Trends in Oncology Vol 5 Issue 1 2023
DOI: 10.37155/2717–5278–0501–5

review

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Advancements in Cancer Hypnotherapy Research

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How to cite: Yuan Jia .Advancements in Cancer Hypnotherapy Research [J]. *Trends in Oncology*, 2023; vol. 5(iss. 1). DOI: 10.37155/2717-5278-0501-5

Abstract: Tumor cells can evade pursuit from the body's immune system through various channels, proliferating extensively within the body and causing harm to normal tissues. With the continuous development of the medical field and the cross-pollination of knowledge from various disciplines such as molecular biology, immunology, and oncology, immunotherapy has been continually refined. Adopting immunotherapy has the advantage of effectively killing tumor cells with fewer and milder side effects, leading to its increasingly widespread application. In comparison to treatments for solid tumors, the evaluation of efficacy in immunotherapy is relatively unique.

Keywords: Tumor; Immunotherapy; Immune evasion; Efficacy

Malignant tumors pose significant risks, and traditional therapies mainly include radiation, chemotherapy, and surgery. While these approaches can inhibit tumor progression, the effectiveness varies depending on the type and stage of the tumor, and they may also harm the overall health of the body. In clinical practice, there is a need to actively explore safe and efficient methods that impede tumor metastasis and growth while minimizing side effects[1]. Immunotherapy, involving deliberate intervention, can activate the immune system to eliminate tumor cells, enhance the body's resilience, and alleviate adverse reactions. This article provides a comprehensive overview of tumor immunotherapy.

1. Analysis of the Mechanisms of Tumor Evasion from Immune Attacks

In terms of evading immune attacks, the mechanisms involved are complex and diverse. Despite the body's inherent immune capabilities and constant immune surveillance, tumors have the potential for continuous development. The primary reasons for tumor evasion from immune attacks include the ability to escape immune surveillance[2]. The evasion mechanisms mainly include:

(1) Regarding tumor cells, the antigen presentation mechanism undergoes changes. Tumor cells may alter surface antigens through processes such as antigen loss, downregulation, and modification, allowing them to evade immune recognition. For example, malignant

melanoma can enhance Melan-A/MART-1 expression to evade T-cell attacks[3].

(2) Negative regulation of cytokines: Tumor cells can produce immunosuppressive factors, including VEGF, IL-10, IDO, and TGF-β, which hinder the activation of T cells. Additionally, Th2 cells can produce IL-13 and IL-14, weakening the tumor-clearing ability.

(3) Inhibition of immune cell subgroups: The immune-suppressive microenvironment near tumors induces the formation of MDSCs, TAMs, and Tregs[4].

(4) Defects in co-stimulatory/adhesion molecules: Inability to efficiently activate T cells leads to negative factor underexpression, including B7-H4.

(5) FasL/Fas interaction: T cells may be deficient or undergo apoptosis due to the reverse action of FasL/Fas.

2. Active Immunotherapy Approaches for Tumors

2.1 Tumor Cell Vaccines

Tumor cell vaccines involve injecting inactivated tumor cells along with corresponding immune adjuvants into the patient's body to stimulate an anti-tumor effect. This vaccine does not require complete knowledge of TAA (Tumor-Associated Antigens), TSA (Tumor-Specific Antigens), etc. All molecules present on the cells are in an exposed state, allowing the immune system to directly exert its effects and form multiple clones, such as CD4+HTL, CD8+HTL, etc. Whole-cell vaccines have poor specificity and weak immunogenicity. Through genetic engineering techniques, utilizing carriers such as retroviruses, adenoviruses, etc., a series of genes can be transduced, including co-stimulatory signal genes and tumor antigen genes. This process can enhance the immunogenicity of the tumor, regulate T cells, make them more responsive and sensitive when facing tumor antigens, and stimulate anti-tumor immune responses effectively[5]. Animal experiments have shown significant efficacy of this vaccine, demonstrating a strong anti-tumor effect.

