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Editorial

Recombinant DNA technology in drug discovery

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ABSTRACT

Recombinant DNA (rDNA) technology has made a revolutionary impact in the area of human healthcare by enabling mass production of safe, pure and effective rDNA expression products. Constructing a recombinant DNA molecule involves cutting the DNA into fragments with restriction endonucleases and rejoining the fragments in novel arrangements with ligase. Currently, several categories of rDNA products, viz. hormones of therapeutic interest, haemopoietic growth factors, blood coagulation products, thrombolytic agents, anticoagulants, interferons, interleukins and therapeutic enzymes are being produced using rDNA technology for human use.

Keywords: Recombinant DNA, Hybridoma technique, Monoclonal Antibodies, Antibiotics, Vaccines

INTRODUCTION

Recombinant DNA technology is the technique of genetic engineering in which recombinant DNA is prepared by cutting the DNA into small fragments and joining different fragments together taken from different organisms.[1] This technique makes it possible to take any gene from any species and place this gene in any other organism or species. It is similar to cloning because when the foreign gene is incorporated in an organism like bacteria then multiple copies are made through cloning to use the gene in different applications.[2]

Drugs produced by recombinant DNA technology[3],[4],[5]: Recombinant DNA technology involves using microorganisms, macroscopic organisms, or hybrids of tumor cells and leukocytes:

- To create new pharmaceuticals;
- To create safer and/or more effective versions of conventionally produced pharmaceuticals;
- To produce substances identical to conventionally made pharmaceuticals more cost-effectively than the latter pharmaceuticals are produced.

Types: The pharmaceutical products of rDNA technology are broadly divided into following four types

1. Human protein replacements (Hormones, clotting factors, tPA, enzymes)
2. Antibiotics/Anticancer (MAb, IFN)/ Autoimmune diseases (MAb)
3. Vaccines
4. Diagnostic kits for infectious diseases/ doping

Applications in Medicine

Recombinant DNA technology had made it possible to treat different diseases by inserting new genes in place of damaged and diseased genes in the human body. It has brought many revolutionary changes in the field of medicine and introduced such methods of treating diseases and delivering the drug which were just imaginary.

Insulin: Insulin is a hormone made up of protein. It is secreted in the pancreas by cells known as islet cells. This hormone is responsible for controlling the glucose level in humans. If a person has decreased amount of insulin in his body, he will suffer from a disease called diabetes. Recombinant DNA technology has allowed the scientists to develop human insulin by using the bacteria as a host cell and it is also available in the market. It is believed that the drugs produced through microbes are safer than the drugs produced traditionally. Eg. Lac operon model in plasmids of E.coli.

Human Growth Hormones: Human growth hormone is a polypeptide hormone. It is responsible for growth, reproduction of the cells and regeneration in humans as well as animals. It is secreted by somatotroph cells present in the pituitary glands. In recent years, scientists have developed many growth hormones using recombinant DNA technology. The disease of dwarfism is treated with this hormone.

Erythropoeitin: It is produced by interstitial fibroblasts in the kidney in close association with peritubular capillary and tubular epithelial cells. It is also produced in perisinusoidal cells in the liver. While liver production predominates in the fetal and perinatal period, renal production is predominant during adulthood. EPO binds to the erythropoietin receptor on the red cell progenitor surface and activates a JAK2 signaling cascade. Erythropoietin receptor expression is found in a number of tissues, such as bone marrow and peripheral/central nervous tissue. In the bloodstream, red cells themselves do not express erythropoietin receptor, so cannot respond to EPO.

