REVIEW ARTICLE

An Overview of Cancer Immunotherapy

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Abstract:

Cancer immunotherapy has emerged as a promising approach in the field of oncology, revolutionizing the landscape of cancer treatment. Unlike traditional therapies such as chemotherapy and radiation, which directly target cancer cells, immunotherapy utilizes the body's immune system to recognize and destroy cancer cells. This approach capitalizes on the inherent ability of the immune system to distinguish between healthy and cancerous cells, thereby offering a more targeted and potentially less toxic treatment option. Various strategies have been developed to harness the immune response against cancer, including immune checkpoint inhibitors, adoptive cell therapy, cancer vaccines, and cytokine therapy. These therapies aim to enhance the anti-tumor immune response or overcome mechanisms by which tumors evade immune surveillance. Despite significant advancements, challenges remain, including immune-related adverse events, resistance mechanisms, and identifying predictive biomarkers to guide treatment selection. Moreover, the efficacy of immunotherapy can vary widely among different cancer types and individual patients. Ongoing research efforts are focused on elucidating the complex interactions between the immune system and cancer cells, refining existing immunotherapeutic approaches, and developing novel strategies to overcome resistance and improve patient outcomes.

Keywords: Immunotherapy; Adoptive cell therapy; Cancer vaccines; Cytokine therapy

1. Introduction

In the nineteenth century, pioneers in medical science laid the groundwork for the revolutionary concept of employing the immune system as a therapeutic weapon against neoplastic diseases. Notably, Wilhelm Busch and Friedrich Fehleisen were among the first to document an epidemiological association between immunological status and cancer. However, it was William Coley who garnered the moniker "Father of Cancer Immunotherapy" for his groundbreaking work. [1-3] In 1909, Paul Ehrlich proposed a seminal theory suggesting that the immune system continuously detects and eliminates cancerous cells. Parallel to Ehrlich's insights, the "cancer immunosurveillance" theory, independently postulated by Sir Frank Macfarlane Burnet and Lewis Thomas, posited that the immune system possesses a mechanism for identifying and targeting tumor-associated neoantigens, akin to rejecting foreign grafts.[4-7] Although the precise mechanism remained elusive initially, clinical observations of melanoma regression in individuals with autoimmune conditions and successful immune responses upon transferring immune cells into tumor-bearing mice provided compelling evidence. [8]

The immune system, comprising intricate networks of lymphoid tissues, B and T cells, and cytokines like interferons and colonystimulating factors, operates as a distributed system spanning various organs and tissues, including lymph nodes. However, cancer cells employ diverse immune evasion tactics, such as recruiting suppressive myeloid cells and T regulatory cells (Tregs), to establish immunosuppressive microenvironments.[9-11] This review explores several strategies in cancer immunotherapy, including the application of monoclonal antibodies, vaccinations, immune checkpoint inhibitors (ICIs), adoptive cell transfer, and cytokines. These approaches aim to overcome the complexities of immune tolerance mechanisms employed by tumors, thus enhancing the immune system's ability to recognize and eliminate cancer cells.

2. Cancer Immunotherapy

The cornerstone of cancer immunotherapy lies in the concept that, when appropriately activated, the immune system possesses the capability to detect and eradicate malignant cells. Acting as a sophisticated network comprising organs, tissues, and cells, the immune system serves as the body's defense against various threats, including cancer cells. [12] However, tumors often develop mechanisms to evade immune detection, posing significant challenges in cancer treatment. The objective of immunotherapy is to counteract



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these evasion tactics and enhance the immune system's ability to combat cancer. [13] Cancer immunotherapy encompasses diverse modalities, each targeting specific aspects of immune function, with the aim of bolstering the body's natural defenses against cancer

