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Assignment Title: Medical biotechnology
Course Title: Introduction to Biotechnology
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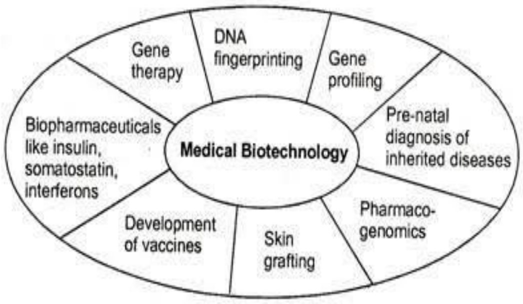
Question
Discuss in details the aspects of medical biotechnology.

Answer
The following are aspects of medical biotechnology:
1. Gene therapy
2. DNA fingerprinting
3. Gene profiling
4. Pre-natal diagnosis of inherited diseases
5. Pharmacogenomics
6. Skin grafting
7. Development of vaccines
8. Biopharmaceuticals like insulin, somatostatin, interferons.



Detection of Genetic Diseases:
The effective treatment of any disease depends on its correct diagnosis. Conventional medicine offers little guarantee of accurate detection, and the diagnosis always contains an element of probability. However, the new techniques of genetic engineering make accurate diagnosis possible by locating and analyzing single genes in a chain of thousands of genes through 'gene probes'. These are the segments of DNA, which match and hence bind with the DNA segments of individual genes. Their binding can be detected just by labelling these DNA segments. Such probes are used to recognize DNA sequences associated with genetic diseases. Genes can now be detected for a varied number of genetic conditions in small tissue samples collected from patients or even from embryos by amniocentesis. These DNA probes can also be used to identify disease organisms, and are used in tests where one may not be able to use antibodies.

Monoclonal Antibodies and Diagnosis:
Antibodies are proteins generated by a body to fight against a disease or an infection. These antibodies are produced by white blood cells as a response to a disease causing organism or infection, which the body recognizes as foreign.
Antibodies work by binding to these foreign substances as they circulate in the blood, and thus prevent them from causing any harm to the body. These antibodies bind with the specific protein (antigen), which has triggered off their production. They can be obtained from the blood of

immunized animals and eventually used for diagnostic and research purposes. Antibodies are of two types. Polyclonal antibodies are not specific in nature, and can recognize many proteins at the same time. Monoclonal antibodies recognize only a specific type of protein. Antibodies, especially the monoclonal ones, are now being widely used for diagnostic purposes. Some of the areas where they find wider application includes pregnancy tests, cancer screening and diagnosis of viral gastro-enteritis, hepatitis B, cystic fibrosis and sexually transmitted diseases like AIDS.

Therapeutic Drugs:
Modem day vaccines have already helped in eradicating diseases like small pox, and reducing the exposure to polio, typhus, tetanus, measles, hepatitis, rotavirus and other dangerous infections. However, standard immunization methods fare poorly when targeted against a particular illness. Genetic material, i.e. DNA and RNA can be used to develop improved vaccines.
The recombinant DNA technology facilitates designing and mass production of such models, as well as greater stability in storage. Furthermore, since these vaccines can be engineered to carry genes from different strains of pathogen, they can provide immunity against several other strains at once.
The idea that genes could be used in creating vaccines was mooted in the 1950-60s. Initial studies revealed that if genetic material was delivered into an animal's cell, it resulted in the synthesis of the encoded proteins and antibodies targeted against those proteins.
Disease causing organisms carry antigens on their surface, which trigger off the body's defense mechanism, and thus help control the damage caused to the body. Special cells found throughout the human body produce antibodies and antigens.
These cells recognize the shape of a particular determinant group of the antigen, and produce specific antibodies to combat not only the vast array of microbial invasions, but also an unlimited range of synthetic chemicals. In short, the mammalian system can bind and deactivate almost any foreign molecule that gets into the system.
Vaccines are prepared from living or dead microorganisms that can be introduced in the human or animal body to stimulate their immunity. They can mimic infectious agents and subsequently help the body develop protective immune responses.
When used on a large scale, vaccines have been a major force in the control of microbial diseases within communities. The major goal of vaccine research is to identify and characterize the individual antigens of infectious agents that can help in developing an immune response.

