Chapter 05

5.Microbial Biotechnology and Infectious Diseases

Microorganisms are etymologically "small organisms," meaning living beings so small that they can only be observed under a microscope. This term encompasses a wide variety of species, whether prokaryotic (bacteria) or eukaryotic (yeasts, algae). Some also include viruses. Microorganisms represent the largest biomass on Earth.

We can define the fields of microbial biotechnology based on the products obtained:

• Production of microbial biomass for animal feed.

• Microbial production of chemicals such as citric acid, glutamic acid, amino acids, etc.

• Microbial or enzymatic production of antibiotics and vitamins.

• Production, from animal or plant cells or genetically modified microorganisms, of antigens, antibodies, therapeutic agents, and diagnostics previously produced from higher organisms.

5.1. Diagnostics

The healthcare sector (both human and veterinary) is increasingly relying on biotechnology to discover, test, and produce new treatments (e.g., vaccines, recombinant proteins, monoclonal antibodies, non-viral cell and gene therapy), but also to diagnose and understand the causes of diseases.

Most scientists working in the medical field tend to view biotechnology advancements as part of a continuum, represented by the ongoing process of refining and developing medical practices. Among the medical techniques, we have vaccination, veterinary diagnostics and treatments, artificial insemination, and genetic crossbreeding. Hundreds of tests used in medical diagnostics have been established. This includes the detection of the HIV virus and other diseases in their initial phase, allowing for the application of appropriate treatment. Home pregnancy tests without medical assistance are also biotechnology products.

Applied Biotechnology in Analysis and Diagnostics has enabled the development of technologies and systems for detecting chemical or biological substances and microorganisms for their application in the characterization of industrial products, food, effluents, etc. The discovery and utilization of microorganisms in medicine has led to revolutionary successes in the field of drug treatment. The first signs of this evolution were the discovery of penicillin, a product of a mold with antimicrobial properties, by Alexander Fleming in 1928/1929. Today, antibiotics account for about half of all drugs derived from biotechnology.

5.2. New Therapeutic Pathways

Biotechnology applied to the pharmaceutical sector encompasses all techniques that use living resources to design and produce active substances.

Associated with genetic engineering, genomics is the foundation of current research in biotechnology. It contributes to new, more rational therapeutic approaches. Indeed, understanding genes and their products, proteins, allows us to understand their roles in a given disease and to define new molecular targets for developing an appropriate treatment. The genomics of *Mycobacterium tuberculosis* has been studied to identify new drug targets and develop new vaccines against tuberculosis.

New vaccines derived from genetic engineering induce effective immune responses and avoid potential side effects; this is why vaccines against Human Immunodeficiency Virus type 1 (HIV1) have been tested in animals.

DNA vaccination (or genetic vaccine) is a new vaccine approach. It is based on introducing DNA into cellular tissues. After DNA administration, the antigen is expressed by the cells, inducing a specific immune response. Thus, two genetic vaccines against toxoplasmosis have recently been developed.

Gene therapy represents another area of research. This therapeutic approach uses genes as medicines, either to compensate for defects in a gene affected by genetic diseases or to modify cellular behavior in the case of other pathologies. It involves introducing a gene into the nucleus of a living cell to induce a therapeutic effect.

The "gene medicine" is introduced into the cell in a targeted manner using gene transfer systems called vectors:

- Viral vectors, attenuated and genetically modified viruses to include the therapeutic gene;
- Synthetic vectors, lipid compounds, polymers, DNA nanoparticles (resulting from recent advancements in nanobiotechnology);
- Bacterial vectors, recombinant bacteria capable of transferring large DNA fragments (especially in the intestinal mucosa).

Vaccines from Recombinant Bacteria

- Vaccination with the recombinant *Mycobacterium microti* vaccine increases protection against tuberculosis. This vaccine induces the immune response of T lymphocytes.
- Ten recombinant proteins derived from *Plasmodium falciparum*, the parasite responsible for malaria, are produced by *Escherichia coli*. These proteins generate antibodies in rats.

- *Brucella abortus* is a Gram-negative intracellular pathogenic bacterium that infects animals or humans through the digestive tract. An antigen from *Brucella abortus* is produced in a recombinant *Lactococcus lactis* bacterium. This is the first step toward the development of live vaccines against brucellosis that can be administered orally.
- A study is underway on cancer vaccination trials. A recombinant protein consisting of an enzyme and an antigen associated with tumors has been expressed by a recombinant *Escherichia coli* strain. When injected into tumor-bearing mice, the recombinant protein shows anti-tumor activity.
- Recent research focuses on using recombinant bacteria as vectors for therapeutic genes.
- Work has been done to transfer a therapeutic gene into the intestinal mucosa by oral administration of a genetically modified, non-pathogenic, invasive *Escherichia coli* bacterium. A similar study aims to develop a recombinant *Escherichia coli* strain as a gene transfer vector in epithelial cells of the respiratory tract. These recombinant bacteria are capable of transferring large DNA fragments and open new perspectives for gene therapy.

Vaccines from Recombinant Viruses

- Research on vaccines against Human Immunodeficiency Virus type 1 (HIV1) is ongoing: recombinant attenuated measles viruses expressing HIV1 antigens have been developed. The immunogenicity of these recombinant vaccines has been tested in animals. The goal of this research is to develop an effective pediatric vaccine simultaneously against measles and AIDS.
- The recombinant Herpes Simplex Virus type 1 (HSV1) is used as a vector for vaccines. However, the immune response after vaccination is diminished in case of HSV1 seropositivity.
- A recombinant virus expressing a stimulating molecule infects dendritic cells and thus stimulates the immune system to counteract the growth of cancer cells. It can be used in cancer immunotherapy.