UNIT 23 GENETICS AND HUMAN WELFARE

Structure **Page No.**

23.1 INTRODUCTION

Genetics, one of the modern branches of biology can be effectively applied for identifying the various inherited disorders and more specifically for preventing the recurrence of the disorder in the human populations. Nature has contrived it in such a way that most the lethal genetic disorders do not surface because the affected embryos.or foetuses are naturally aborted before the complete development takes place. This is true of many of the chromosomal disorders. It is also true that several genetic disorders, especially arising out of the abnormalities in the structure and number of chromosomes result in the sterility of the individuals concerned so that the disorders are not transmitted to the subsequent generations. We discussed in Units 9 and 10 of Block 2 the abnormalities in chromosomal structure and number, and said that many abnormalities result in mental retardation and decreased I. Q. of the individuals. Such individuals are less likely to be married and therefore have no chance of contributing their defective genes to the gene pool. Even if they were to marry, they tend to raise fewer children. You could observe from these statements that nature has devised a number of ways by which it could selectively prevent the spreading of the lethal and sublethal genes in the population. Nevertheless, the genetic disorders do occur and there is a need to diagnose and arrest their transmission to the subsequent generations. In other words, ways and means should be found to prevent the burdening of the population with unwanted genes, a phenomenon come to be known as genetic load. The study of genetics must be used as an effective tool to promote the human genetic welfare.

This unit aims at the study of the genetic counselling phenomenon for the promotion of human welfare, Further we also discuss at length one of the recent advances in molecular genetics, namely the recombinant DNA technology. With the advent of this technique the science of Genetics has opened new vistas for promoting human welfare. The technology has wide possibilities in areas of

medicine, agriculture as well as industry. We shall discuss the applications of the recombinant DNA technology, otherwise known as genetic engineering technique in various fields related to human welfare.

Objectives:

After studying this unit you should be able to:

- define the term genetic counselling
- distinguish between informative counselling and supportive counselling
- discuss the concept of genetic diagnosis with special reference to amniocentesis and chorionicvillus biopsy
- explain the principle behind the recombinant DNA technology and
- list the applications of genetic engineering technique.

23.2 WHAT IS GENETIC COUNSELLING

One of the recent trends in health care and human welfare is genetic counselling. The main aim of the counselling process is to identify individuals or families who may run a high risk for genetic disorders. Such genetic disorders may arise because of the exposure of individuals to certain special circumstances (such as radiation effects) or due to the occurrence of the disorders among the members of the family or the relatives. In short genetic counselling can be defined as a communication process which deals with the human problems associated with the occurrence or the risk of occurrence of a genetic disorder in a family. (Definition provided by a group of genetic counsellors–Committee on genetic counselling 1975, Genetic counselling, *American Journal of Human* Genetics 27, 240-242). By this process a trained person tries to help an individual or a family to understand the various aspects of the genetic disorder, the contribution of heredity to the disorder., the probability of its future occurrence in the family and the possible steps to be taken for avoiding the recurrence of the disorder in the family.

Genetic counselling has several components in it. The first component is the diagnosis of the genetic disorder. The diagnosis itself is done by the medical specialists after performing certain special tests that are available. Once the diagnosis is done; the next step in the counselling process is the preparation of the pedigree of the affected individual. Once the pedigree chart is made and analysed it would throw light on the type of disorder--either it is an autosomal or sex linked trait or whether it is a dominant or a recessive trait. The pedigree chart is drawn essentially based on the information obtained by way of interviews with the family members and the information obtained from the laboratory tests.

On the basis of the conclusion arrived by the above methods, the counsellor would advise the individual or the family on the risks involved in their children inheriting the genetic disorder. They are told of the probability that a child will not be affected and other courses of action if any. Such a counselling process is designated as informative counselling, Another aspect of the counselling process, the supportive counselling would provide the affected individuals professional help that may be needed to understand the intensity of the problem. For this purpose the counsellor should have had training in more specific areas of genetics.

23.2.1 Diagnosis through Genetic Counselling

For the diagnosis of any possible genetic disorder in unborn babies the extensively used method is the prenatal diagnosis. This diagnosis is done on samples of amniotic fluid (Fig, 23.1) collected from the mother and the process of collection is

called **amniocentesis.**The collection of the sample is done after the 14th week of pregnancy and before the 20th week. The fluid contains the foetal cells which are cultured in the laboratory and subjected to the karyotype analysis. Amniocentesis and subsequent karyotyping are the most commonly used tests in prenatal

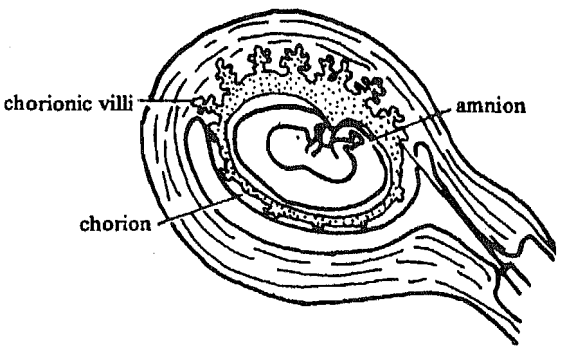


Fig. 23.1: Figure showing the chorionic villi, the amnion and the amniotic fluid surrounding a human foetus.

diagnosis. The karyotype analysis will reveal the structural or numerical chromosomal abnormalities if any that the developing foetus has. In case an abnormality is diagnosed (such as Down syndrome) the counsellor may advise the couple to have the pregnancy terminated.

