Current Trends of Immune System Engineering in Healthcare Applications

K.Vivekanandan

Senior Lecturer, Kongu Polytechnic College, Perundurai.

E-mail: anandankkv@gmail.com

Abstract

Immune system engineering presents significant challenges as well as great opportunities for biomedical engineers. Human immunity is critical to both health and disease, and immune system activation plays a critical role in disease prevention. The malfunctioning of the human immune system will result in autoimmune disorders, cardiovascular disease, cancer, and other serious diseases. Immune engineering responds to the immune system's complex challenges by targeting a variety of cellular and molecular processes, such as improving antigen presentation, reviving worn-out tumour cells, engineering immune effectors and cells, and improving drug delivery to targeted immune tissues or cells. By reprogramming specific biological responses and developing technologies for early disease detection, numerous opportunities will emerge to boost the human immune system while keeping costs under control. This article discusses about the current trend of using immune engineering in healthcare.

Keywords: Immuno-engineering, immune system, biomedical engineers, tumor cells, immune response

1. Introduction

Engineering and medicine have always collaborated together to solve various problems related to healthcare in order to find solutions for various problems related to healthcare. Recent advances in mass cytometry, next-generation sequencing, and high-resolution imaging techniques have provided biomedical research and healthcare with tools that should help them advance. Immune engineering targets numerous cellular and molecular processes,

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simulating the complex nature of immune system. These processes include improving the antigen presentation, reviving worn-out T cells, engineering immune molecules and cells, enhancing drug delivery to the target immune cells or tissues, and developing new components for immunotherapy.

Immune system: A system of biological processes called the immune system protects an organism against disease. It diagnoses and reacts to a wide range of pathogens, separating them from organism's original healthy tissue including viruses, worms, cancer cells, and things like wood splinters [1].

Immunology: One of the most significant areas of medical and biological sciences is immunology, which is the study of immune system. Through a number of layers of protection, the immune system guards against infection. Diseases including cancer, allergies, and autoimmunity can develop if the immune response is not operating properly.

Immunologist: A scientist or physician who is specialized in immunology is known as an immunologist. Many immunologists do their research in a lab setting, either in academics or the industry sector.

Immunoengineering: Applying engineering principal's and algorithms to the study and development of immune system is known as immunoengineering. Immunoengineering is a crucial technique since immune system malfunction is a major factor in a number of disorders, including inflammation, cancer, autoimmune, and transplant rejection. Therefore, the therapy of these disorders depends on innate immunity and engineering techniques based drugs [2].

Understanding the function of immune system has been the focus of intensive scientific research for more than a century because it is essential in protecting one's health. In particular, the objectives have been achieved in understanding of immunological components and function over the past three decades. Almost every organ in the human body contains this extensive system of cells and proteins that are released. Our immune systems control activities ranging from pathogenic bacteria to tissue formation, playing significant roles in both homeostasis and diseases [9-11]. Parallel to these discoveries are those in the domains of genetics and cellular engineering, materials science, and immunoengineering, which were created as a result of the application of these fields to immunology. This article highlights some recent developments in the field of adaptive immune system engineering, which incorporates antibodies and T cells. The below figure 1 represents the human immune therapy

