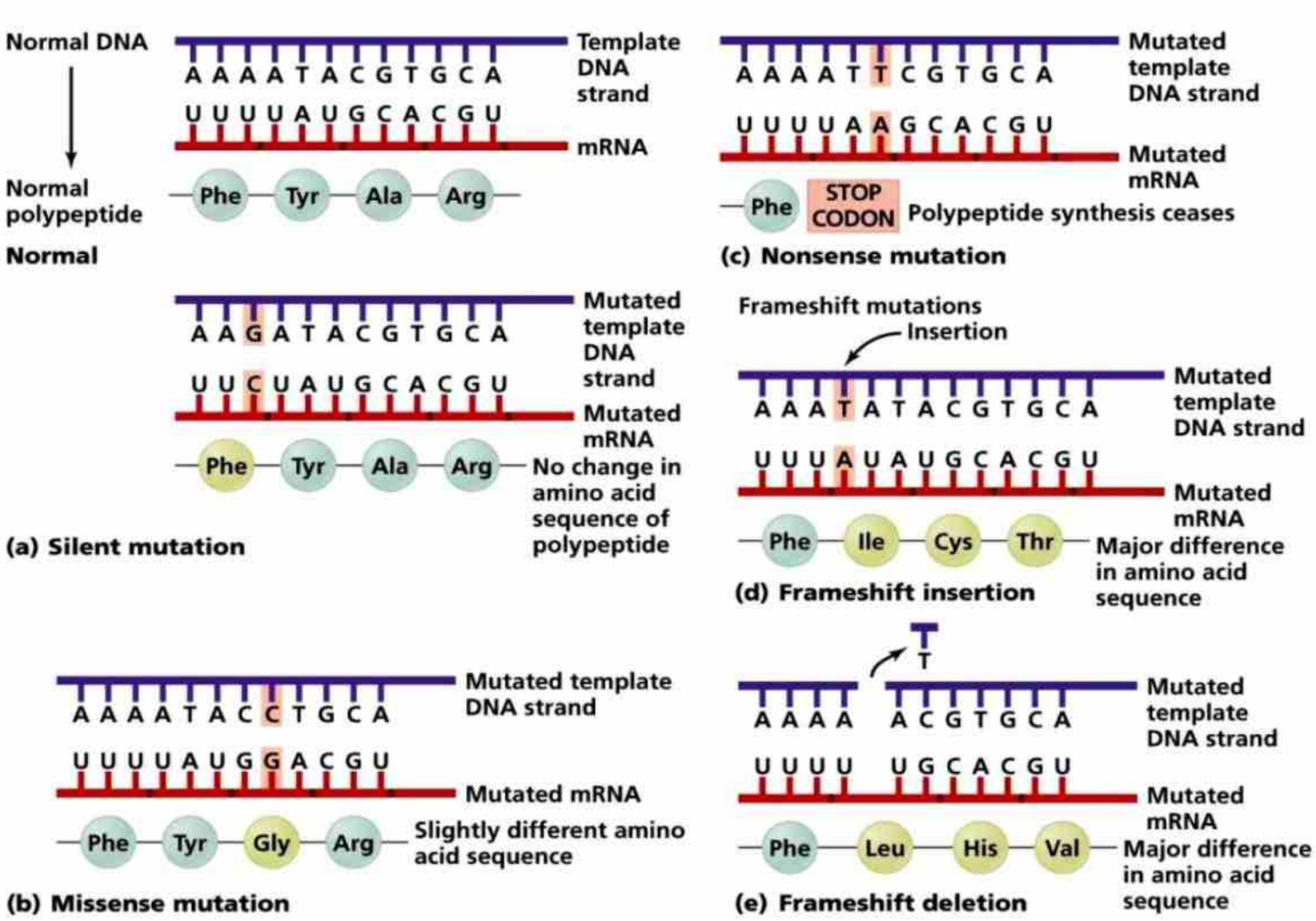


Fig.22.19.Gene mutation

If the change occurs at specific genetic code(s) this type of gene mutation is called **point mutation**. The change in nucleotide sequence at gene develops change in the sequence or type of amino acids, due to these changes in amino acid the nature of protein also alter. It may develop non-functional protein or different protein which develops new character in organism following are the two example of point mutation.