A relatively less commonly used technique for the diagnosis is the **chorionic** villus **biopsy. In** this technique a sample of chorionic villi surrounding the foetus is removed and the karyotype of the cells is determined. In such a diagnosis there are possibilities for an error because certain differences may arise postzygotically between the foetal cells and the placental cells. It is said that in certain cases normal embryos have been aborted based on the abnormal karyotype of the chorion. Contrarily a normal chorionic karyotype may be associated with an abnormal foetal karyotype.

In general the prenatal diagnosis is done only in high risk pregnancies. For chromosomal abnormalities the high risk indicators are the advanced maternal age, prior birth of a child with a genetic disorder and the information that one of the parents has abnormal chromosomal rearrangement that can generate meiotic mispairing.

SAQ 1:

State whether the following statements are true or false.

1. Pedigree charts throw light on the type of genetic disorder-either it is an autosomal dominant or recessive trait or a sex linked dominant or recessive trait. True/False.
2. Supportive counselling provide the affected individual professional help needed to understand the intensity of genetic disorder. True/False.
3. In aminocentesis there are possibilities for an error because certain differences may arise postzygotically between foetal cells and the placental cells. True/False.
4. Prenatal diagnosis is done only in low risk pregnancies. True/False

23.2.2 Genetic Screening

Genetic screening has been defined as a "systematic search in a population for persons of certain genotypes". Genetic screening is a useful concept in that, the occurrence of many of the inherited diseases could be prevented, if parents at risk could be diagnosed and treated before they plan to have the child or if the affected newborns are identified and treated before degenerative changes occur. Recessive

genotypes are the ones that need to be screened rigorously since these alleles lie usually hidden and unsuspected.

Genetic screening is usually done at three levels: i) identifying the potential parents ii) identification by prenatal screening iii) For identification of the affected new borns.

Screening Potential Parents:

The genetic diseases caused by the recessive alleles essentially arise because of the marriage between the heterozygous parents. The only solution for such a problem is that by suitable pedigree charts the heterozygous individuals need to be identified. Marriage between such heterozygous individuals can be avoided. Alternatively, if the heterozygous individuals marry then they should avoid producing children. The third possibility is that they could have the pregnancies monitored to detect affected homozygotes. It should be made clear that the children do not run into the risk of inheriting a genetic disease unless both the parents are heterozygous for mutant alleles at the same locus.

Prenatal Screening:

There are several methods by which the genetic disorders could be detected in embryos and foetuses. Malformation if any could be detected by ultrasound techniques. The non-closing of the spinal chord, spina bifida, a high risk neural tube defect can be identified by high levels of a-foetoprotein (AFP) circulating in the maternal blood. We earlier mentioned the amniocentesis and chorionic villi biopsy as effective tools for identifying the structural and numerical chromosomal abnormalities.

Screening of New Borns:

Once the new borns have inherited the genetic disorder then every attempt must be made to prevent the disorder assuming serious dimensions. Any therapy should be done before irreversible physiological damage is done to the individual. In USA and Europe it is a legal requirement that the newborns be screened for hypothyroidism and phenylketonuria, the two diseases that could be treated effectively if detected very early.

23.2.3 Therapy for Inherited Diseases

Therapy for inherited diseases has taken various forms. Inherited defects in vision are treated by the use of various prosthetic devices such as eye glasses. New born children suffering from the inherited metabolic disorder galactosemia need to have milk omitted from their diet. Some diseases such as enzyme deficiences in liver may require drastic treatment such as liver transplants. Bone marrow transplants have become a common treatment for certain inherited diseases and the transplanted cells express the normal gene products.

It could be generalised that the transplantation of a genetically normal tissue into a patient with a defective gene function could be termed as gene therapy. But the term gene therapy is now come to be used in a more restricted sense namely it refers to the introduction of a specific gene into a patient to correct the genetic defect he suffers from. The technique of gene therapy revolves around the introduction of a vector carrying the normal gene into the cells of the affected individual. Many vectors such as viruses or plasmids are available for use with E. *Coli*, yeast, mamalian cells and plants. The entire technique of introducing a foreign gene into a host through a vector is come to be known as the recombinant DNA technique and is dealt with in the subsequent sections. Another technique' known as transfection refers to the direct injection of DNA into mouse eggs resulting in the incorporation of some of the DNA into the host chromosome. The incorporated DNA then replicates alongwith the host genome.

Any type of gene therapy corrects the genetic deficiency only in a clone of somatic cells, There is no alteration in the genotype of the germ cells. This means that the defective gene would continue to be transmitted on the mendelian pattern. But the gene therapy does correct the defect permanently in the individual who was given such a therapy. Like any physical disorder the occurrence of genetic disorder is better prevented than cured.

SAQ2:

I. Match the following:

a)	Screening potential parents	i)	Screening of infants for purpose of therapy
b)	Prenatal screening	ii)	Avoidance of marriage between heterozygous individuals
c)	Screening of newborns.	iii)	Amniocentesis and chorionic villus biopsy

II. Fill in the blanks:

i) Therapy for inherited defects on vision are treated by the use of ....

ii) New born infants suffering from ..... should avoid taking milk as a diet.

iii) Transplantation of a genetically normal tissue into a patient with a defective gene function is .....