2.1. Cancer Vaccine

Cancer vaccines, at the forefront of cancer immunotherapy, capitalize on the immune system's ability to recognize and combat cancer cells. These vaccines stimulate immune responses against tumor-associated antigens (TAAs) or neoantigens, training the immune system to identify and attack cancer cells bearing these markers [14, 15]. Types of cancer vaccines include peptide-based vaccines, dendritic cell vaccines, and whole-cell vaccines, each leveraging distinct strategies to provoke anti-tumor immunity. While some cancer vaccine trials have shown success in terms of prolonged survival and positive outcomes, challenges persist, including tumor heterogeneity and immune evasion mechanisms. Combining cancer vaccines with other immunotherapies, such as checkpoint inhibitors and CAR-T cell therapy, presents a synergistic approach for enhanced efficacy [16]. Personalized cancer vaccines, tailored to individual genetic and immunological profiles, emerge as a promising avenue. Advances in identifying predictive biomarkers for vaccine response contribute to refining personalized treatment strategies. Next-generation vaccine technologies, including RNA-based and viral vector vaccines, showcase ongoing efforts to broaden the applicability and improve the effectiveness of cancer vaccines. Cancer vaccines, with their potential to harness the immune system against cancer, contribute significantly to the multifaceted landscape of cancer immunotherapies shape a promising trajectory in the fight against cancer.

2.2. CAR-T cell Therapy

Auto-T cell remedy, a zenith of cancer immunotherapy, involves rooting a case's T cells and genetically modifying them to express fantastic antigen receptors(buses). These buses enable T cells to fete and target specific cancer cell antigens with remarkable perfection. Clinical successes are most pronounced in hematological cancers, demonstrating unknown remittals and cures in leukemia and carcinoma cases. [20] Despite these achievements, challenges persist, particularly in applying Auto-T remedy to solid excrescences. Ongoing exploration explores strategies to enhance its efficacity in this environment. Safety enterprises, similar to cytokine release pattern (CRS) and neurological venom, demand scrupulous operation approaches and nonstop enhancement. Understanding mechanisms of resistance, including antigen loss and immunosuppressive microenvironments, is pivotal. Experimenters are developing innovative strategies, like binary-targeted Auto-T cells, to overcome resistance and enhance treatment issues [21]. Integration with other immunotherapies and traditional treatments in combination with curatives further broadens the remedial diapason. individualized Auto-T remedy is consummate, acclimatizing treatments to individual case biographies. relating prophetic biomarkers for treatment response contributes to a more targeted approach. Next-generation Auto-T technologies, similar to armored and commutable Auto-T cells, pledge to further upgrade perfection and effectiveness in cancer treatment. In conclusion, Auto-T cell remedy exemplifies a transformative force in cancer treatment. Its success in hematological cancers and ongoing exploration addressing challenges emphasize its implicit to reshape the oncological geography [22]. As substantiated and perfectionacquainted curatives continue to evolve, Auto-T cell remedy emerges as a lamp of a stopgap in the fight against cancer, offering unknown possibilities for cases and clinicians.

2.3. Checkpoint blockers

Checkpoint inhibitors (PD-1, PD-L1, or CTLA) target immune checkpoints that cancer cells use to evade detection and evade detection. The immune system normally responds to these immune checkpoints, but checkpoint inhibitors disrupt the mechanisms that reactivate the immune system, leading to new immune responses. Combination therapies combine checkpoint inhibitors for synergy effects. Patients continue to respond well to checkpoint inhibitors, with durable responses and increased survival rates across a variety of cancers [23]. Combination therapies also integrate with traditional treatments such as chemotherapy, improving outcomes. More research is being conducted to identify biomarkers that predict patient response and to broaden the applicability of checkpoint inhibitors across diverse cancers. By tailoring treatments based on patient profiles, there is hope for more targeted and effective cancer therapies. Checkpoint blockers continue to revolutionize cancer immunotherapy. Their transformative impact is undeniable

2.4. Combination therapies

Cancer immunotherapy has witnessed a paradigm shift with the emergence of combination therapies, strategically integrating different approaches to potentiate the immune system's ability to combat cancer. The rationale lies in addressing tumor heterogeneity and enhancing the durability of treatment responses. Pairing PD-1/PD-L1 inhibitors with CTLA-4 inhibitors demonstrates exceptional efficacy, leveraging distinct pathways to unleash a more potent immune response. Integrating immunotherapy with traditional treatments, such as chemotherapy or radiation, enhances the overall anti-cancer effect by creating a favorable microenvironment. Combining CAR-T cell therapy with checkpoint inhibitors presents a multi-faceted assault on cancer, leveraging the precision of CAR-T cells and the broader immune activation from checkpoint inhibitors [24]. Administering cancer vaccines