Sickle Cell Anemea

It is a disorder of Hemoglobin impairment. Affected individuals contain erythrocytes that under low oxygen tension become elongated and curved because of the polymerization of hemoglobin.

The normal individual has homozygous genotype Hb^A Hb^A while the affected individuals have homozygous genotype Hb^s Hb^s. The heterozygous individuals do not suffer from this disease because over half of their hemoglobin is normal.

Symptoms: At severe stage of a sickle cell anemia person feel fatigue, pain, fever, fast heartbeat, breathlessness and damage of various organs.

Cause: The genetic code at sixth position for **glutamic acid** in β-chain of hemoglobin is replaced by genetic code of **valine**, develop sickle shaped R.B.C due to this point mutation.

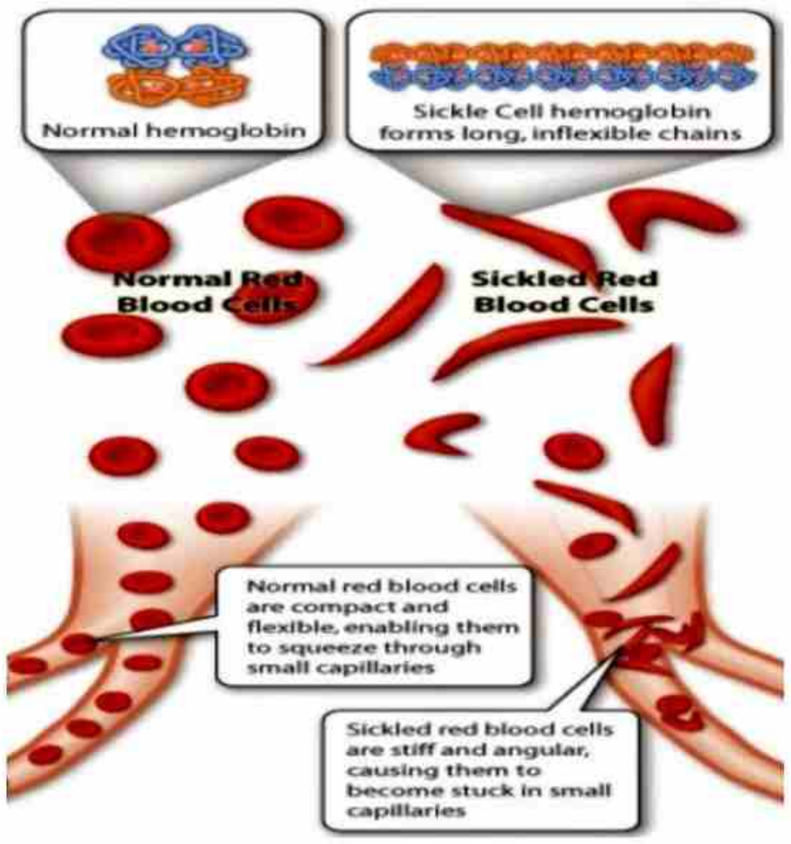


Fig.22.20.Sickle cell anemia

Effect of Sickle Shape R.B.C

The abnormal hemoglobin in sickle shape R.B.C lost oxygen binding capacity so these cells deliver less O_2 and accumulate in blood vessels.

Treatment: Blood transfusion, analgesic and use of high quantity of fluid. Bone marrow transplantation is the long term treatment of sickle cell anemia.

Phenyl Ketonuria (PKU)

Inherited disorder where a new born baby is unable to convert Phenylalanine, amino acid into Tyrosine called **PhenylKetonuria**. It is due to the fact the baby is unable to synthesize an enzyme Phenylalanine hydroxylase. The gene for the synthesis of this enzyme becomes defective due to point mutation. This point mutation converts phenylalanine into phenyl Ketone instead of Tyrosine which damages the nervous system. It appears in homozygous recessive person.