23.3 RECOMBINANT DNA TECHNIQUE

The recombinant DNA technology widely known as genetic engineering or gene cloning aims at the isolation of required DNA fragment and recombining of the

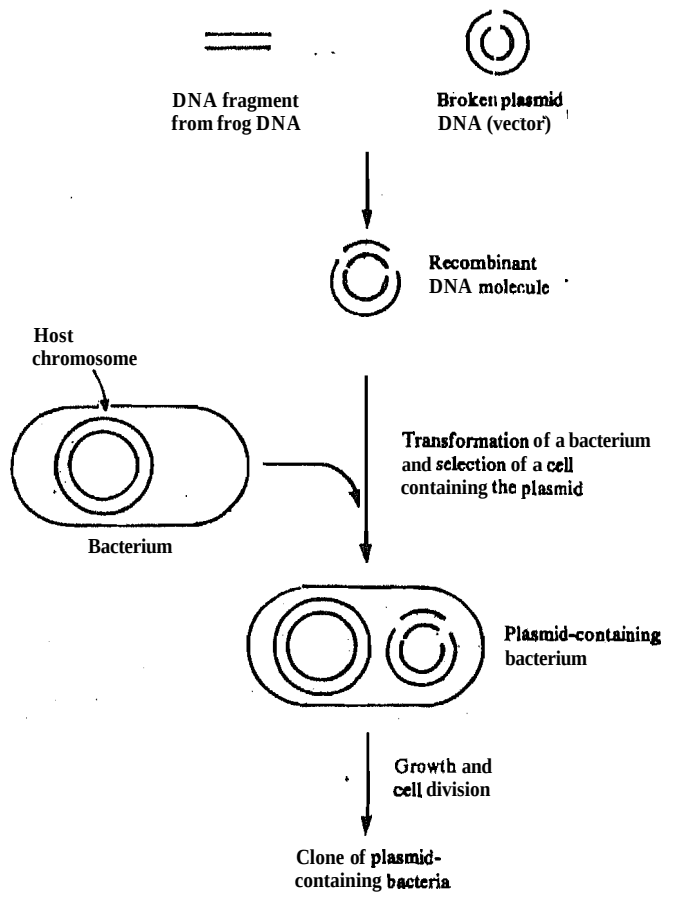


Fig. 23.2: Recombining and cloning of a DNA fragment.

isolated fragment by suitable procedures. More specifically two **DNA** molecules are isolated and cut into fragments by specific enzymes and then joined together in a desired combination. Such a reconstructed gene is restored to a cell by suitable procedures for replication and reproduction (Fig. 23.2). In this section you will learn in detail the methods adopted in the creation of recombinant **DNA** molecule and the process by which such a molecule is amplified in a bacterial cell-the gene cloning process.

In order to create a recombinant **DNA** molecule the required **DNA** fragment has to be incorporated into a suitable genome. Such a genome is known as a vehicle or a **vector.** To be useful in the cloning process a vector or a cloning vehicle should have the following properties.

- It must a small and a well characterised molecule.
- It must have a replication origin, enabling self-replication as well as the replication of inserted segment.
- It should be amenable for the selection of the hybrid molecules.

There are many vectors currently used for cloning. They are the small circular **DNA** molecules — the plasmids and phage particles such as the λ phage with 15 to 20 kilobases (kb) of **DNA.** We shall first look into the isolation of the **DNA** fragment by appropriate enzymes known as restriction enzymes and then the joining of the isolated **DNA** with the vector.

23.3.1 Restriction Enzymes

Restriction enzymes also known as restriction endonucleases are those enzymes which recognise specific base sequences in a **DNA** molecule and make two cuts, one in each strand. Such an action results in generating a 3' hydroxyl and a 5' phosphate termini.

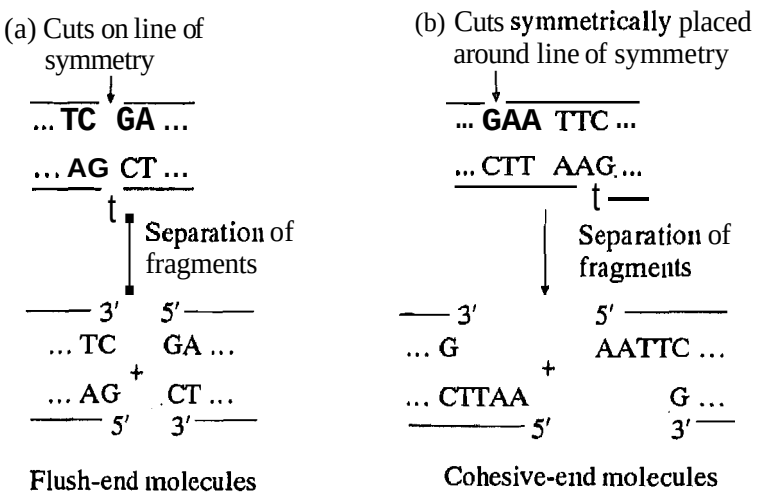


Fig. 23.3 The types of cuts made by restriction enzymes

Restriction enzymes used in recombinant **DNA** are capable of making breaks in the **DNA** molecules by two distinct arrangements.

One type of cleavage results in blunt ended **DNA** fragment and the other type of cleavage generates cohesive ended molecules. The blunt ended molecules are produced when a restriction enzymes acts on the line of symmetry and the cohesive ended molecules are produced when a restriction enzyme acts around the line of symmetry (Fig. 23.3).

