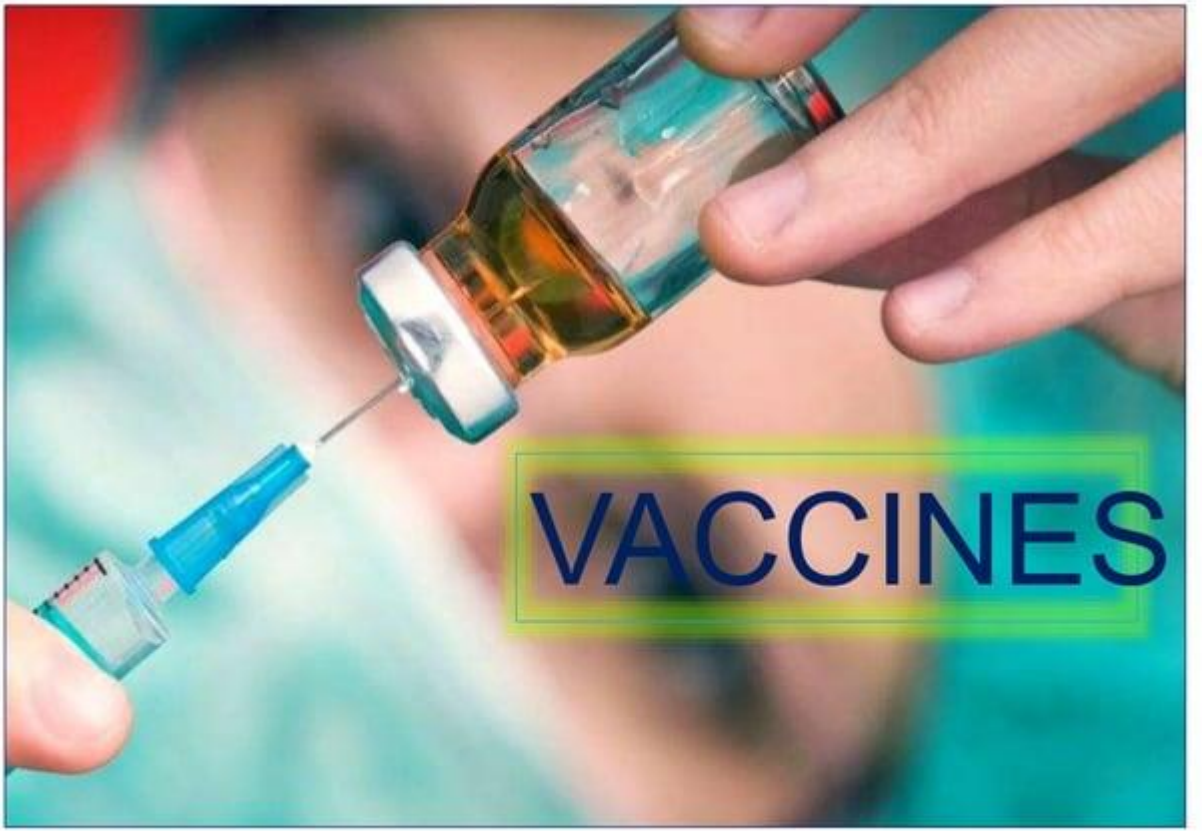
APPLICATION OF GENETIC ENGINEERING IN MEDICINE

INTRODUCTION

- The manipulation of genetic make up of living cells by inserting desired genes through a DNA vector, is called as genetic engineering
- Genetic engineering has been gaining importance over the last few years
- It will become more important in the current century as genetic diseases become more prevalent and agricultural area is reduced
- Genetic engineering plays significant role in the production of medicines

- Microorganisms and plant based substances are now being manipulated to produce large amount of useful drugs, vaccines, enzymes and hormones at low costs
- Genetic engineering is concerned with the study (inheritance pattern of diseases in man and collection of human genes that could provide a complete map for inheritance of healthy individuals

- The main applications of genetic engineering in medicine are
  - VACCINES
  - HORMONES
  - LYMPHOKINES
  - SOMATOSTATIN
  - PRODUCTION OF BLOOD CLOTTING FACTORS
  - MONOCLONAL ANTIBODIES
  - GENE THERAPY
  - TISSUE ENGINEERING


VACCINES

- Recombinant DNA Technology is also used in production of vaccines against diseases
- A vaccine contains a form of an infectious organism that does not cause severe disease
- But it cause immune system of body to form protective antibodies against infective organism
- Vaccines are prepared by isolating antigen or protein present on the surface of viral particles
- When a person is vaccinate against viral disease, antigens produce antibodies that acts against the viral proteins and inactivate them