2.2 DC-Based Tumor Vaccines

Dendritic cells (DCs) belong to professional antigen-presenting cells and have been found to play a crucial role in the body's anti-tumor mechanisms. In recent years, there has been increasing interest in DC-based tumor vaccines. The principle behind these vaccines involves cultivating DCs in vitro, expanding them using cytokines, modifying them with tumor antigens through genetic engineering or direct contact methods, generating sensitized DCs, and then infusing them back into the patient. This process induces an anti-tumor immune response[6]. Regarding tumor antigens, they are easily collected and convenient to prepare. The impact method of tumor antigen is commonly used during the clinical preparation of sensitized DCs. Currently, this vaccine is mainly used for the treatment of malignant gliomas, malignant melanomas, renal cancers, etc. DC vaccines carry various genes, such as those encoding cytokines and tumor-associated antigens. They have strong capabilities in antigen presentation, processing, and uptake, enhancing the anti-tumor efficacy[7]. In a study by Jiao Qingfang and colleagues, a recombinant adenovirus vector containing the HPV16 E6E7 gene was used to modify DC vaccines in vitro. This gene induction had a stimulating effect on cytotoxic T lymphocytes (CTLs), accelerating the apoptosis process of cancer cells and improving the efficacy of cervical cancer treatment.

2.3 Tumor Peptide Vaccines

Tumor peptide vaccines primarily utilize two therapeutic methods: one involves introducing genes into viral vectors, and the other focuses on isolation and purification. In comparison to whole-cell vaccines, peptide vaccines are more cost-effective, can be produced quickly and simply through artificial synthesis, stimulate the body, evoke specific immune responses, and generally carry a lower risk of immune suppression and autoimmune reactions. This type of vaccine includes various tumor antigens, with common examples being protein core peptides, P53 protein, CEA, heat shock proteins, etc. Scholars like Yan Xiaoli proposed using Hansen's yeast as a base, extracting B16 and gp96 to obtain gp96 tumor vaccines, which exhibit significant immunogenicity. These vaccines can activate cytotoxic T lymphocytes (CTLs), generate anti-tumor immune responses, and lay a solid foundation for vaccine preparation[8]. Due to the drawbacks of peptide vaccines, such as susceptibility to degradation, weaker immunogenicity, and relatively small molecular mass, when adopting a core matrix, it is advisable to choose low-immunogenicity amino acids with small molecular masses. For antigenic epitope monomers, typically 4-8 are selected, interlinked to form a Multiple Antigenic Peptide (MAP), which helps overcome

the aforementioned limitations and enhance vaccine effectiveness. Scholars like Liao and Tang Xudong suggest that, compared to effector cells made from heparinase, MAP exhibits stronger anti-tumor immune effects and simultaneously demonstrates safety and broad-spectrum characteristics[9].

3. Monoclonal Antibody Therapy

In the past 20 years, monoclonal antibodies have experienced rapid development. When selecting a carrier, ensuring high specificity is crucial. Monoclonal antibodies can directly deliver cytotoxic molecules to the site of the lesion, exerting a specific cytotoxic effect with a high success rate in treating tumors. Monoclonal antibodies can act on the tumor cell membrane, targeting the blockade of receptor-ligand binding, inducing apoptosis in nearby tumor cells, inhibiting receptor dimerization, interrupting signal transduction across the membrane, and exerting cytotoxic effects. In clinical treatment of non-Hodgkin's lymphoma, Rituxan can be employed[10].