An important property of restriction enzymes is that a particular enzyme recognises

a unique sequence of **DNA** bases. (Table **23.1)** This essentially means that any given restriction enzyme can make only a limited number of cuts in the **DNA.** For instance a restriction enzyme can creale only a few hundred lo few thousand **DNA** fragments from **a** bacterial chromosome which contains around **3** million base pairs. The genome of a plasmid which is a much smaller **DNA** molecule may have less than ten cutting sites. Such a specificity of restriction enzymes generates unique family of fragments from a **DNA** molecule. The **DNA** fragments produced by the aclion of a restriction enzyme arc called reslriction fragments.

Table 23.1 Some restriction endonucleases and their cleavage sites

Microorganisu	Name of enzyme	Target sequence and cleavage sites
Generates cohesive ends		
E. coli	EcoRI	G A A ¦ T T C C T T ¦ A A G
Bacillus amyloliquefaciens H	BamHI	G G A ¦ T C C C C T ¦ A G G
B. globigii	BglII	A G A ¦ T C T T C T ¦ A G A
Haemophilus aegyptius	HaeII	Py G C ¦ G C Py Py C G ¦ C G Py
Haemophilus influenza	HindIII	A A G ¦ C T T T T C ¦ G A A
Providencia stuartii	PstI	C T G ¦ C A G G A C ¦ G T C
Streptococcus albus G	SalI	G T C ¦ G A C C A G ¦ C T G
Thermus aquaticus	TaqI	T C ¦ G A A G ¦ C T
Generates flush ends		
Brevibacterium albidum	BalI	T F G ¦ C C A A C C ¦ G G T
Haemophilus aegyptius	HaeI	(A/T) G G ¦ C C (T/A) C C ¦ G G
Serratia marcescens	SmaI	C C C ¦ G G G G G G ¦ C C C

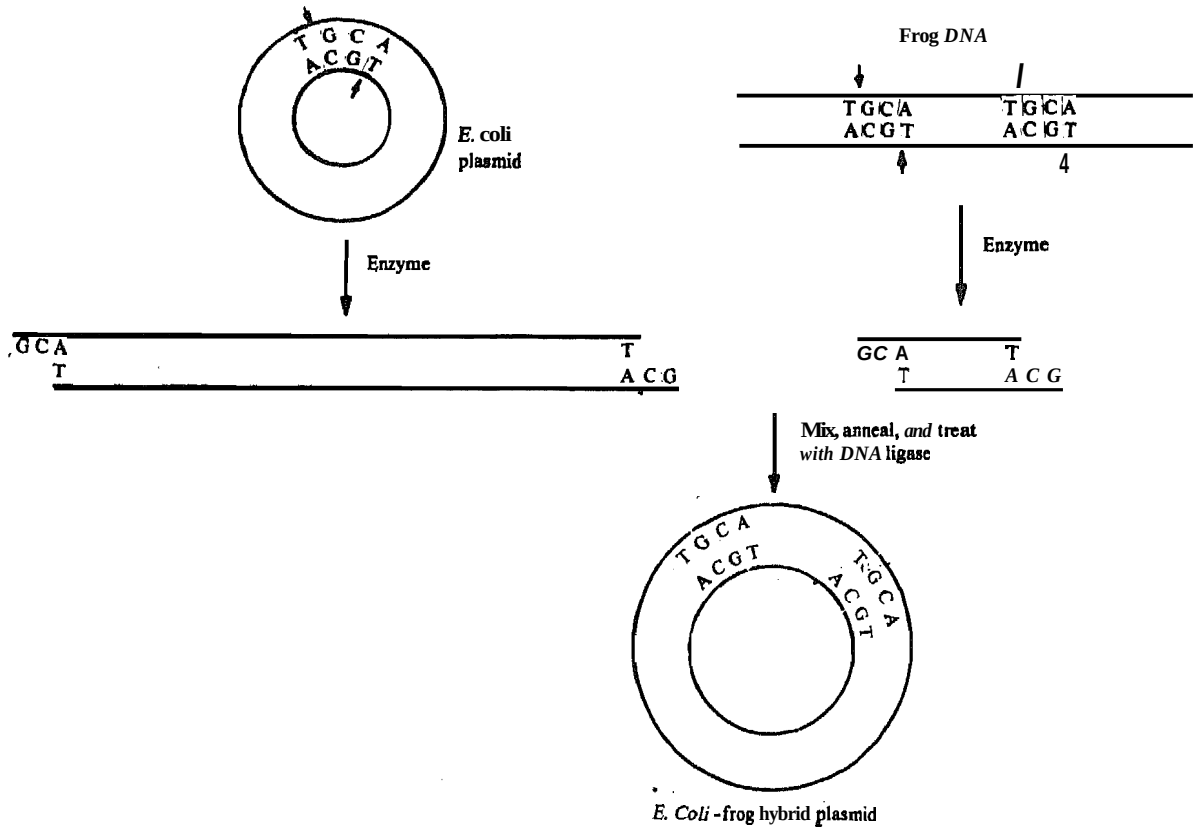
Note: The vertical dashed / indicates the axis of dyad symmetry in cnch sequcncc: Arrows indicate the sites of cutting.

Table 23.4: A general form of nucleotide palindrome sequence

We earlier said that each restriction enzyme recognises only an unique sequence. All such unique sequences have been shown to be palindromic sequences or inverted repeal sequences. Such a sequence consists of four to six complementary bases (Fig. **23.4).** The dashed or interrupted vertical line in Fig. 23.4 is the line of symmetry. The double stranded segment to the right of the line of symmetry can be superimposed on the one to the left.