- Today, the microorganism (such as: yeast) is used to produce virus antigen used as a vaccine, that stimulate human immune system against the virus
- This procedure has been done successfully for development of a vaccine against hepatitis B virus (HBV) that is now widely used
- Genetically engineered vaccines hold great promise for the future!
- GE vaccines may be useful to prevent diseases that have resistant to traditional vaccination , including HIV, tuberculosis…

- With recombinant DNA technology, scientists have been able to transfer the genes for some viral sheath proteins to vaccinia virus which was used against small pox
- Vaccines produced by gene cloning are contamination free and safe
- It is because they contain only coat proteins against which antibodies are made
- A few vaccines are being produced by gene cloning,E.g.
  - vaccines against viral hepatitis influenza
  - herpes simplex virus
  - virus induced foot and mouth disease in animals


Hormones

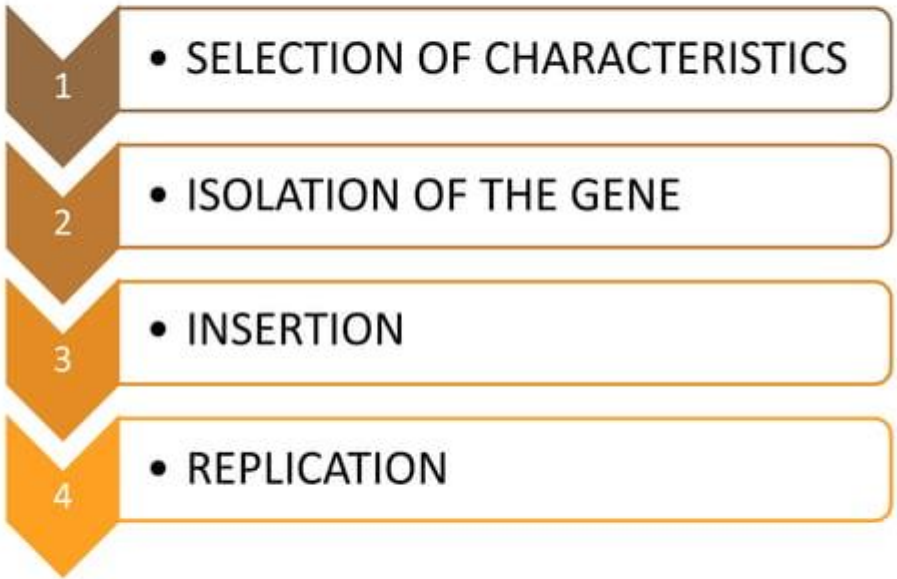
- Until recently the hormone insulin was extracted only in limited quantities from pancreas of cows and pigs
- The process was not only costly but the hormone sometimes caused allergic reactions in some patients of diabetes
- The commercial production of insulin was started in 1982 through biogenetic or recombinant DNA technology
- The medical use of hormone insulin was approved by food and drug administration (FDA) of USA in 1982

- Human insulin gene inserted into the bacterium *E.coli* to produce synthetic "human" insulin(humilin) , for the treatment of insulin-dependent diabetes

PRODUCTION OF INSULIN

- Insulin is a protein hormone produced in the pancreas which has an important function in the regulation of blood sugar levels
- Insulin facilitates the transport of glucose into cells
- A deficiency in insulin is one of the causes of the disease diabetes mellitus or sugar diabetes in which the sugar levels in the blood become raised resulting in harmful consequences

- At least 3% of the world's population is affected by diabetes mellitus and sufferers of the disease require insulin injections to manage the disease
- Before genetic engineering, insulin used for treatment was sourced from the pancreas of slaughtered pigs and cattle
- This source of insulin had minor differences in the amino acid composition to the insulin produced in humans and also contained trace impurities
- As a result some patients were allergic to insulin sourced from animals and had damaging side effects as a result of treatment from these injections
- The solution to this problem was solved by genetic engineering


1
• SELECTION OF CHARACTERISTICS
2
• ISOLATION OF THE GENE
3
• INSERTION
4
• REPLICATION

The insulin production gene is identified from amongst all the other in the DNA of the donor organism.

The identified insulin production gene is cut out from the rest of the DNA by a special enzyme called a restriction enzyme which acts as a chemical scissor.