Biopharmaceuticals:
Many pharmaceutical products are compounds derived either from synthetic chemical processes or from natural sources like plants and microorganisms, or are combinations of both. Such compounds are used to regulate essential body functions and to combat disease-causing organisms.
Efforts are now on to harness the human body's own regulatory molecules, which are normally found in very small concentrations. Limited quantities of some of these compounds have historically been derived from the organs of cadavers or from blood banks. Genetic engineering is now being recognized as a practical means of generating some of these scarce molecules in larger quantities. This involves inserting the necessary human derived gene construct into a suitable host microorganism that will produce therapeutic protein (biopharmaceutical) in quantities related to the scale of operation. Such products carry no risk of contamination from extraction of cadavers (like the degenerative brain disease). Creulzfelt-Jakob disease has also been associated with the administration of human hormone from early extraction.

The successful development of biopharmaceuticals requires:
1. Advanced biochemical or biomedical research to identify and characterize the native compounds.
2. Skilled molecular biology and cloning technology to identify the relevant gene sequences and insert them into a mammalian or microbiological host.

3. Bioprocess technology to grow the organisms to isolate, concentrate and purify the chosen compounds.
4. Clinical and marketing expertise.

Some of the important biopharmaceuticals already in use:

1. **Insulin:**

Millions of people suffer from diabetes due to insulin deficiency. These patients have to depend on external insulin intake. Conventionally, the insulin used by diabetic patients had been extracted from pigs and cattle. This has been discontinued due to its adverse side effects. We now use recombinant human insulin, which is free from any contamination and has proved extremely effective against the disease.

2. **Somatostatin:**

This growth hormone has been extremely difficult to isolate from animals. However, the cloning of the human gene for somatostatin into bacterium has enabled its large-scale production. This has proved to be a boon for the treatment of hypo pituitary dwarfism, which occurs due to the deficiency of this hormone.

3. **Interferon's:**

Interferon's are glycoproteins (proteins with attached sugar molecules), believed to be instrumental in controlling many types of viral infections including the common cold. They also inhibit the growth of cancer cells and stimulate the body's natural immune defenses against them.
In 1957, two British researchers recognized these interferon's as substances produced within the body that could make the cells resistant to virus attacks. However, the scarcity of these compounds has consistently hampered the efforts to understand the extent of their effectiveness. Of late using modem techniques we have been able to produce interferon molecules, which have a role in controlling various infections.

4. **Lymphokines:**

These are proteins produced by lymphocytes (a part of the body's immune system) and are deemed important to immune reactions. They have the capability of enhancing and restoring the capacity of the immune system to fight infections, diseases and cancer. Interleukin-2 is the most commonly used lymphokine that is being produced by genetic engineering. Each of these compounds has helped scientists achieve new levels of realistic pharmaceutical drug delivery. Recombinant DNA technology has enabled the synthesis of large quantities of these products. This molecular pharmacy is becoming quite successful in the production of human pharmaceuticals in transgenic animals as well.

Gene Therapy:
This promising technology uses genes as drugs to correct hereditary genetic disorders. Using gene therapy, a faulty or missing gene can be replaced to correct genetic cause of a disease. This is done by determining the normal gene's function in human cells, the kind of protein it instructs the cell to produce, and the level, quantity, and time of protein formation. This can further indicate whether the right protein is being formed at the right time or place, and how to counter the effects of any failure. Gene therapy is of two types: Germ Cell Gene Therapy and Somatic Cell Gene Therapy. In Germ Cell Therapy, changes are directed towards the individual genetic makeup and can be passed

on to the offspring. In the Somatic Cell Gene Therapy on the other hand, functional genes are introduced into body cells that lack them. The effects of the therapy are not passed on to the subsequent generation.

DNA Fingerprinting:
The development of DNA fingerprinting technique has proved to be extremely significant in identifying criminals and establishing parentage. The fundamental principle of this technique is based on the fact that no two individuals can have the same genetic composition.
The DNA fragments of the person in question can be taken from a tissue or blood sample using a restriction enzyme. This fragment can then be studied to establish the exact genetic composition of the individual. This technique offers such a high rate of polymorphism that the possibility of two persons having the same DNA characteristics is very remote.

Pre-natal Diagnosis of Inherited Diseases:
Molecular genetics holds significant application in pre-natal diagnosis of inherited disorders like haemoglobinopathies. For instance, the technique for analyzing DNA to diagnose sickle cell anaemia from the amniotic fluid cells was devised in 1978.