23.3.2 Joining of the Cohesive Ended Restriction Fragment with the Vector

In the previous subsection you have learnt about the generation of cohesive and blunt



Fi. 23.5 The mechanism of consturction of a hybrid DNA between a bacterial plasmid and frog DNA

ended restriction fragments by the action of restriction enzymes. The restriction fragments thus generated have to be joined with the vector, either a **plasmid** or a phage before it is cloned into a bacterium where the gene could be amplified.

Cohesive ended restriction fragments, as shown in Fig 23.3 have single stranded terminal at each end that are complementary. The joining procedure takes advantage of the complementary single stranded termini. You may also recall that the fragments produced by a particular enzyme acting on two different **DNA** molecules have the same set of single stranded ends. This is because both the **DNA** molecules have the same restriction sequence recognised by the **enzyme.** Let us now look into the technique **that** enables the joining of **DNA** molecules from two different sources such as an E. ***coli*** **plasmid** and a frog (Fig. **23.5).**

You can see from Fig. 23.5 that both the **plasmid DNA** molecule and the frog **DNA** have similar restriction sequences **(TGCA).** Moreover the **plasmid** has only one cleavage site for the restriction enzyme. Once the enzyme has independently cleaved the **plasmid** and the frog **DNA,** the two sources of **DNA** are mixed, annealed and treated with **DNA** ligase to obtain a permanent joining. The interspecific hybrid **plasmid** thus produced is also called a chimera. The hybrid **plasmid** can then be introduced into a bacterium where the **DNA** fragment would replicate as a part of the **plasmid.**

23.33 Joining of blunt ended restriction fragments with the vector

The joining of the blunt ended restriction fragments is achieved by the addition of a homopolymer tail to the 3' hydroxyl group to produce an extended single stranded segment of a **DNA** chain. The homopolymer tail is essentially a sequence of a few similar nucleotides. For examples it could be a poly **A** or a Poly T tail (Fig. 23.6).

The **molecules** to be joined **are** first treated with a **5'** specific exonuclease that

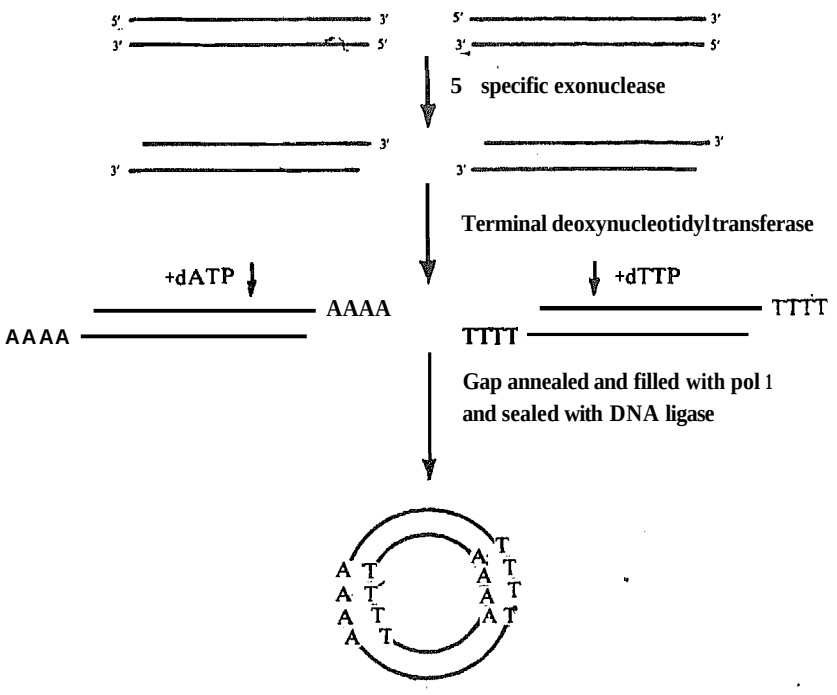


Fig 23.61 Joining *of two DNA* fragments with complementary homopolymer tails.

removes a few terminal nucleotides from each strand at the 5′ ends of the molecule. Such an exonuclease treated **DNA** is mixed with dATP (deoxy adenosine triphosphate) and a specific enzyme, the terminal nucleotidyl transferase. This unusual polymerase obtained from animal tissues adds the nucleotides to the 3' end of a single stranded **DNA** molecule. We call this enzyme an unusual polymerase in the sense that unlike the normal **DNA** polymerase it does not require a template strand for the addition of the nucleotides. In the reaction mixture a poly **A** tail will be formed at the 3′ends of a double stranded **DNA** molecule. If instead of dATP, dTTP (deoxy thymidine triphosphate) is added, then the second molecule will have a homopolymer tail of dT. Once the complementary homopolymer tails are attached to the two different **DNA** fragments, they are joined by the gap filling **DNA** polymerase-I and sealed with **DNA** ligase.

23.4 THE CLONING OF THE HYBRID DNA INTO A HOST

So far we described the methods of generating restriction **DNA** fragments, the vector systems and the joining mechanisms to produce recombinant **DNA** molecules. The recombinant **DNA** has to be introduced into a suitable host for'its propagation. There are two approaches followed to cloning a specific gene. In the first approach all the fragments from a restriction digest are cloned non-selectively into a host and then screening for a desired gene is done. This non-selective method of cloning random **DNA** fragments into a host is called shot gunning method (Fig.23.7). This results in the creation of a gene bank or a gene library from which specific gene could be screened. In this method the hybrid plasmids or the phages containing the gene library represent the entire genome of the organism. Each plasmid or phage may carry a different small fragment of the genome. The second approach consists of using a purified probe for the gene for selecting the appropriate restriction fragment and then cloning that specific fragment.