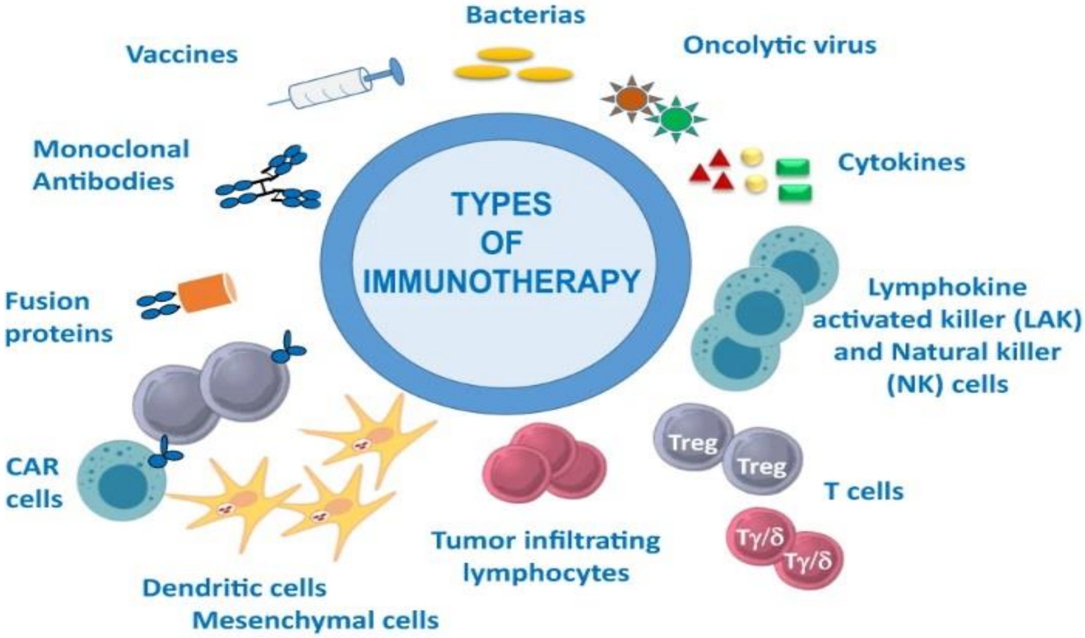

Figure 1. Types of immunotherapy

2. History of immune system

Louis Pasteur and Robert Koch, both scientists, who discovered crucial immune system functions, should have been able to regard their research as complement, but they ended up fighting.

- One of the most significant founders of **medical microbiology** was Pasteur, a French chemist and microbiologist who was born in Dole, France, on December 27, 1822, and died in Saint-Cloud on September 28, 1895.
- German physician Koch, one of the pioneers of bacteriology, was born in Germany on December 11, 1843.He identified the germs that cause cholera (1882), tuberculosis (1876), and the anthrax illness cycle (1876). (1883). Both individuals were competitors throughout their careers, probably fuelled by nationality, a language issue, criticism of one another's work, and jealousy. They both contributed to the development of the germ theories of diseases.[11]

3. Engineering in Human Immune system

The quick-acting "innate" immune systems as well as the highly-targeted “adaptive” immune system are the main immune systems of many cell types and signalling molecules

[12]. Different phenotypes of immune cells might activate to respond to the body's stresses. Exposure to a disease or its antigen is necessary for active immunity. WBCs are the primary immune cells produced by hematopoietic stem cells during the haematopoiesis process [13]. Table 1 represents the immune cells, its origin and the implementation of the same in immunology towards various applications.

Table 1. Type of human cells, origin and its functions towards immunoengineering

Cell type	**Origin of a cell**	**Functions of the cell**
Lymphoid cells	Thymus and bone marrow	Pathogens and tumors
Natural killer (NK) cells	Hematopoietic stem cells	Cells with a viral infection or tumor
T-lymphocytes	Bone marrow progenitors	Fights cancer
B-lymphocytes	Bone marrow	Creates antibody
Myeloid cells	Bone marrow	Tissue repair(skin wounds)
Mast cells	Skin, near blood vessels and lymph vessels, in nerves, and in the lungs and intestines.	Treats cancer cells
Basophils	Bone marrow	Immune body against allergens
Macrophages	White blood cell	Regenerating damaged tissue

3.1 Cancer therapy

The inborn immune system cells found in the human body is responsible for eliminating any foreign substances discovered. T cells are one of these types of cells; they eliminate malignant or undesirable cells while sparing healthy cells. Furthermore, certain cancer cells release specific antigens that the immune system cannot recognise, preventing it from attacking and curing them. Since there are multiple sources of T cell donor. The business can still use its own DNA to instruct the cell what to do, such as which malignant cell to kill, but they can also use gene editing to alter the T cell's receptor so it won't kill cells that are harmful to the patient.

Immune cells called **macrophages** explore the body for possible threats like bacteria, viruses, and cancer cells before engulfing and eliminating them. Cancerous tumours, they release chemicals that "switch" incoming macrophages from about their tumor-killing state to tumor-promoting state, which suppresses the body's immune response, promotes the blood vessel growth to supply the tumour, and aids in the metastasis of the tumour. The tumours persistently switch macrophages backward to their pro-tumor state, making it impossible to remove them from the body, induce them into their cancer form, and then return them to fight cancer.