Vaccines: Vaccine is a biological substance which is prepared to from the suspension of weak or dead pathogenic cells. It is injected in the body to enhance the production of antibodies against particular antigen. Recombinant DNA technology enables the scientists to develop vaccines by cloning the gene used for protective antigen protein. Viral vaccines are most commonly developed through this technology for example, Herpes, Influenza, Hepatitis and Foot and Mouth Disease. Recombinant vaccines can be broadly grouped into two kinds**:**

(i) **Recombinant protein vaccines**: This is based on production of recombinant DNA which is expressed to release the specific protein used in vaccine preparation. Eg – cholera vaccine

(ii) **DNA vaccines:** Here the gene encoding for immunogenic protein is isolated and used to produce recombinant DNA which acts as vaccine to be injected into the individual. The mode of delivery of DNA vaccines include: direct injection into muscle; use of vectors like adenovirus, retrovirus etc; invitro transfer of the gene into autologous cells and reimplantation of the same and particle gun delivery of the DNA. Eg: vaccinia virus.

Advantages:

(i) Since it does not involve actual pathogen, recombinant vaccines is considered to be safe than the conventional vaccines.

(ii) It induces both humoral and cellular immune response resulting in effective vaccination.

Monoclonal Antibodies: When a foreign object enters the body, immune system of the body releases a specific protein called as antibody. Hybridoma technology has made it possible to produce monoclonal antibodies. In this technique, the lymphocytes or B cells are joined with myeloma cells; the resulting substance is called as Hybridoma. This Hybridoma produces unlimited antibodies in the culture. The antibody produced is called as monoclonal antibody. These antibodies are used to produce vaccines against different viral infections.

Interferon: A glycoprotein which has the ability to block the multiplication or division of viruses in the cells or in the nearby cells is called as interferon. Interferon can be used to treat cancer like hairy cell leukemia. Recombinant DNA technology produces this protein using E. coli. Interferon alpha is used to treat lymphoma and myelogenous leukemia; small imidazoquinoline molecules (Imiquimod) activate TLR7 - actinic keratosis, superficial basal cell carcinoma, papilloma and external genital warts; hepatitis B and hepatitis C, viral respiratory diseases

Interferon beta-1a and interferon beta-1b - slowing disease progression and activity in relapsing-remitting multiple sclerosis and reducing attacks in secondary progressive multiple sclerosis.

Antibiotics: Antibiotics are the chemical substances which are used against bacterial infections. They can be produced by microorganisms as well as in the laboratory. They have the ability to destroy bacteria or other harmful microbes which cause infections in the body. Alexander Fleming discovered penicillin for the first time in 1928 using recombinant DNA

technology. Other biotechnological techniques are also being used to produce antibiotics. Penicillin (P. chrysogenum) and cephalosporins.

Infectious Diseases: Many diseases are diagnosed by conducting certain tests. Recombinant DNA technology has allowed the development of many tests which are being used to diagnose diseases like TB and cancer. Other diseases like measles, small pox and hepatitis are also diagnosed through tests and if they are not diagnosed properly, they can be a threat to human health. In the diagnosis process, certain pathogens are isolated and identified, and then diagnostic kits are produced when the genome of the specific pathogen is known to kill it or block its pathogenic activity.

rDNA Product	Trade name	Application / Uses
Insulin	Humulin	Diabetes
Growth hormone	Protropin/Humatrope	Pituitary dwarfism
Interferon	Intron A	Hairy cell leukemia
Hepatitis B vaccine	Recombinax HB/ Engerix	Hepatitis B
Tissue plasminogen activator	Activase	Myocardial infarction
Factor vIII	Kogenate/Recombinate	Hemophilia
Dnase	Pulmozyme	Cystic fibrosis
Erythropoietin	Epogen/rocrit	Severe anemia with kidney damage

Recombinant EPO is chemically slightly different from the made in the body version, and this can be used on blood tests to determine whether or not an athlete is doping.

Conclusions

Based on biotechnological processes, new substances with different therapeutic applications, with a central focus on quality of life and public health, have been developed and produced on a large scale. The application of these techniques covers a wide range of drug classes such as antibiotics, blood factors, hormones, hematopoietic growth factors cytokines, enzymes, vaccines and monoclonal antibodies.

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