The introduction of the hybrid plasmid or phage is done by transformation. And bacteria such as *E. coli* can be made permeable to **DNA** by treatment with calcium

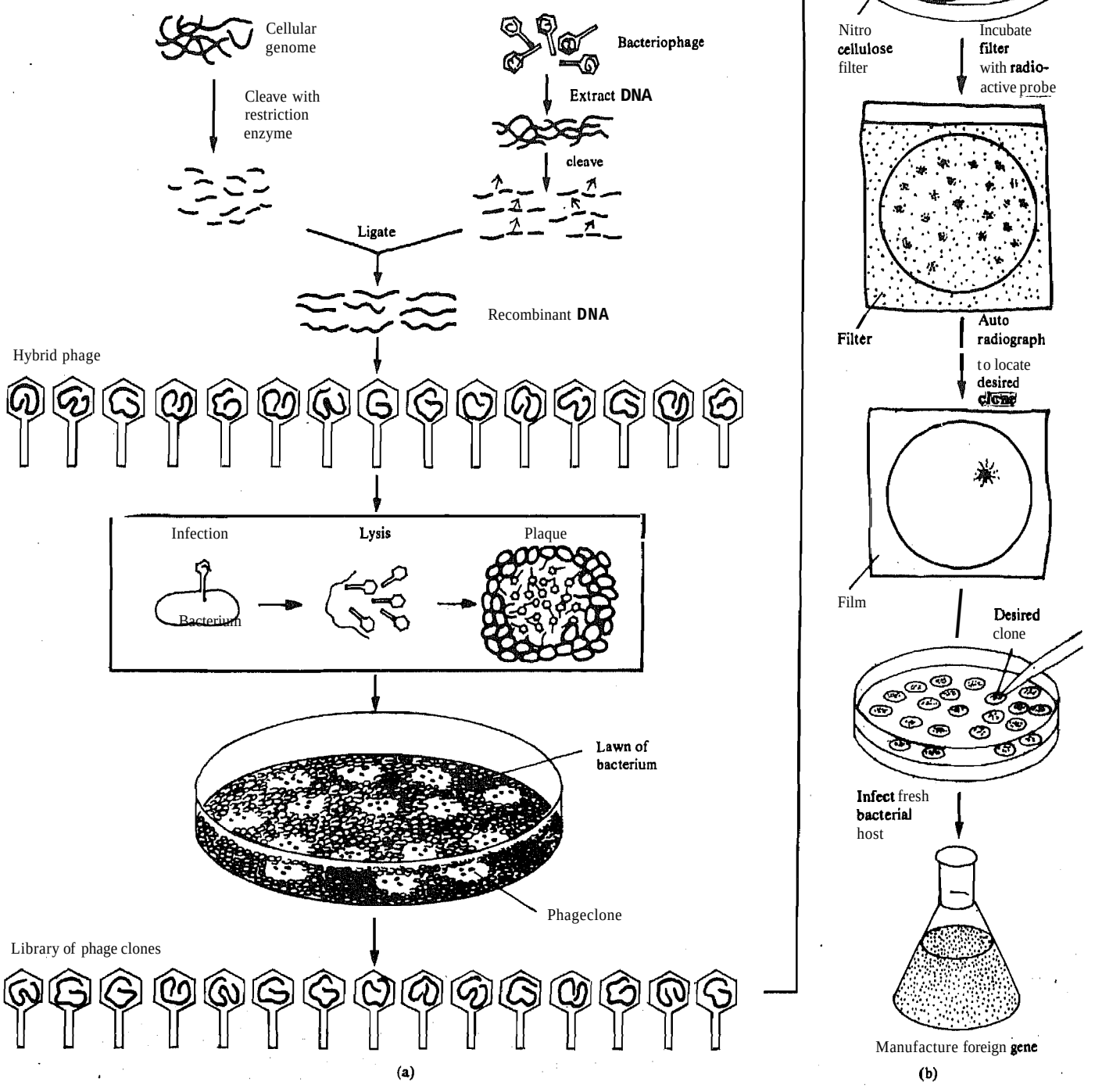


Fig. 23.7 The method of shotgunning, creating a gene **library** and **selecting** for **the** desirtd gene. a) The **creation** of **recombinant DNA genome from** an **eukaryotic genome** and a **bacteriophage genome b)** hybrid **phages.** c) **Each hybrid phage is** allowed to **infect** a bacterium and **multiply. d) The plaque pattern** is **transferred** to a **nitrocellulose filter** and the **phage protein** is dissolved **leaving** only the **recombinant DNA. c) The** filler is **incubated** with the radioactively **labelled** probe. **The** probe **is** actually a DNA copy of the messenger RNA **representing** the **desired** gene. f) **The autoradiography** reveals **the position of the** clone having the **desired** gene. g) **The desired** clone is then selected and **transferred** to a **fresh bacterial** host to obtain multiple copies **recombinant** DNA.

chloride (for detailed discussion on transformation refer to Unit 12 of **LSE-03).** The foreign DNA after it is cloned into a bacterium becomes part of the replication mechanism of the bacteria and the gene product is elaborated.

SAQ 3:

State whether the following statements are true or false.

