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EDITORIAL

Tumor immunotherapy: A crucial area for immediate focus

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Recent years have seen significant breakthroughs in tumor immunotherapy, with the treatment method offering numerous cancer patients a renewed prospect of survival, with the treatment method offering a renewed prospect of survival to numerous cancer patients. The therapeutic armory of immunotherapy comprises a variety of medications, including immune checkpoint inhibitors, drugs related to adoptive cell therapy, cancer vaccines, and cytokine drugs. The mechanism of action of immunotherapy involves activating the immune system to target and destroy tumor cells, a process that can be precise and effective in minimizing damage to normal tissues. The broad spectrum of immunotherapy applications, encompassing numerous tumor types, has a significant advantage over other therapeutic modalities. Furthermore, the capacity for combination therapy, in which immunotherapy is utilized with other treatments such as radiotherapy and chemotherapy, further enhances the therapeutic outcomes. Despite the evident benefits of immunotherapy, considerable challenges must be addressed to ensure its optimal efficacy and broad application in cancer treatment. These challenges will impede the enhancement of therapeutic efficacy and hinder its application across a broader range of patient demographics.

A salient feature of immunotherapy is its heterogeneity in terms of efficacy among patients, with some demonstrating notable responses while others exhibit minimal or no response. To illustrate this point, a survey of 27 elderly patients with advanced tumors who underwent immunotherapy revealed that 7.4% experienced complete remission, 48.1% experienced partial remission, 18.5% were in stable condition, and 25.9% experienced disease progression.[1] This individual variation may be related to the tumor microenvironment heterogeneity, the state of the patient's immune system, and the tumor mutational load.

In addition to the heterogeneity of efficacy outcomes, a significant challenge confronting immunotherapy is the occurrence of immune-related adverse events. The therapeutic modality of immunotherapy involves activating the patient's immune system to target tumor cells. However, this process may result in the immune system's misdirected attack on normal tissues, leading to immune-related adverse events. These adverse reactions have the potential to affect multiple organ systems in the body, including the skin, endocrine, cardiovascular, pulmonary, hepatic, renal, gastrointestinal, musculoskeletal, and neurological systems, and can occur during treatment or after discontinuation of the drug.[2] Adverse reactions of this nature have the potential to be life-threatening in severe cases. Effectively managing such reactions without compromising efficacy is a significant clinical challenge.

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Immunotherapy has proven to be highly efficacious in many cancer patients; however, the phenomenon of drug resistance is widespread, with tumor cells often evading immune cell attacks through various mechanisms. Both primary and adaptive resistance arise from a combination of intrinsic and extrinsic factors. Intrinsic factors include antigen deletion, antigen presentation abnormality, genetic alterations leading to T-cell rejection, or insensitivity to T-cells. Extrinsic factors encompass inhibitory immune cells, immune checkpoint molecules, and immune-suppressing cytokines within the tumor microenvironment. Acquired resistance can additionally manifest as the loss of T-cell function, downregulation of tumor antigen expression, mutations that hinder T-cell recognition, and escape mutations in tumor cells, amongst others.[3] Developing effective strategies to overcome drug resistance and prolong progression-free survival in patients represents a significant research direction with considerable potential for future advances.

In recent years, there has been a surge in research focusing on combining immunotherapy and other therapeutic modalities, yielding promising. Integrating nanomedicine, radiotherapy, and immunotherapy has shown positive outcomes, though it must be noted that this approach has its challenges. These challenges include the intricate physicochemical properties of nanoparticles, the complexity of assessing their distribution, metabolism, and toxicity *in vivo*, and their susceptibility to clearance by the reticuloendothelial system. Additional issues include reduced bioavailability of tumor sites, difficulties in tumor targeting and penetration, nanoparticle toxicity, and differences between pre-clinical models and patient tumors. Furthermore, challenges persist regarding the appropriate timing of radiotherapy and immunotherapy, determining optimal radiotherapy dosing, the direct effects of radiotherapy on T-cells, and the identification of biomarkers for predicting patient response to combination therapy.[4,5] Addressing these issues will require further basic and clinical research.

Biomarkers play a significant role in the immunotherapy of tumors, serving as crucial tools for treatment planning and predicting treatment response and prognosis. However, the currently available biomarkers (e.g., programmed death-ligand 1 expression and tumor mutation load) have limitations that prevent them from fully meeting clinical needs. Therefore, there is a clear need to develop more definitive biomarkers to enhance the efficacy of immunotherapy for patients with tumors.

The elevated manufacturing expenses associated with immunotherapy medications contribute to their high cost, thereby imposing a substantial financial strain on patients. This high cost significantly impacts the broad utilization of these medications, influencing patients' treatment options. Many patients lack access to these advanced treatments in regions with limited resources. The reduction of treatment costs, the enhancement of accessibility for a broader patient population, and the improvement of immunotherapy accessibility are crucial issues that necessitate consideration.

Immunotherapy has precipitated a paradigm shift in managing tumors, yet numerous challenges persist. Resolving these issues necessitates a multifaceted collaborative effort encompassing basic research, clinical practice, drug development, and policy support. We urge research institutions, pharmaceutical companies, and government agencies worldwide to collaborate to promote the advancement of immunotherapy, thereby extending hope to more patients.

Conflict of interest

Xianbin Kong is an Editorial Board Member of this journal but was not in any way involved in the editorial and peer-review process conducted for this paper, directly or indirectly. Separately, other authors declared that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

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