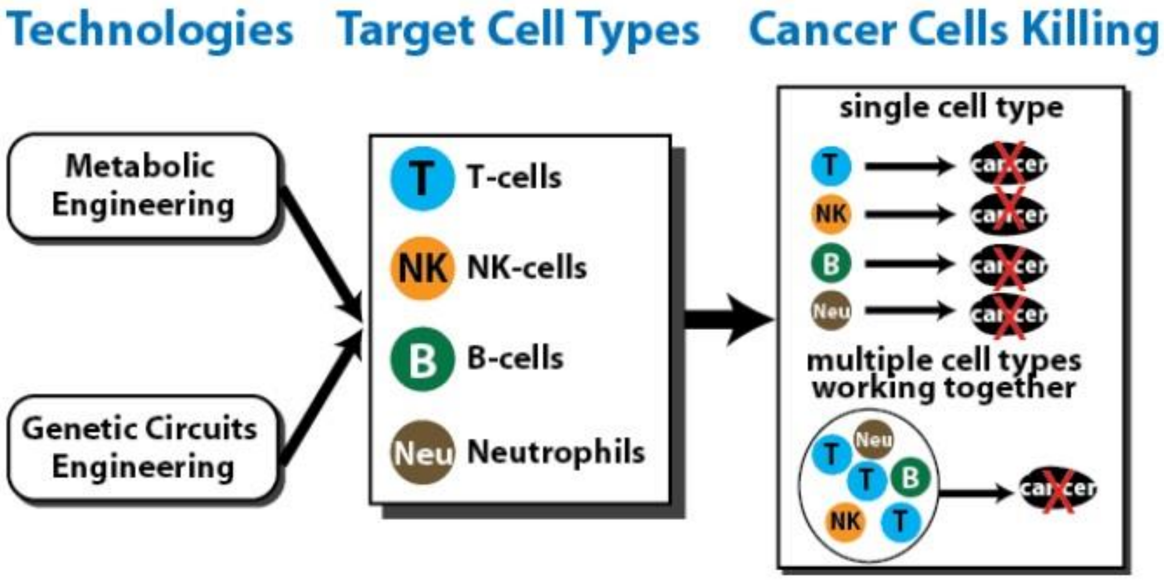

Figure 2: Technologies in fighting cancer cells [8]

Advantages: Apply nanotechnology to help medications reach immune cells inside a way that enhances the targeted anti-tumor response. Investigates how the immune system reacts to bio-materials, then use your understanding to treat cancer and promote tissue regeneration**.**

The Immunoengineering center is also looking into how to deliver immunological and other treatments directly to cancer cells using nanoparticles, which are objects 100 times smaller than a single cell. In the future, nanoparticles help biomaterials treat cancer patients.

Disadvantages: Low solubility as well as permeability, first pass metabolism, degradation by gastro intestinal flora and poor bio-availability are all issues that prevent unconscious people from taking medication.

3.2 T-cell therapy

By modifying immune cells known as T cells (a kind of white blood cell) in the lab, chimeric antigen receptor (CAR) T-cell therapy makes it possible for these cancer-fighting T cells to locate and eliminate cancer cells. Because CAR T-cell therapy involves changing the genes in T cells to enable them to fight cancer, it is occasionally referred to as a form of cell-based gene therapy. By locating proteins known as antigens on the exterior of those cells, the immune system can identify foreign substances within the body. T cells, which are immune cells, have their own specific proteins receptors that connect to foreign substances and aid in causing other immune system components to start destroying the foreign object. Cancer cells include antigens as well, but if the immune cells lack the proper receptors, they won't be able to bind towards the antigens and aid in the destruction of the cancer cells [3].

Disadvantages: The immune system can be strengthened as a result of the vast quantities of cytokines that CAR T cells have the capacity to discharge into the blood as they grow. This release's potentially harmful negative effects include: Severe nausea, vomiting, high fever and chills, trouble breathing, feeling dizzy or lightheaded, and headaches.

3.3 Tissue Engineering

Tissue engineering combines the recent developments in materials science and cell biology to enable the in vitro production of semi-synthetic tissues and organs. These tissues are made up of living cells expanded by using cell culture techniques, as well as biocompatible scaffolding material that eventually breaks down and is absorbed. The ultimate goal is to replace the damaged or sick organs with complete organs made of various tissue types. The sections that follow discuss the specific contributions of each biomaterial, delivery system, and cell transplantation to the biological signals as well as their ability to induce an immune response.

Disadvantages: Biopolymer and its compounds used in tissue engineering have a weak mechanical strength and reduced cell adhesion, which are considered as major challenges. By adding appropriate elements to alginate and alginate-based compounds, these restrictions are reduced. Alginate that has been altered by ceramics, peptides, and polymers is a viable candidate material for cell adhesion, differentiation, and proliferation.

