Veterinary Oncology Immunotherapies

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KEYWORDS

• Veterinary immunotherapy • Antibody-based therapy • Cancer vaccines

KEY POINTS

- The immune system is generally divided into 2 primary components: the innate immune response and the highly specific but more slowly developing adaptive or acquired immune response.
- Immune responses can be further separated by whether they are induced by exposure to a foreign antigen (an active response) or if they are transferred through serum or lymphocytes from an immunized individual (a passive response).
- The ideal cancer immunotherapy agent should be able to discriminate between cancer and normal cells (ie, specificity), be potent enough to kill small or large numbers of tumor cells (ie, sensitivity), and be able to prevent recurrence of the tumor (ie, durability).
- Tumor immunology and immunotherapy are among the most exciting and rapidly expanding fields; cancer immunotherapy is now recognized as a pillar of treatment alongside surgery, radiation, and chemotherapy.

The term immunity derived from the Latin word immunitas, which refers to the legal protection afforded to Roman senators holding office. Although the immune system is normally thought of as providing protection against infectious disease, the immune system's ability to recognize and eliminate cancer is the fundamental rationale for the immunotherapy of cancer. Multiple lines of evidence support a role for the immune system in managing cancer. These include (1) spontaneous remissions in patients with cancer without treatment; (2) the presence of tumor-specific cytotoxic T cells within tumor or draining lymph nodes; (3) the presence of monocytic, lymphocytic, and plasmacytic cellular infiltrates in tumors; (4) the increased incidence of some types of cancer in immunosuppressed patients; and (5) documentation of cancer remissions with the use of immunomodulators.[1,2] With the tools of molecular biology and a greater understanding of mechanisms to harness the immune system, effective tumor immunotherapy is now a reality. This new class of therapeutics offers a more targeted and,

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therefore, more precise approach to the treatment of cancer. Cancer immunotherapy is now recognized as a pillar of treatment, alongside surgery, radiation, and chemotherapy.

TUMOR IMMUNOLOGY

Cellular Components

The immune system is generally divided into 2 primary components: the innate immune response and the highly specific but more slowly developing adaptive or acquired immune response. Innate immunity is rapid acting, although typically not very specific, and includes physicochemical barriers (eg, skin and mucosa); blood proteins, such as complement, phagocytic cells (macrophages, neutrophils, dendritic cells [DCs], and natural killer [NK] cells); and cytokines, which coordinate and regulate the cells involved in innate immunity. Adaptive immunity is thought of as the acquired arm of immunity that allows for exquisite specificity, an ability to remember the previous existence of the pathogen (ie, memory); differentiate self from nonself; and, importantly, the ability to respond more vigorously on repeat exposure to the pathogen. Adaptive immunity consists of T and B lymphocytes. The T cells are further divided into CD8 and major histocompatibility complex (MHC) class I cytotoxic helper T cells (CD4 and MHC class II), NK cells, and regulatory T (Treg) cells. B lymphocytes produce antibodies (Abs; humoral system), which may activate complement, enhance phagocytosis of opsonized target cells, and induce Ab-dependent cellular cytotoxicity. B-cell responses to tumors are thought by many investigators to be less important than the development of T-cell–mediated immunity; however, there is little evidence to fully support this notion.[3] The innate and adaptive arms of immunity are not mutually exclusive. They are linked by (1) the innate response's ability to stimulate and influence the nature of the adaptive response and (2) the sharing of effector mechanisms between innate and adaptive immune responses.

Immune responses can be further separated by whether they are induced by exposure to a foreign antigen (an active response) or if they are transferred through serum or lymphocytes from an immunized individual (a passive response). Although both approaches have the ability to be extremely specific for an antigen of interest, an important difference is the inability of passive approaches to generally confer memory. The principal components of the active or adaptive immune system are lymphocytes, antigen-presenting cells, and effector cells. Furthermore, responses can be subdivided by whether they are specific for a certain antigen or a nonspecific response whereby immunity is attempted to be conferred by upregulating the immune system without a specific target. These definitions are helpful because they allow methodologies to be more completely characterized, such as active-specific, passive-nonspecific, and so forth.

Immune Surveillance

The idea that the immune system may actively prevent the development of neoplasia is termed cancer immunosurveillance. Sound scientific evidence supports some aspects of this hypothesis,[4–7] including (1) interferon (IFN)-γ protects mice against the growth of tumors, (2) mice lacking IFN-γ receptor were more sensitive to chemically induced sarcomas than normal mice and were more likely to spontaneously develop tumors, (3) mice lacking major components of the adaptive immune response (T and B cells) have a high rate of spontaneous tumors, and (4) mice that lack IFN-γ and B or T cells develop tumors, especially at a young age.