8. Dendritic Cell-based Immune Therapy: Concept, Design, Present Limitations, and Future Projections

Dendritic Cell (DC)-Based Therapy as Immune Therapy in Clinical Medicine

Immune therapy seems to be a rational therapeutic choice for treating patients with immune-mediated anomalies. In some diseases, immune-related factors are primarily responsible for disease pathogenesis. Autoimmune diseases are a typical example. In addition, an immune-mediated phenomenon is related to rejection of organ transplants. Thus, immune therapy may be used for treating autoimmune diseases. Rejection of transplanted organs may be delayed or blocked by immune intervention strategies.

In addition to a direct role of immunity in disease pathogenesis, the immune responses of the hosts play critical roles during the initiation, progression, and complications of many pathological conditions such as chronic microbial infections, cancers, and allergic diseases. Microbial agents are primary etiological factors of different microbial infections. However, the clinical course of the disease depends on the immune responses of the hosts to the microbial agents. If the host immune responses against the microbial agents are adequate and purposeful, the microbes are eradicated or controlled after an acute and self-limiting infection. On the other hand, chronic infections are established in some patients because of impaired immune responses of the hosts to invading pathogens.

Genetic mutations in critical genes of the hosts, various environmental factors, and microbial agents are related to initiation of tumorigenesis. However, this is usually controlled by the host immune system, and rarely are clinically visible tumors detected. Progression of cancer indicates failure of host immune surveillance mechanisms.

Thus, either exacerbated or decreased immune responses are related to the pathogenesis of various diseases. In this context, the concept of immune therapy has surfaced. Immune therapy may be broadly divided into two categories. Some immunomodulatory drugs have been used for a long time for treatment of different pathological conditions. Corticosteroid is a representative member of this group. Different immunosuppressive and immunomodulator drugs are commercially available and are used in clinics. A second type of immune therapy may be regarded as an evolving or emerging immune therapeutic approach. This type of immune therapy is designed by evaluating the role of immune responses in different pathological conditions. Most of these immune therapeutic approaches are started as pilot studies.
Cell-based immune therapy represents one of the most promising evolving and emerging immune therapeutic approaches in clinical medicine. Among cell-based therapies, dendritic cell (DC)-based immune therapy has emerged as a means of inducing antigen-specific immunity in patients with cancers. Studies in animal models of cancers revealed that DC-based immune therapy possesses potent immunomodulatory and therapeutic efficacy against cancer. In patients with cancer, DC-based therapy has shown some therapeutic efficacy, but more potent regimens of DC-based therapy are needed in the clinic. In this chapter of the book, we mainly discuss the concept, design, present limitations, and future projections of DC-based therapy in patients with cancer as well as those with chronic viral infections.

Types of Immunity and Their Putative Roles in Host Defense

Different types of immune therapy have been applied to treat patients with different pathological conditions, but few of them could stand the test of time. There may be several underlying factors for lack of general acceptability of immune therapy, which seems to be more relevant in the context of evolving and emerging immune therapies. The final purpose of immune therapy in different pathological conditions is to modulate host immunity so that it can cure the disease or control the progression of different diseases. Immune therapy is a generalized term; however, the purpose of immune therapy should be specific and clear when this is applied to treat patients with different pathological conditions. For example, the purpose of immune therapy for patients with cancers is different from that of patients with autoimmunity. Again, the aim of immune therapy for patients with chronic microbial infections is different from immune therapies of patients with cancers and autoimmunity.

As shown in Fig. 1, different types of immune responses may be seen in vivo. Some of them may also be induced by different immune therapeutic approaches. There is lack of consensus about the nomenclature of these immune responses. Immune surveillance is an inherent property of living organisms, and this type of immunity is induced in the hosts when they are challenged with non-self agents or dangerous elements. Recent studies also indicate that hosts are usually protected from unwanted attack by autoantigens because of the presence of immune surveillance mechanisms. Immune surveillance against tumors is one of the common mechanisms that allow the host to block the growth of clinically visible tumors.

Immune ignorance is seen in some patients after being infected with some microbial agents or after development of transformed cells or precancerous cells. In spite of harboring abundant amounts of harmful agents, these subjects do not exhibit adequate levels of immunity against these agents. It seems that these agents have been either completely or partially ignored by the host immune system.

Protective immunity provides protection against various harmful agents, which can be induced by vaccines in normal individuals. Protective immunity can also be developed after development of acute inflammatory diseases following microbial infections, as is also detected in some patients with chronic viral infections spontaneously or after antiviral therapy. The nature of protective immunity in patients with tumors is not clearly defined because of incomplete understanding