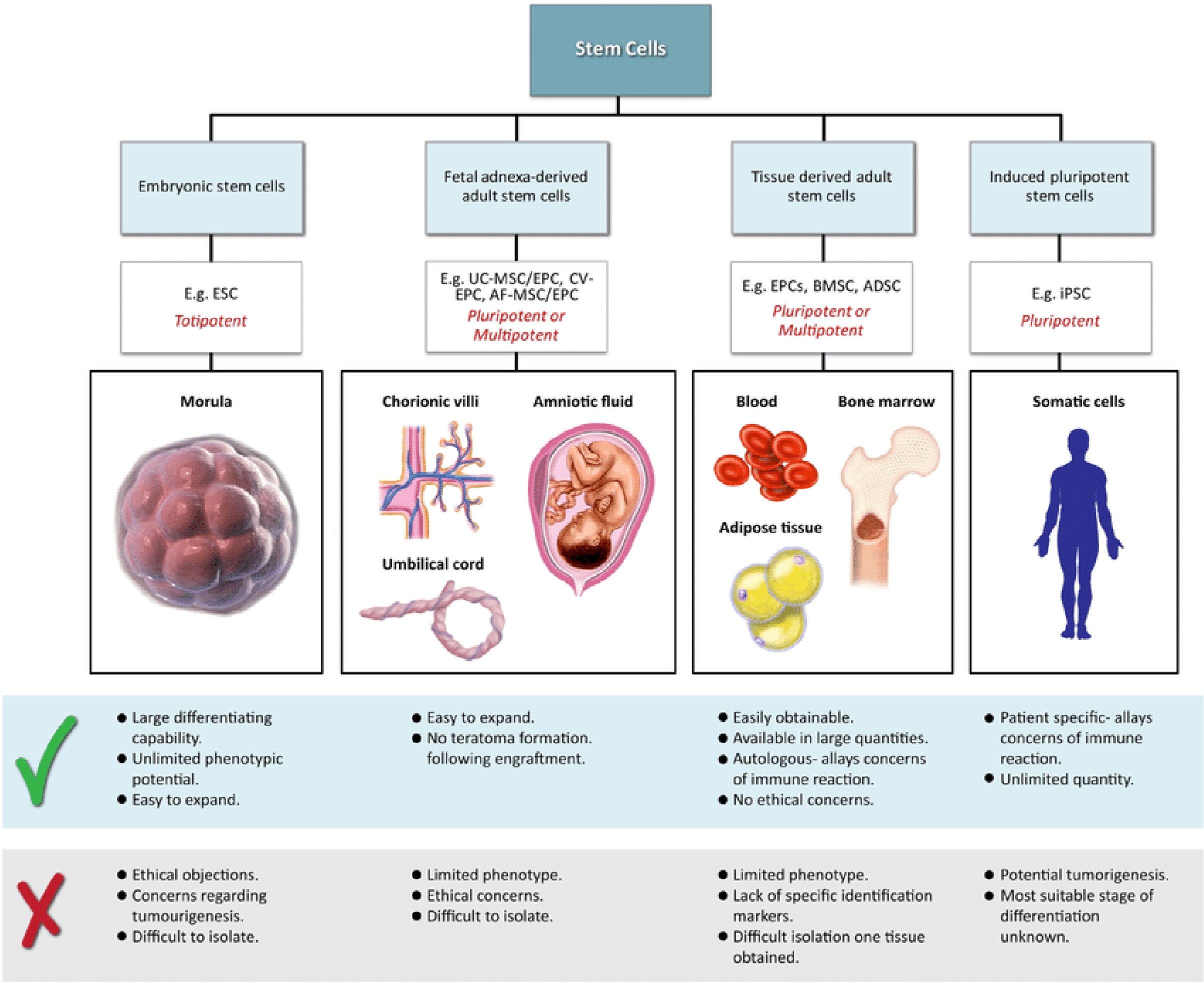

Figure 3. Advantages and disadvantages of tissue engineering [4]

3.4 Immune engineering for Type 1 diabetics

Insufficient insulin production and on-going hyperglycemia brought on by pancreatic beta-cell degeneration remain as the major cause for type 1 diabetes (T1D). In contrast to insulin injection, cell transplantation is a desirable alternative strategy. Immune rejection can be prevented by encapsulating the transplanted cells, which creates a barrier between the cells and the patient's immune system. By creating a barrier that is selectively permeable between both the hosts and the transplanted cells, cell encapsulation has the potential to limit the host's immunological reactions and the rejection of islets or T-cells. Promising methods in the field of encapsulation technology have been made possible by biomaterials, conformal nano-coatings, and modulations [5].