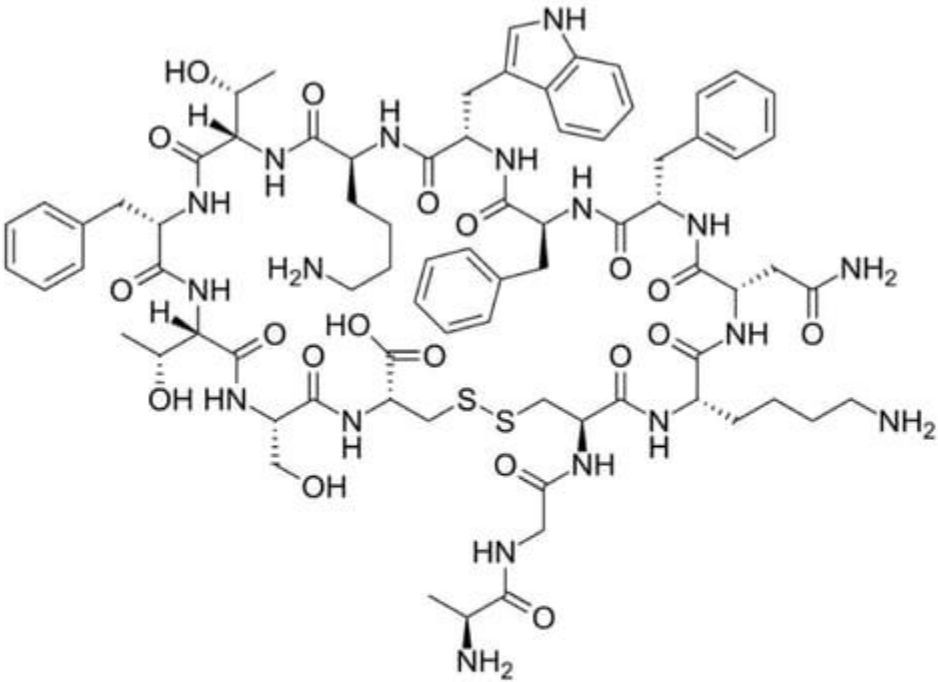
The separated insulin production gene needs to be inserted in a vector. A circular piece of DNA called a plasmid found in bacterium is a commonly used vector. The plasmid is extracted from the bacterium. A particular section of the plasmid is removed by cutting it with the restriction enzyme and the insulin producing gene is placed in the plasmid. The modified plasmid is inserted in a new bacterium.

The bacteria multiply rapidly. The more the bacteria divide the more insulin it produces. Thus, in this way a lot of insulin is produced.

LYMPHOKINES

- Lymphokines are proteins which regulate immune system in human body
- α -Interferon is one of the example
- Interferon is used to fight viral diseases such as hepatitis, herpes, common colds as well as cancer
- Such drugs can be manufactured in bacterial cell in large quantities
- Lymphokines can also be helpful for AIDS patients
- Genetically engineered interleukin-II, a substance that stimulates multiplication of lymphocytes is also available and is being currently tested on AIDS patients

SOMATOSTATIN



- It is a fourteen aminoacid polypeptide hormone synthesized by hypothalamus was obtained only in a small quantity from a human cadavers
- Somatostatin used as a drug for certain growth related abnormalities appears to be species specific
- The polypeptide obtained from other mammals has no effect on human, hence its extraction from hypothalamus of cadavers
- Genetic engineering technique has helped in chemical synthesis of gene which is joined to the pBR 322 plasmid DNA and cloned into a bacterium
- The transformed bacterium is converted into somatostatin synthesising factory