Treatment: Avoid phenylalanine containing diet at childhood, and at adult stage. An especial milk formula Lofenalac is available for PKU infant.

SUMMARY

- Chromosomal theory of inheritance states that the genes are located at chromosome inherits through gametes.
- Chromosome are thread like structure made up of highly condensed chromatin material, appear during cell division.
- Replication of DNA is semi-conservative process.
- Replication of DNA require helicase, DNA polymerase I, II, III, primase and Ligase.
- Replication is the process which provide stability of genes from generation to generation but if any charge occur in DNA before replication, it leads to variation.
- Gene expression is the process where information of gene is used to produce functional product.
- Gene expression is consist of two steps i.e. Transcription and translation.
- Transcription is the process where information present on a specific part of DNA is copied in a complementary form of mRNA.
- Translation process of converting information of mRNA into correct sequences of amino acid synthesize protein.
- Genetic code is the set of rules to store the genetic information within DNA for a particular protein synthesis.
- CODON is the triplet of nitrogenous bases on mRNA which encode one amino acid.
- Before translation, the transcribed introns are spliced, cap and tail are added to mRNA in Eukaryotic gene.
- The process of turning ON and OFF a gene is called regulation of gene expression.
- Introns are not useless part of gene, they play important role in positive regulation of gene expression.
- Mutation is the failure to store genetic information faithfully.
- The mutation may be sportenous or induced, may be chromosomal or genic, may be negative, positive or neutral.
- Chromosomal mutation may be change in number of chromosome or change in structure of chromosome.

EXERCISE

1. Encircle the correct answer:

i) W. Sutton and Theodor observed this behavior of chromosomes.
(a) Formation (b) Distribution
(c) Staining (d) Replication

ii) Which is not the part of chromosomal theory of inheritance.
(a) Gametes do not make equal hereditary contribution
(b) Chromosome segregate during meiosis
(c) Nucleus is the room of hereditary material
(d) Gametes have one copy of homologous chromosome

iii) Newly formed chromosome has two.
(a) Chromatids (b) Heterologous
(c) Centromere (c) Pairs

iv) The complex of histone octamer and two loops of duplex DNA is.
(a) Chromomer (b) Chromatin
(c) Nucleosome (d) Heterochromatin

v) Small part of DNA which has information to synthesize specific polypeptide chain is.
(a) Genome (b) Locus
(c) Gene (d) Nucleotide

vi) According to replication model, the parental double helix remain intact and conserved called.
(a) Semi conservative (b) Conservative
(c) Disposed (d) Eukaryotic replication

vii) A protein which prevents the re-binding of complementary strand during replication at fork is.
(a) DNA helicase (b) Ligase
(c) SSB (d) Primase

viii) The DNA strand which continuously replicate in the direction of 5' → 3' called.
(a) Lagging strand (b) Leading strand
(c) Primer (d) Okazaki fragment

ix) Process where information present on gene is used to produce a functional product by living organism called.
(a) Transcription
(b) Translation
(c) Gene expression
(d) Regulation of gene expression

x) The set of rules used to store the genetic information within a DNA for particular protein synthesis is.
(a) Gene (b) Genetic codes
(c) Codon (d) Anticodon

2. Write short answer of the following:

i) Why DNA is negatively charged molecules?
ii) Why replication is called semi-conservative process?
iii) Do genes of prokaryotic cell and eukaryotic cells are different in structure? If so give the main differences between them?
iv) What are leading and lagging strand of DNA?
v) Give the name of enzymes involved in replication of DNA, also give their brief functions.
vi) Do introns are transcribed, and involve in translation?
vii) Give changes occur in mRNA during transport from nucleus to cytoplasm.
viii) Give site at ribosome and their functions during translation.
ix) Draw structure of tRNA and give functions of their different sites.
x) Do mutation is always harmful? Justify you answer.

3. Give detail answer of following questions:

i) Describe the chromosomal theory of inheritance?
ii) Describe the semi conservative process of DNA replication?
iii) Describe the chemical structure of chromosome.
iv) Describe the process of transcription during gene expression.
v) What is gene regulation how gene regulate during expression?