Disadvantages: Although patients achieve postoperative insulin independence, this method has limitations, including as a 1-3% postoperative death risk, lifelong immunosuppression, and a shortage of donor pancreas.

3.5 Immune system engineering to fight against COVID 19

Usage of biomaterials on improving COVID-19 immunotherapeutic for vaccination prevention, infection therapy, tissue healing and regeneration after infection resolution. By stimulating the growth of lengthy memories B and T cells in addition to plasma cells, which make antibodies, effective vaccinations induce long-term antigen-specific responses. It is possible to increase patient compliance and vaccination effectiveness using a number of vaccination approaches. Vaccinations can be administered nasally, pulmonary, intravenously, and subcutaneously using hydrogels, nano and micro particles, and micro needles. Using biomaterials-based engineering techniques, more potent vaccinations can be created. It is possible to create particle vaccinations that efficiently drain to lymph nodes. To offer areas for immune cell programming, the hydrogel/scaffold vaccination can also function as transient artificial lymph nodes [6].

Disadvantages

- Poor immune responses
- High viral intensity at the lung's primary infection site
- Tissue damage toward the lungs
- Reduced heart functionalities
- Raise in risk due to neuro related issues

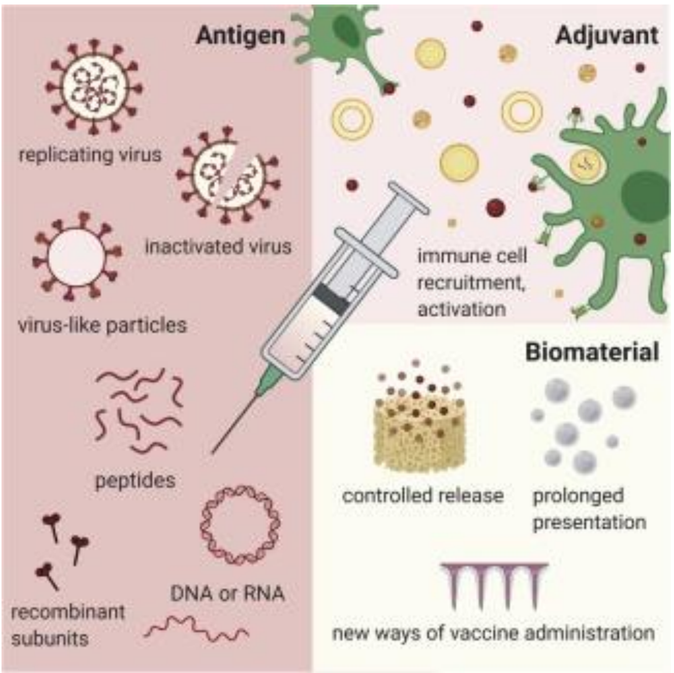

Figure 4. Immune engineering in COVID 19 vaccine case

3.6 Immunoengineering for Kid's

New advancements in paediatric vaccination are being made possible via immunoengineering and sophisticated delivery technologies. An immune reaction that lowers the infection risk and prevents disease is the aim of vaccination. Since the bulk of vaccines used low virulence organisms, which were frequently particle in origin and inherently contained the numerous and essential immune-stimulating signals, delivery techniques were initially redundant. New-borns and young infants are particularly exposed to infections with harmful microorganisms, including bacteria like Listeria spp. and Salmonella spp, viruses like the respiratory syncytial virus, herpes simplex virus and intracellular pathogens of great importance like HIV, tuberculosis, and malaria. This is because they have essentially differed and delayed T cell-mediated immunity. For the creation of paediatric vaccines, nanoparticle-based formulations may show considerable promise. Numerous promising vaccine technologies with a great deal of promise to drive innovation in paediatric vaccination have been produced as a result of advances in immunoengineering and innovative delivery mechanisms [7].