4. Adoptive Immunotherapy for Tumors

Adoptive immunotherapy involves selecting appropriate immune cells to ensure the presence of anti-tumor activity, which is then infused into cancer patients. This approach not only directly attacks the tumor but also activates the body's anti-tumor immune response, thereby treating the cancer. Implementing this therapy activates various cells such as CIK, CD3AK, TIL, and LAK cells. CIK cells, classified as heterogeneous cells, are cultivated in conjunction with IFN-γ, CD3 McAb, and others. Targeting TCR and MHC, CIK cells exhibit immunoreactivity and possess restrictions. Specifically targeting T lymphocytes, CIK cells demonstrate significant anti-tumor activity, while also exhibiting limiting cytotoxic effects on NK cells[11]. Hontscha and others proposed that, compared to CD3AK, TIL, and other approaches, the use of CIK cells yields more promising results. CIK cells exhibit faster proliferation rates, a broad spectrum of tumor-killing capabilities, and strong anti-tumor activity. Even in the case of multi-drug resistant tumor cells, CIK cells maintain high sensitivity and low toxicity. Particularly when used in conjunction with dendritic cells (DC), the anti-tumor efficacy can be enhanced. In vitro experiments with Dong and others showed that, compared to CIK cells from cancer patients, CIK cells from healthy individuals demonstrate stronger tumor-killing abilities and clearer proliferative capabilities. The cytotoxicity and amplification effects of CIK cells form the foundation for anti-tumor activity. LAK cells, derived from peripheral blood mononuclear cells (PBMC), can be cultured in vitro by adding an appropriate amount of IL-2 and maintaining the culture for 4-6 days. Through induction, nonspecific cytotoxic cells can be obtained, capable of killing various tumor cells. This is particularly effective for individuals with lower sensitivity to NK and CTL. In vitro, LAK cells exhibit a broad-spectrum anti-self activity, and they can enhance their activity against allogeneic tumors. However, it is important to note that LAK cells have relatively weak killing power, and the addition of a large amount of IL-2 is required during amplification. The use of LAK cells is subject to certain limitations due to these factors. TIL (tumor-infiltrating lymphocytes) are a type of lymphocyte that can infiltrate solid tumors, including activated NK cells, T cells, and non-B and T cells. Compared to LAK cells, TILs have higher potential anti-cancer activity and generally exhibit minimal adverse reactions. Through in vitro cultivation with the addition of an appropriate amount of IL-2 to stimulate their growth, TILs can proliferate rapidly. In comparison to LAK cells, TILs demonstrate stronger tumor-killing capabilities, estimated to be 50-100 times more potent than the latter. Research suggests that the in vivo anti-tumor efficacy of TILs and LAK cells is essentially similar. CD3AK (CD3-activated killer) cells are peripheral blood mononuclear cells, and their foundation lies in anti-CD3 monoclonal antibodies. When used in conjunction with low doses of IL-2, CD3AK cells exhibit strong anti-tumor activity and can produce cytokines, thereby exerting immunomodulatory effects. Research by Hu Wei and others has shown that the use of CD3AK cells for the treatment of advanced malignant tumors results in improved immune function in patients, with favorable changes in the proportion of T cell subsets[12]. CD3AK cells are primarily cultured in vitro, requiring only a small amount of cytokines. They are easily amplified, reaching therapeutic quantities rapidly. CD3AK cells are less likely to induce toxic side effects, and they can circumvent the limitations associated with TILs and LAK cells. This approach is

cost-effective, helps prevent side effects resulting from excessive IL-2 dosage, and, when implemented after tumor radical surgery, can reduce the recurrence rate.

5. Evaluating the Efficacy of Immunotherapy

Assessing the effectiveness of immunotherapy is crucial for supporting subsequent research and treatments. Currently, for evaluating the efficacy of bone and soft tissue tumors, standards proposed by RECIST or WHO are often considered as gold standards. One month after treatment, observations are made to determine if new lesions have developed. The size of solid tumors is measured to assess the therapeutic effects [13]. However, after implementing immunotherapy, patients may experience a phenomenon known as pseudoprogression in the short term. The causative factor is not tumor growth but rather the local infiltration of immune cells before the therapeutic effects manifest. Additionally, small lesions that may have been overlooked during examination could be detected due to the influence of local infiltration. Hence, the mentioned evaluation standards have certain limitations. To address these limitations, Wolchok and others recommend the use of irRC (immune-related response criteria). When evaluating, particular attention is given to baseline/total tumor burden, observing changes to determine whether new lesions have emerged. In assessing efficacy, emphasis should be placed on both short-term and long-term outcomes. Apart from evaluating tumor efficacy and monitoring adverse reactions, considerations should also include clinical benefits and quality of life. Strengthening tumor diagnosis through the examination of tumor markers enhances specificity and sensitivity. By examining tumor markers before and after immunotherapy, prognosis can be assessed. In a study by Du Chunjuan and others, patients receiving GVAX treatment showed a significant decrease in Treg content when examined.

6. Conclusion

In conclusion, compared to traditional therapies, tumor immunotherapy demonstrates remarkable efficacy with strong specificity and minimal side effects. From a theoretical perspective, the benefits of immunotherapy are evident for various types of tumors, particularly in the early stages where the body's immune function is robust, leading to more prominent effects. Even in the advanced stages, immunotherapy can effectively suppress disease progression. However, relying solely on this approach may not eradicate tumors, necessitating combination with other modalities. Subsequent research should delve into areas such as proteomics, bioinformatics, and genetic aspects to enhance the therapeutic effects of immunotherapy.

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