- ADA (adenosine deaminase) deficiency is a disease like combined immune deficiency which killed the bubble boy David in 1984
- The children with ADA deficiency die before they are two years old
- Bone marrow cells of the child after removal from the body were invaded by a harmless virus into which ADA has been inserted
- Erythropoietin, a genetically engineered hormone is used to stimulate the production of red blood cells in people suffering from severe anaemia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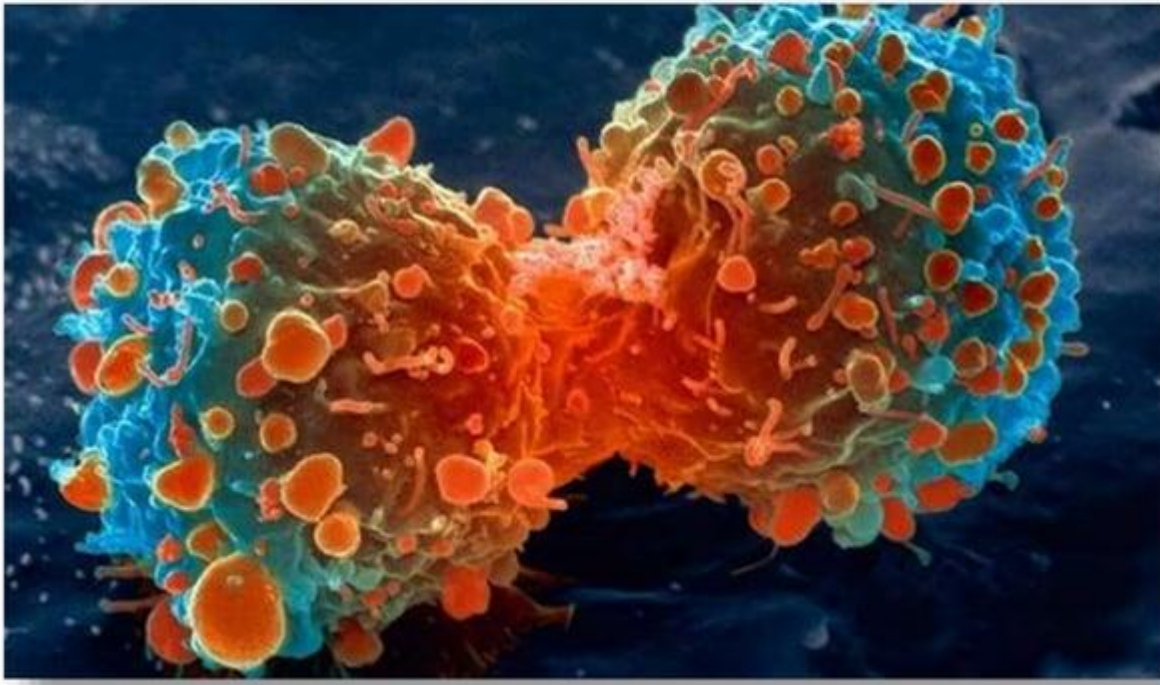
- Normally heart attack is caused when coronary arteries are blocked by cholesterol or blood clot
- Plasminogen is a substance found in blood clots
- Genetically engineered tissue plasminogen activator (tPA) enzyme dissolves blood clots in people who have suffered heart attacks
- The plasminogen activator protein is produced by genetech company
- Which is so potent and specific that it may even arrest a heart attack underway