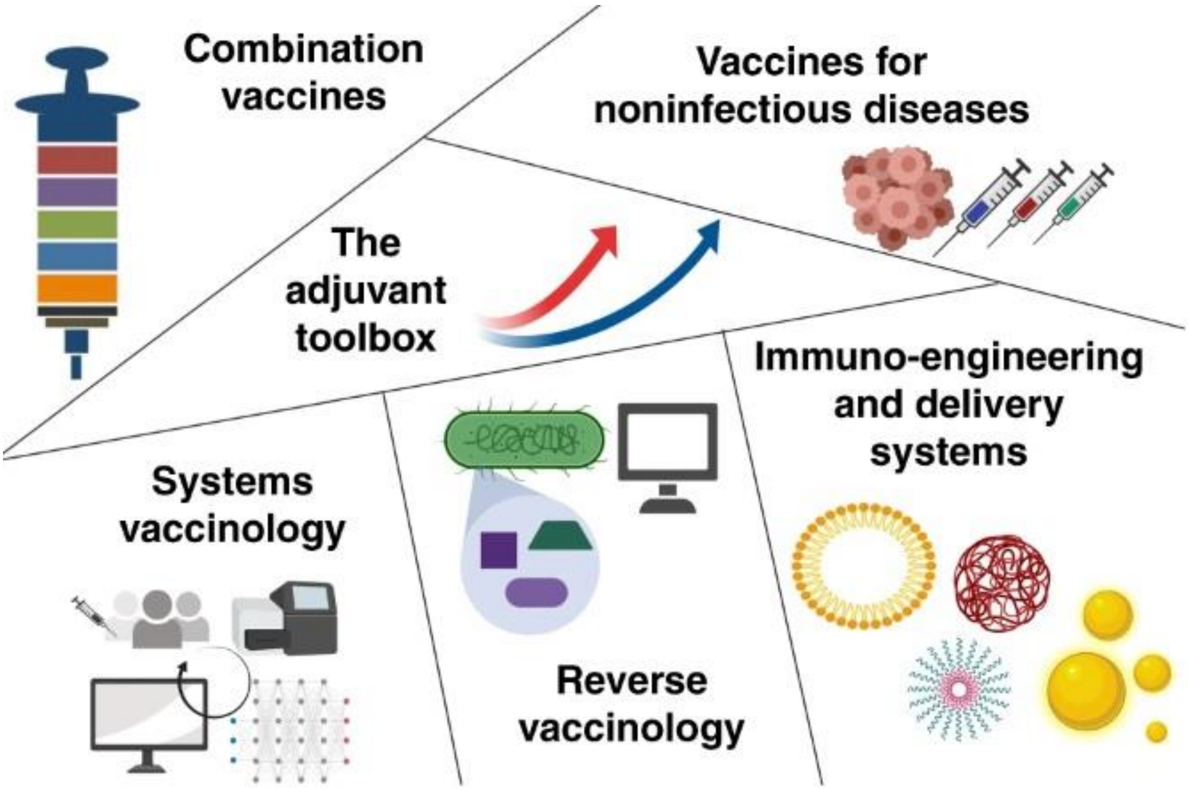

Figure 5. Paediatric vaccinology using immuno-engineering

4. Limitations in Immune system engineering

The most important phase is the limitation towards current **animal models**. Due to a variety of factors, including the use of immune compromised animals, variations in biological metabolism, transport, and variations in the tumour microenvironment, some models that may performed exceptionally well when analysing a response to therapy **may not be appropriate** to a **human patient** with the same disease.

5. Upcoming researches

The below are the few recent researches in process with immuno-engineering

- Regeneration of 3D skin via stem cell treatment
- Adaptive immunity
- Malignancies of the immune system's pathobiology
- BPTF protein's function in treating breast cancer
- Metabolism in immunity
- Cancer Immunosuppressive Mechanisms
- Vaccines

6. Conclusion

An interdisciplinary field known as immunoengineering combines engineering methods and ideas with immunological ideas to maximize the potential of an immune system. Through the quantitative analysis of immune tissues and cells and the development of novel treatment approaches, immunoengineering research seeks to understand how the immune system regulates itself and operates to prevent various diseases. This article summarizes the current and emerging trends in immune engineering for the diagnosis and treatment of various diseases emerge around the world.

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Author’s Biography

K. Vivekanandan Completed his master's degree in National Collge, Trichy. He has more than 25 years of teaching experience and 2 years of Industrial experience. Currently working as Senior Lecturer in the Departement of Chemistry at Polytechnic College, India.