alongside checkpoint inhibitors primes the immune system, amplifying the anti-tumor activity. Overcoming resistance remains a challenge, and combination therapies, like checkpoint inhibitors with targeted therapies, aim to circumvent resistance mechanisms. Personalized approaches consider individual patient profiles, optimizing treatment precision and selecting combinations based on predictive biomarkers for response [25]. While promising, combination therapies bring challenges, including heightened risks of immune-related adverse events. Ethical considerations, ensuring equitable access, informed consent, and addressing potential disparities, are integral to responsible advancement. Ongoing research explores novel combinations, incorporating emerging technologies like oncolytic viruses, microbiome modulation, and advanced delivery systems. Focusing on patient-centric approaches involves considering overall well-being, quality of life, and long-term outcomes, emphasizing a holistic perspective. In conclusion, the evolution of combination therapies signifies a transformative era in cancer immunotherapy, bringing us closer to more effective and personalized interventions against a diverse array of malignancies

3. Challenges of Immunotherapy

Cancer immunotherapy, while transformative, confronts several challenges that necessitate careful consideration for the advancement of the field. The emergence of resistance mechanisms in tumors poses a formidable barrier, demanding a deeper understanding of the intricate interactions between cancer cells and the immune system. Patient variability in treatment responses underscores the need for personalized approaches, calling for the identification of reliable predictive biomarkers. The occurrence of immune-related adverse events accentuates the delicate balance required to maximize therapeutic efficacy while minimizing side effects [24, 25]. Overcoming the success achieved in hematological cancers compared to solid tumors remains a persistent challenge, requiring innovative strategies to enhance the effectiveness of immunotherapy in diverse cancer types. The immunosuppressive tumor microenvironment and the optimization of combination therapies present further hurdles, emphasizing the ongoing need for refined treatment strategies. Beyond challenges, future directions in cancer immunotherapy offer promising avenues, such as personalized treatments, exploration of next-generation immune targets, sophisticated combination strategies, advancements in cancer vaccines, integration of artificial intelligence, overcoming resistance, early-stage application of immunotherapy, and fostering global collaboration [26, 27]. Through a concerted effort to address challenges and explore innovative avenues, the future of cancer immunotherapy holds great potential, offering renewed hope in the relentless fight against cancer.

4. Conclusion

In conclusion, cancer immunotherapy stands as a forefront revolutionary treatment, utilizing the body's innate defense system to combat cancer. The transition from conventional methods to harnessing the immune system has yielded remarkable successes, introducing therapies such as checkpoint inhibitors, CAR-T cell therapy, and cancer vaccines. However, moving forward presents its share of challenges, including resistance mechanisms, patient variability, and the imperative for vigilant management of immune-related adverse events. As we confront these hurdles, the future of cancer immunotherapy appears promising, with personalized treatments, innovative combination approaches, advancements in vaccine technologies, and the integration of artificial intelligence poised to reshape the landscape. The ongoing commitment to surmounting challenges and exploring new frontiers reflects a collective dedication to enhancing outcomes for cancer patients worldwide. Cancer immunotherapy, with its transformative potential, remains a beacon of optimism, ushering in a new era of hope and progress in the relentless fight against cancer.

References

- Schuster M, Nechansky A, Kircheis R. Cancer immunotherapy. Biotechnology Journal: Healthcare Nutrition Technology. 2006 Feb;1(2):138-47.
- [2] Dillman RO. Cancer immunotherapy. Cancer biotherapy & radiopharmaceuticals. 2011 Feb 1;26(1):1-64.
- [3] Mellman I, Coukos G, Dranoff G. Cancer immunotherapy comes of age. Nature. 2011 Dec 22;480(7378):480-9.
- [4] Farkona S, Diamandis EP, Blasutig IM. Cancer immunotherapy: the beginning of the end of cancer?. BMC medicine. 2016 Dec;14(1):1-8.
- [5] Esfahani K, Roudaia L, Buhlaiga NA, Del Rincon SV, Papneja N, Miller WH. A review of cancer immunotherapy: from the past to the present, to the future. Current Oncology. 2020 Apr;27(s2):87-97.
- [6] Sarella PN, Thammana PK. Potential applications of Folate-conjugated Chitosan Nanoparticles for Targeted delivery of Anticancer drugs. Research Journal of Pharmaceutical Dosage Forms and Technology. 2023 Oct 1;15(4):281-8.
- [7] Fukumura D, Kloepper J, Amoozgar Z, Duda DG, Jain RK. Enhancing cancer immunotherapy using antiangiogenics: opportunities and challenges. Nature reviews Clinical oncology. 2018 May;15(5):325-40.
- [8] Lesterhuis WJ, Haanen JB, Punt CJ. Cancer immunotherapy-revisited. Nature reviews Drug discovery. 2011 Aug;10(8):591-600.

