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Immunome Research

Commentary

Relationship between Antigen-Specific and Non-Specific Immunotherapy in Cancer Treatment

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DESCRIPTION

Immunotherapy is a type of cancer treatment that helps your immune system fight cancer. Immune system helps your body to fight infections and other diseases. It consists of white blood cells and the organs and tissues of the lymphatic system. Immunotherapy is a type of biological therapy.

Historically, the goal of anticancer therapies has been to eradicate the colony-forming potential of cancer cells. The basics of treatment: surgery, chemotherapy, and radiotherapy aim to rid the host of every last cancer cell with growth potential by resection or cytotoxic death. Although progress has been made in improving therapeutic modalities, these therapies remain largely unable to eradicate malignancy once it has spread. Exploiting the potential of the immune system to eradicate advanced cancer has again come to the forefront of cancer research in recent years. The ability of the host immune system to identify and eradicate malignant cells with little systemic toxicity remains the holy grail of cancer immunotherapy.

Immunotherapy

There is an increased incidence of cancer in mice and Immuno compromised humans. Immuno-deficient rag2−/− mice develop cancer three times faster than immuno competent counterparts when exposed to carcinogens and also have higher rates of spontaneous benign and malignant tumorigenesis [1]. Similarly, immunosuppressed people such as AIDS patients or transplant patients are also at increased risk of malignancies [2], a risk that is not limited to viral tumours. Furthermore, cancer patients have been shown to have deficient circulating levels of certain immune cells compared to healthy adults [3]. The integrity of the host immune system is also associated with outcomes in patients treated with cytotoxic therapies. For example, a prospective study of squamous cell carcinoma of the head and neck treated with radiotherapy demonstrated that the level of circulating natural killer T-cells before treatment was an independent prognostic factor even after adjustment for age [4]. Patients with elevated cell levels had a 3-year overall survival rate of 92%, compared with 75% and 39% for those with intermediate and low levels, respectively. The growing evidence for the importance of the host immune response in cancer treatment and the promise of harnessing the immune system to fight cancer has not gone unnoticed. Humoral immunotherapies using monoclonal antibodies such as transtuzumab and bevacizumab have shown clinical success. However, these therapies target specific receptors on cancer cells but do little to promote the host's inherent antitumor immunity.

Antigen-specific antitumor immune responses

Another potential reason for the shortcomings of some immunotherapies is that much of the research and therapies have focused on antigen-specific immune responses. The idea of tumor-specific antigens was proposed by Burnet [5] and its existence was demonstrated in experimental animal models by Old and Boyse [6]. Since then, the concept of cancer antigens has been modified from tumor-specific antigens to tumor-associated antigens, which include inappropriately/overexpressed tissue antigens, oncofetal antigens, viral oncogenes, fusion proteins, idiotypic antigens, and altered post-translationally modified glycoproteins. In melanoma, the ability of tumor-infiltrating immune cells to recognize tumor-associated antigens and lyse malignant cells that express them has been described. These findings have been verified in various malignancies and also apply to humoral immunity.

Antigen-nonspecific immunotherapy

Although any immunotherapy will ultimately require the identification and eradication of malignant cells to be successful, some therapies focus less on inducing responses against an antigen or set of antigens and more on inducing large-scale changes that, in the ever-evolving battle between the malignancy and the host's immune system, hope the pendulum swings in favour of the immune system. These therapies may be less sensitive to the shortcomings of antigen-specific therapies. Such therapies are also known as immunomodulatory therapies and, although not antigen specific, tend to involve both the innate and adaptive parts of the immune system. These therapies may include cytokines such as interleukins and interferon's, immuno-

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stimulatory agents such as CpG oligonucleotides or BCG, receptor-targeted antibodies such as agonistic CD40 or inhibitory CTLA-4 antibodies, and enzyme inhibitors such as those targeting cyclooxygenase or indoleamine -2,3-dioxygenase.

Combination of antigen-specific and non-specific immunotherapy

One area where further understanding is needed is the role played by antigen-specific and non-specific immune responses in cancer immunotherapy. This is particularly important with regard to cytotoxic T-cell responses. Neither antigen-specific nor non-specific strategies have been widely successful by themselves. There is reason to believe that antigen-nonspecific therapy may avoid some of the pitfalls of antigen-specific therapy and that a combination of the two strategies may provide better results. The use of immuno modulators can induce innate immunity and an antigen-nonspecific T-cell response that can reduce tumor volume, increase antigen release, change the tumor microenvironment from suppressive to permissive, and induce a pro-inflammatory cytokine milieu. all of which may promote the development of antigen-specific immune responses and provide an environment where antigen-specific therapies are better able to induce and maintain long-term responses.

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