1. **A** vector to be of use as a cloning vehicle must have a replication origin, capable of self replication and replication of a inserted segment.

   True/False.

2. Blunt ended restriction fragments are produced when a restriction enzyme acts around the line of symmetry.

   True/False.

3. Specificity of restriction enzymes generates unique family of fragments from a DNA molecule.

   True/False.

4. Homopolymer tail is essentially a sequence of four different nucleotides.

   True/False.

5. Terminal nucleotide transferase is a unique polymerase because it requires a template strand for the addition of nucleotides.

   True/False.

6. Cloning on the introduction of hybrid plasmid or phage is done by transformation.

   True/False.

23.5 APPLICATIONS OF GENETIC ENGINEERING

Genetic engineering has many practical applications. The following are the major benefits of the application of genetic engineering technique now come to be widely known as biotechnology.

- Production of a number of biochemicalssuch as enzymes and drugs as well as commercially important chemicals.
- Production of specific RNA and protein molecules in abundant quantities.
- Creation of new varieties of plants with particular desirable characteristics such as disease resistance or less fertiliser requiring.
- Isolation of a particular gene or a region of genome and its characterization.
- Creation of organisms with economically important features.

We shall look into a few chosen examples of the applications of the genetic engineering technique and the benefits derived therefrom.

23.5.1. Applications to Agriculture

An important application of recombinant DNA technology is to alter the genotype of plants for purposes of high yield, disease resistance and less fertilizer consumption. The first genetically engineered plant of commercial **value** was produced in 1985. Glyphosate is a commonly used weed killer and this it does by

inhibiting a particular essential enzyme in many plants. But glyphosate is not specific towards weeds alone but kills the useful crops also. It was discovered that the target gene of glyphosate is present in a bacterium ***Salmonella typhimurium. A*** mutant of *S. typhimurium* is resistant to glyphosate. The mutant gene was cloned to E. ***coli*** and then recloned to ***Agrobacterium tumefackns*** through its plasmid T_i. Infections of plants with purified T_i containing the glyphosate resistant gene has yielded a variety of crops such as maize, cotton and tobacco, all of which are resistant to glyphosate. This makes possible to spray the crop fields with glyphosate to kill the weeds specifically.

23.5.2 Applications to Medicine

Clinical medicine is one of the areas where genetic engineering technique will be employed extensively in future. The technique has been quite useful in developing microorganisms that would overproduce antibiotics which in turn would reduce the production cost. Also some of the biologically active compounds useful in therapy such as insulin, somatostatin and a-interferon are produced by recombinant DNA technique. Somatostatin–afourteen amino acid polypeptide hormone synthesised by the hypothalamus was earlier obtained from the human cadavers and that too in very small amounts. Somatostatin administered as a drug for certain growth related abnormalities appears to be species specific and that obtained from other mammals has no effect on humans; hence the extraction from the hypothalamus of cadavers. With the advent of genetic engineering technique the gene is chemically synthesised, joined to the pBR-322 plasmid DNA and then cloned into a bacterium. The bacteria is converted into a somatostatin synthesising factory. A similar story could be told with reference to insulin and genetically engineered insulin is now commercially available as humilin.

Another example of the product of biotechnology is the antiviral agent a interferon. The substance is presumed to act by supressing the infection duration of a virus and is found to be effective against herpes virus, infection of the eye, multiple sclerosis, atherosclerosis in rats and may possess the antitumor activity. Genetically engineered interleukin-11, a substance that stimulates the multiplication of B-lymphocytes is also available and is being currently tested on AIDS patients.

Biotechnology has also attempted to make vaccines for disease prevention. Although there are certain problems in cloning and purifying the genes for the viral antigens, such as their poor antigenecity and thermal instability attempts are underway to develop vaccines using the anti-smallpox agent, the ***Vaccinia*** virus as a carrier. The method consists of genetically engineering the viral antigens present on the surface of the viral particles onto the coat of ***Vaccinia. Vaccinia*** hybrids with surface antigens of hepatitis B, influenza virus and vesicular stomatitis virus which kills cattle, horses and pigs have been prepared and used in antimal tests. Attempts are also underway to obtain an antimalaria vaccine against the surface antigens of the ***Plasmodium falciparum.***

23.5.3 Applications to Industry

Yet another area where the genetic engineering techniques are being extensively used is industry. The aim is to produce bacteria with novel phenotypes by combining the features of several bacteria. For instance several genes from different bacteria have been introduced to a simple plasmid and then cloned into a bacterium, resulting in an organism that metabolises oil spills in the oceans, thus getting the ocean water cleaned.

Genetically designed bacteria are put into use for synthesising industrial chemicals. Creation of organisms that are capable of cornposting waste very efficiently, fix nitrogen to reduce the fertilizer input but yet increase the fertility of the soil and convert biological waste into alcohol are some of the attempts that are made by people who are actively involved in biotechnological research.

Biotechnology can cut down on expenditure on pestcides and improve the quality of the environment as well. Maize and soyabean are extensively damaged by black cut worm. *Pseudomonas flourescens* lives in association with maize and soyabean. *Bacillus thuringiensis* contains a gene pathogenic to the pest. The pest has over the years not only become dangerous to the crops but has developed resistance to a number of pesticides. In preliminary studies the pathogenic gene from B. *thuringiensis* is cloned into ***Ps. flourescens*** and inoculated into the soil. It is found that the genetically engineered ***Ps. flourescens*** could cause the death of cut worms.