MONOCLONAL ANTIBODIES

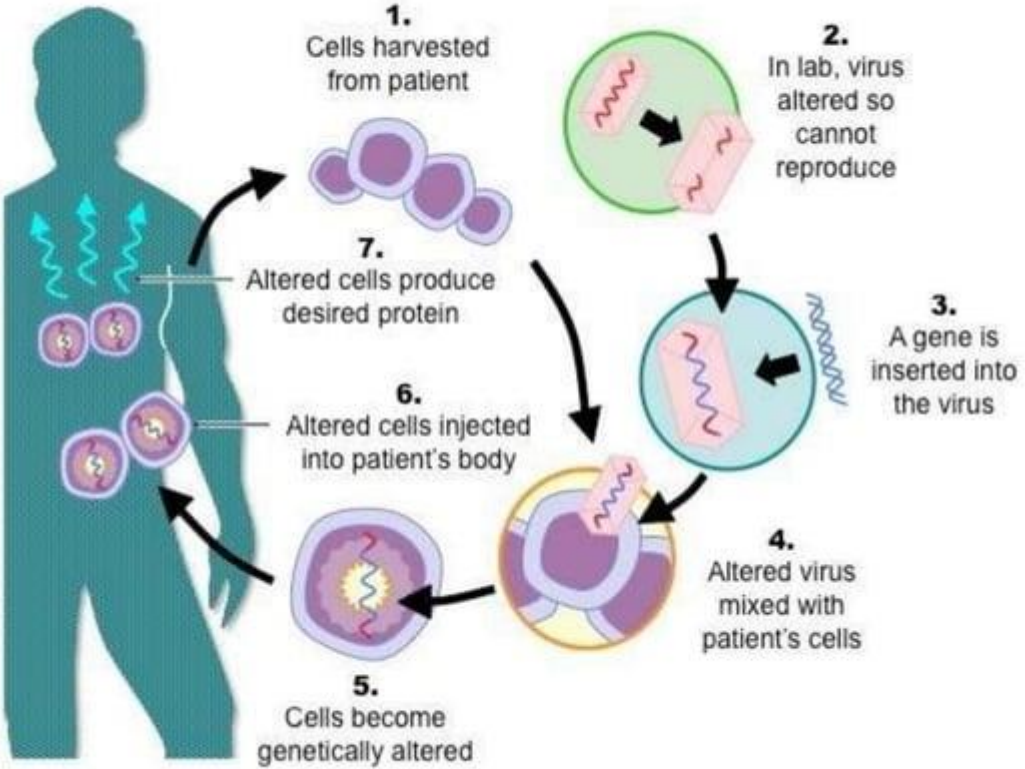


- Antibodies cloned from a single source and targeted for a specific antigen (monoclonal antibodies) have proved very useful in cancer treatment
- Monoclonal antibodies have been target with radioactive elements or cytotoxins like Ricin from castor seed to make them more deadly
- Such antibodies seek cancer cells and specifically kill them with their radioactivity or toxin

GENE THERAPY

- Somatic gene therapy is designed to introduce functional gene(s) to body cells, which enable the body to perform normal functions thus providing correction for genetic abnormalities
- This will cause treating individuals by targeting the therapy to body cells such as bone marrow or blood cells
- Gene therapy has been successfully used to treat Chronic lymphocytic leukaemia (CLL) and Parkinson's disease
- Gene therapy is also being tested as a treatment for cystic fibrosis, skin cancer, breast cancer, brain cancer, and AIDS

- However, most of these treatments are only partially successful , The major reasons for these failures is inefficient vectors
- In the future, as more efficient vectors are engineered, gene therapy is expected to be a common method for treating a large number of genetic disorders

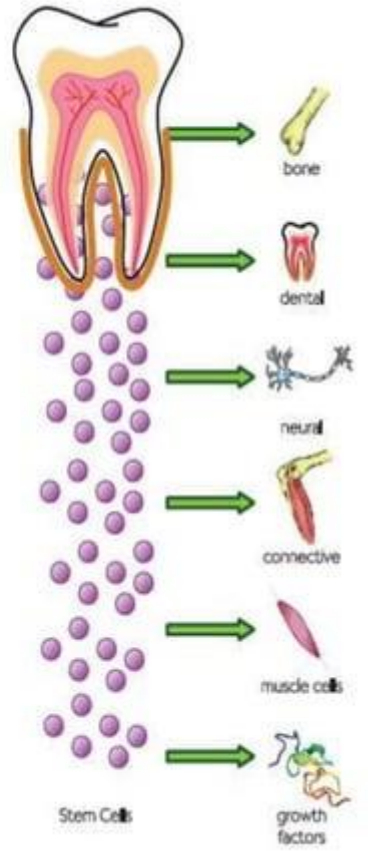

1.
Cells harvested from patient
2.
In lab, virus altered so cannot reproduce
3.
A gene is inserted into the virus
4.
Altered virus mixed with patient's cells
5.
Cells become genetically altered
6.
Altered cells injected into patient's body
7.
Altered cells produce desired protein

- Germ line gene therapy it is changing the genes of embryo used in IVF, before they are implanted
- These babies are "designed" to achieve more desired looks, skills, or talents such as: (gender, hair and eye colour, or intelligence…etc.) and the baby will be free of the disease under consideration
- If the gene is inserted into the germ line cell such as (fertilized ova) it can be passed down to that person's descendants

TISSUE ENGINEERING

- According to their source stem cells are divided into "adult “ which are multipotent, and "embryonic" stem cells, that are mostly pluripotent
- Stem cells can become almost any other kind of cell, they are waiting for a signal that will tell them what kind of tissue cell to become
- stem cells may be useful for the repair of damaged tissues, or may be used to grow new organs

- Stem cells in the pulp of primary teeth, characterized as multipotent cells, have the potential to be used in both dental and medical applications
- such as: treatment of periodontal disease, diabetes, spinal cord injury, stroke, heart attack, burn, rheumatoid arthritis and Parkinson's and Alzheimer's, and regenerate many types of tissue in the body



OTHER APPLICATIONS

- Producing human growth hormone
  to treat growth retardation (dwarfism)
- Producing follistim injection
  (contains the FSH hormone) for treating infertility
- Making human albumin, anti-haemophilic factors and many other drugs
- Other biopharmaceuticals
  under development through genetic engineering, include

anti-cancer drug and a possible vaccine for AIDS, malaria etc..

Genetically engineered bacteria can produce growth hormones for human use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