- [9] Martin JD, Cabral H, Stylianopoulos T, Jain RK. Improving cancer immunotherapy using nanomedicines: progress, opportunities, and challenges. Nature Reviews Clinical Oncology. 2020 Apr;17(4):251-66.
- [10] Baxevanis CN, Perez SA, Papamichail M. Cancer immunotherapy. Critical reviews in clinical laboratory sciences. 2009 Aug 1;46(4):167-89.
- [11] Mannaa S, Lakshmia US, Racharlaa M, Sinhab P, Kanthala LK, Kumara SP. Bioadhesive HPMC gel containing gelatin nanoparticles for intravaginal delivery of tenofovir. Journal of Applied Pharmaceutical Science. 2016 Aug 30;6(8):022-9.
- [12] Gajewski TF. Cancer immunotherapy. Molecular oncology. 2012 Apr 1;6(2):242-50.
- [13] Tan S, Li D, Zhu X. Cancer immunotherapy: Pros, cons and beyond. Biomedicine & Pharmacotherapy. 2020 Apr 1;124:109821.
- [14] Posinasetty B, Madhu C, Galgatte UC, Kommineni S, Basavaraj H, Rao BA, Narla D, Ande SN. Design and Evaluation of Polyherbal Nanogel for The Treatment of Rheumatoid Arthritis. Journal of Advanced Zoology. 2023 Sep 4;44.
- [15] Whiteside TL, Demaria S, Rodriguez-Ruiz ME, Zarour HM, Melero I. Emerging opportunities and challenges in cancer immunotherapy. Clinical Cancer Research. 2016 Apr 15;22(8):1845-55.
- [16] McNutt M. Cancer immunotherapy. Science. 2013 Dec 20;342(6165):1417-.
- [17] Christofi T, Baritaki S, Falzone L, Libra M, Zaravinos A. Current perspectives in cancer immunotherapy. Cancers. 2019 Sep 30;11(10):1472.
- [18] Davis ID. An overview of cancer immunotherapy. Immunology and cell biology. 2000 Jun;78(3):179-95.
- [19] Hegde PS, Chen DS. Top 10 challenges in cancer immunotherapy. Immunity. 2020 Jan 14;52(1):17-35.
- [20] Stagg J, Johnstone RW, Smyth MJ. From cancer immunosurveillance to cancer immunotherapy. Immunological reviews. 2007 Dec;220(1):82-101.
- [21] Goldberg MS. Improving cancer immunotherapy through nanotechnology. Nature Reviews Cancer. 2019 Oct;19(10):587-602.
- [22] Kruger S, Ilmer M, Kobold S, Cadilha BL, Endres S, Ormanns S, Schuebbe G, Renz BW, D'Haese JG, Schloesser H, Heinemann V. Advances in cancer immunotherapy 2019–latest trends. Journal of Experimental & Clinical Cancer Research. 2019 Dec;38(1):1-1.
- [23] Voena C, Chiarle R. Advances in cancer immunology and cancer immunotherapy. Discovery medicine. 2016 Feb 26;21(114):125-33.
- [24] Liu M, Guo F. Recent updates on cancer immunotherapy. Precision clinical medicine. 2018 Sep 1;1(2):65-74.
- [25] Irvine DJ, Dane EL. Enhancing cancer immunotherapy with nanomedicine. Nature Reviews Immunology. 2020 May;20(5):321-34.
- [26] Melief CJ. Cancer immunotherapy by dendritic cells. Immunity. 2008 Sep 19;29(3):372-83.
- [27] Ribas A, Wolchok JD. Cancer immunotherapy using checkpoint blockade. Science. 2018 Mar 23;359(6382):1350-5.

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