23.5.4 Production of Proteins from Cloned Genes

Genetic engineering aims at the production of large quantity of a simple proteins that may not be otherwise possible to obtain. Theoretically it is possible to insert a foreign gene into a bacterium adjacent to a promotor and get the gene transcribed. Assuming a high copy number hybrid plasmid is involved in the cloning process, as high as 5% gene product could be harvested. But there are several practical constraints in the expression of a eukaryotic gene in a prokaryotic system. The major problems are:

- The non-recognisition of eukaryotic promoter by bacterial RNA polymerase.
- Lack of a specific nucleotide sequence in the eukaryotic mRNA for binding to bacterial ribosomes.
- Absence of mechanisms in prokaryotic systems for eukaryotic mRNA processing.
- Inability of the prokaryotic system to bring about the post-translational changes of a nascent eukaryotic polypeptide.

  Finally eukaryotic proteins are often cleaved by the bacterial proteinases and being regarded as foreign proteins.

In this unit we have briefly discussed two different aspects of modern genetics that have far reaching implications for human welfare. Under genetic engineering not only we discussed the methods of constructing a recombinant DNA molecule and cloning it into a suitable organism but also the applications of the technique to agriculture, medicine and industry. In the last one decade the genetic engineering techniques have invited the attention of many a researchers. Over 250 biotechnology companies have focussed their attention on manufacturing products through genetic engineering process. There are many a journals and books devoted exclusively to the study of genetic engineering worldwide. It is multicrore rupee project and would remain so far many years to come.

SAQ 4:

Match the following:

1. *Salmonella typhimurium*	a) anti-smallpox agent
2 *Vaccinia virus*	b) pathogenic gene for cutworms
3. *Pseudomonas flourescens*	c) anti-cancer agent
4. a interferon	d) glyphosate
5. Somatostatin	e) pBV 322 plasmids

23.6 SUMMARY

In this unit you have studied that:

- Genetic counselling is one of the important aspects of health care. Counselling

helps to assess the genetic risks involved in giving birth to children with inherited disorders and to assist the parents in dealing with the risk.

- Whereas informative counselling aims at imparting the parents the knowledge to understand the risks and the probability that a child will not be affected, supportive counselling offers professionalto help the parents to effectively deal with the risks.
- Genetic diagnosis means the identification of genetic disorders either prior to the marriage of the couple, prior to the birth of the child or in the new borns.
- Amniocentesis and chorionic villus biopsy are the two recognised tests for prenatal diagnosis with the former being more effective than the latter.
- The recombinant **DNA** technology involves the introduction of a foreign gene into a plasmid or a phage genome known as a vector and the amplification of the recombined **DNA** in a suitable host such as bacteria.
- The restriction endonucleases are molecular scissors that cleave a **DNA** molecule at a specific sequence to generate cohesive ended or blunt ended restriction fragments. Each restriction enzyme can only specifically act on a given four to six palindromic nucleotide sequence to produce the restriction fragments.
- The plasmids or the phages are the efficient vectors in which a **DNA** fragment could be recombined to generate a new **DNA** molecule. The amplification or the replication of the recombined **DNA** can be done in a suitable bacterium after the introduction of the **DNA** into the host by the transformation process.
- The recombinant **DNA** technique has a wide range of applications in the fields of agriculture, medicine, industry as well as the genetic research.

23.7 TERMINAL QUESTIONS

1. Define the term genetic counselling? What are the components of genetic counselling process?

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2. How can amniocentesis and chorionic villus biopsy be advantageously used in prenatal diagnosis?

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3. What do you understand by genetic screening?

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4. Give a brief account of restriction enzymes.

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5. Describe any two applications of genetic engineering technique.

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23.8 ANSWERS

Self-assessment Questions

1) 1) True 2) False 3) False 4) False

2) I. a) (ii) b) (iii) c) (i)

II. i) Prosthetic devices ii) Galactosemia iii) gene therapy.

3) 1) True 2) False 3) True 4) False 5) False
6) True.

4) 1) (d) 2) (a) 3) (b) 4) (c) 5) (e)

TERMINAL QUESTIONS

1. Genetic counselling can be defined as a communication process which deals with human problems associated with the occurrence or the risk of occurrence of a genetic disorder in a family. The different components of genetic counselling are i) diagnosis of genetic disorder, ii) counselling process leading to preparation of pedigree chart iii) drawing appropriate conclusion based on pedigree analysis.

2. Both amniocentesis and chorionic villus biopsy are useful prenatal diagnostic tests for detecting possible genetic disorder in the newborn babies. Both techniques depend on obtaining foetal cells (either from amniotic fluid or from chorionic villus surrounding foetus) and culturing them in *vitro*. The cultured

cells are then analysed for their chromosomes and karyotyping is done. Chromosomal abnormalities, if any, can be identified and suitable measures evolved to combat the problem.

3. Genetic screening would refer to systematic search in a population for persons of certain genotypes. The screening would enable to prevent occurrence in, future of many of the genetic disorders in the population. The screening is done at three levels i) identification of potential parents ii) identification by prenatal screening iii) identification of affected new borns.

4. Restriction enzymes are enzymes which recognise specific base sequences in a DNA molecule and make two cuts in each strand. This generates DNA fragments with a 3' OH and 5' phosphate termini. There are two types of restriction enzymes. i) enzymes which act on the line of symmetry of the cleavage site ii) enzymes that act around the line of symmetry of the cleavage site.

5. Refer to Section **23.5**