BIOTECHNOLOGY AND ITS APPLICATIONS

BIOTECHNOLOGICAL APPLICATIONS IN MEDICINE

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(1) Genetically Engineered Insulin

It is a proteinaceous hormone having 51 Amino acids arranged in two polypeptides A and B having 21 and 30 Amino Acids, respeCtively and joined by S-S disulphide bridges.

Sir Edward sharpy-Shafer (1916) was the first to note that diabetes of some persons was because of failure of some islands of pancreas to produce a substance which he called insulin (Derived from the latin, insula, meanning island).

Banting and best (1921) were the first to isolate insulin from dog's pancreas and used it to cure diabetes in man.

The first genetically engineered insulin obtained by recombinant DNA technique with the help of E-Coli was produced by the American firms, Eli-Lilly on July 5, 1983. It has been given the trade name humulin and has been approved for clinical use.

Insulin used for diabetes was earlier extracted from pancreas of slaughtered cattle and pigs. Insulin from an animal source, though caused some patients to develop allergy or other 'types of reactions to the foreign protein. Insulin consists of two short polypeptide chains: chain A and chain B. that are linked together by disulphide bridges. In mammals, including humans, insulin is synthesised as a prohormone (like a pro-enzyme, the pro-hormone also needs to be processed before it becomes a fully mature and functional hormone) which contains an extra stretch called the C peptide.

This C peptide is not present in the mature insulin and is removed during maturation into insulin. The main challenge for production of insulin using rONA techniques was getting insulin assembled into a mature form. In 1983, Eli Lilly an American company prepared two DNA sequences corresponding to A and B, chains of human insulin and introduced them in plasmids of E coli to produce insulin chains. Chains A and B were produced separately, extracted and combined by creating disulfide bonds to form human insulin.

(2) Gene Therapy :

- A new system of medicine gene therapy, may develop to treat some hereditary diseases such as SCID, haemophilia etc.
- Gene therapy is a collection of methods that allows correction of a gene defect that has been diagnosed in a child/embryo. Here genes are inserted into a person's cells and tissues to treat a disease. Correction of a genetic defect involves delivery of a normal gene into the individual or embryo to take over the function of and compensate for the non-functional gene.

  The first clinical gene therapy was given in 1990 to a 4-year old girl with adenosine deaminase (ADA) deficiency. This enzyme is crucial for the immune system to function. The disorder is caused due to the deletion of the gene for adenosine deaminase. In some children ADA deficiency can be cured by bone marrow transplantation; in others it can be treated by enzyme replacement therapy, in which functional ADA is given to the patient by injection. But the problem with both of these approaches that they are not completely curative. As a first step towards gene therapy, lymphocytes from the blood of the patient are grown in a culture outside the body. A functional ADA eDNA (using a retroviral vector) is then introduced into these lymphocytes, which are subsequently returned to the patient. However, as these cells are not immortal, the patient requires periodic infusion of such genetically engineered lymphocytes. However, if the gene isolate from marrow cells producing ADA is introduced into cells at early embryonic stages, it could be a permanent cure.

(3) Medical Diagnosis of Disease (Molecular diagnosis)

You know that for effective treatment of a disease, early diagnosis and understanding its pathophysiology is very important. Using conventional methods of diagnosis (serum and urine analysis, etc.) early detection is not possible. Recombinant DNA technology, Polymerase Chain Reaction (PCR) and Enzyme Linked Immunosorbent Assay (EUSA) are some of the techniques that serve the purpose of early diagnosis.

Presence of a pathogen (bacteria, viruses, etc.) is normally suspected only when the pathogen has produced a disease symptom. By this time the concentration of pathogen is already very high in the body. However, very low concentration of a bacteria or virus (at a time when the symptoms of the disease are not yet visible) can be detected by amplification of their nucleic acid by PCR. PCR is now routinely used to detect HN in suspected AIDS patients. It is being used to detect mutations in genes in suspected cancer patients too. It is a powerful techqnique to identify many other genetic disorders.

A single stranded DNA or RNA, tagged with a radioactive molecule (probe) is allowed to hybridise to its complementary DNA in a clone of cells followed by detection using autoradiography. The clone having the mutated gene will hence not appear on the photographic film, because the probe will not have complimentarity with the mutated gene.

EUSA is based on the principle of antigen-antibody interaction. Infection by pathogen can be detected by the presence of antigens (proteins, glycoproteins, etc.) or by detecting the antibodies synthesised against the pathogen.