TISSUE REGENERATION:

Skin Grafting:
Skin is probably one of the only organs that can be artificially synthesized from cell culture, and used for grafting when it is severely damaged. Skin cells (keratinocytes) make up ninety per cent of the epidermis of the skin. The proliferation of these cells is facilitated by fibroblasts present in the dermal layer of skin. Fibroblasts are useful for culturing skin cells. These fibroblast cells, called 3T3 cells, are used along with the necessary chemicals and stem cells. However, only about one to ten per cent of the epidermal cells proliferate. Sub-culturing to fresh media prompts further growth of these cells. Skin grafting enables quick recovery and normalization of damaged skin. Regenerated keratinocytes have also been used to cure a number of other diseases. For instance, skin scars can be removed using cultured skin, and cultured oral keratinocytes can be used to regenerate the epithelium of the mouth. Cultured urethra keratinocytes have been used to repair congenital penile defects. Chronic ulcers have also been treated with successful culmred grafts, and allographs (skin from another individual) have been successful in curing these ulcers.

Fertility Control:
Indian scientists have successfully developed drugs like Centchroman for anti-fertility (contraceptive), which have shown excellent results without any side effects. Immunological approaches have also been used to develop anti-fertility vaccines.
Birth control vaccines have now been developed using the HCG (Human Chorionic Gonadotrophin) hormone. The vaccine elicits antibodies against both tetanus and pregnancy hormone HCG. This has substantially reduced the impact of tetanus, which is a major cause of natal deaths in India due to unhygienic conditions especially in the rural sector.

Genetic Counseling:
This application has cropped up due to increasing awareness among people who want their children to be free from congenital diseases. A genetic counselor tells the patient about the consequences of a particular genetic defect. Subjecting amniotic fluid to various tests can examine these congenital disorders and the results obtained could be discussed with the patient. This will allow prospective parents to think over the defect in the fetus well in advance.

Pre-implantation Genetic Diagnosis:

Pre-implantation Genetic Diagnosis (PGD) came into existence, when through Assisted Reproductive Technology (ART) the umbilical cord stem cells of yet unborn (only foetus) were used to cure a six year- old suffering from fanconi anaemia. When the fetus was merely a ball of blastomere cells, researchers at the Reproductive Genetic Institute at Illinois Masonic Medical Centre separated some of these cells.

These cells were analyzed and not only found to be free of the fanconi anaemia gene, but also compatible in terms of Human Leukocyte Antigens (HLA). The researchers implanted the rest of the ball of blastomere cells back into the mother's uterus. The mother gave birth to a healthy child. After a month's time, his, umbilical cord stem cells were, infused into his sister.

This process was made possible thanks to an inherent development process called 'indeterminate cleavage'. Like any other vertebrate, an eight-celled human embryo (known as pro-embryo) can continue developing even after one or two cells are removed.

In PGD, embryos obtained for in-vitro fertilization are subjected to many tests (biopsies). Next, the genetic makeup is thoroughly examined, and only those cells are transferred back to the mother, which are free from genetic diseases. This technique is a great help in the diagnosis of genetic disorders.

Pharmacogenomics:

The intervention of molecular tools in the pharmaceutical domain has given birth to a new area of Pharmacogenomics. A merging of pharmaceutical science and genetics, pharmacogenomics combines traditional pharmaceutical sciences including biochemistry, the molecular structure of the gene, and its behavior and function at the protein level.

It basically involves the study of how an individual's genetic makeup affects the body's response to drugs. This upcoming field holds a great promise of the day when it will be possible to tailor drugs for individual patients in keeping with their genetic architecture.

Gene Profiling:

Modem biotechnological tools have virtually revolutionized the medical field. One such tool, the microarray, has been found to be exceptionally advantageous. This technique makes it possible to pinpoint the molecular differences among the various genes being expressed.

The detailed molecular picture obtained by this technique will help in designing molecular medicines, just like high-resolution radiographic imaging methods have assisted in treating diseases at anatomical levels. One of the recent studies using gene expression based on DNA micro-arrays was for the molecular classification of cancer.

It was reported that the profiling helped in distinguishing distinct pathological strains, such as acute myeloid leukemia and acute lymphoblastic leukemia, based on their distinctive gene expression pattern. DNA micro-arrays have also helped in revealing other new diseases.