Insights of Pharmatech, 1 (1), 2025, 50-52.
Available at amepurvapub.com

Insights of Pharmatech
Official Journal of Amepurva Forum

SHORT REVIEW

New Frontiers In Immunotherapy For Cancer Treatment

Ganesh Sonawane[1*], Kajal Pansare[1], Chandrashekhar Patil[1], Sunil Mahajan[1], Deepak Sonawane[1]
[1]*Divine College of Pharmacy, Satana Dist. Nashik-423301, Maharashtra (India)*
**Corresponding author: gbsonawane8@gmail.com*
Received on: 01/12/2024 Accepted on: 20/12/2024 Published on: 26/03/2025

ABSTRACT

Cancer immunotherapy has revolutionized oncology by leveraging the immune system's ability to target and eliminate cancer cells. This review explores the latest advancements in immunotherapy, including immune checkpoint inhibitors, CAR-T cell therapy, bispecific antibodies, oncolytic viruses, and cancer vaccines. It also highlights the emerging role of natural killer (NK) cell therapy and discusses strategies to overcome challenges such as tumor heterogeneity, immunosuppressive microenvironments, and therapy-related toxicities. Additionally, the review emphasizes future directions in combination therapies, biomarker discovery, gene editing, and cost-effective solutions to improve accessibility. These innovations hold the potential to redefine cancer care, offering hope for improved survival and quality of life for patients worldwide.

KEYWORDS: Cancer immunotherapy, CAR-T cell therapy, Bispecific antibodies, Oncolytic viruses, Cancer vaccines, Tumor microenvironment

INTRODUCTION

Cancer immunotherapy has fundamentally transformed oncology by harnessing the immune system's natural ability to combat malignancies. Unlike conventional treatments such as chemotherapy and radiation, which often have broad systemic effects, immunotherapy offers targeted mechanisms that improve specificity, reduce off-target toxicity, and enhance long-term remission. This article highlights the latest advancements in immunotherapy, including immune checkpoint inhibitors, CAR-T cell therapy, and emerging approaches.

Immune Checkpoint Inhibitors: Revolutionizing Cancer Treatment

Immune checkpoints, such as programmed death-1 (PD-1), programmed death-ligand 1 (PD-L1), and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), are crucial regulators of immune responses. Tumors exploit these checkpoints to evade immune surveillance.

- **Anti-PD-1/PD-L1 Agents**: Drugs like pembrolizumab and nivolumab inhibit PD-1/PD-L1 interactions, reactivating T cells to target tumors. These therapies have shown durable responses in melanoma, NSCLC, and renal cell carcinoma. (1, 2)

Anti-CTLA-4 Agents: Ipilimumab, an anti-CTLA-4 antibody, was one of the first checkpoint inhibitors approved for metastatic melanoma. It blocks CTLA-4, enabling enhanced T-cell activation and proliferation. (3)

Despite their success, many patients develop resistance, either intrinsic or acquired. Ongoing research focuses on overcoming resistance through combination therapies, such as pairing ICIs with chemotherapy, radiation, or other immune-modulating agents.(4)

CAR-T Cell Therapy: Engineering the Immune System

Chimeric Antigen Receptor T-cell (CAR-T) therapy involves genetically engineering a patient's T cells to express receptors that target specific tumor antigens.

- **Success in Hematologic Malignancies**: CAR-T therapies like tisagenlecleucel (Kymriah) and axicabtagene ciloleucel (Yescarta) have demonstrated groundbreaking efficacy in treating B-cell malignancies, including acute lymphoblastic leukemia (ALL) and diffuse large B-cell lymphoma (DLBCL). (5, 6)

Challenges in Solid Tumors: Expanding CAR-T therapy to solid tumors is complex due to factors like immunosuppressive microenvironments, antigen heterogeneity, and poor T-cell trafficking to tumor sites. Researchers are exploring innovative designs, such as dual-targeting CARs and armored CAR-T cells that resist tumor-mediated immunosuppression [7].

EMERGING MODALITIES IN CANCER IMMUNOTHERAPY

1. Bispecific Antibodies

Bispecific antibodies are engineered to simultaneously bind tumor antigens and T cells, promoting immune-mediated cytotoxicity.

Clinical Success: Blinatumomab, a bispecific T-cell engager (BiTE), has shown remarkable activity in B-cell precursor ALL by linking CD19 on tumor cells to CD3 on T cells [8].

2. Oncolytic Viruses

These are genetically modified viruses designed to selectively infect and kill cancer cells while stimulating systemic anti-tumor immunity.

Example: Talimogene laherparepvec (T-VEC), an oncolytic herpes simplex virus, is approved for melanoma treatment. It not only induces tumor lysis but also enhances antigen presentation, boosting T-cell responses. (9)

3. Cancer Vaccines

Therapeutic vaccines aim to prime the immune system against tumor-specific or associated antigens.

Proven Models: The HPV vaccine demonstrates efficacy in preventing cervical cancer by targeting high-risk human papillomavirus strains. Efforts are underway to develop vaccines for other cancers, such as prostate and breast cancers. (10)

4. Natural Killer (NK) Cell Therapy

NK cells, a critical component of innate immunity, can target tumor cells without prior sensitization.

Advancements: Efforts to expand and engineer NK cells, including CAR-NK cells, are enhancing their therapeutic potential in hematologic and solid cancers. (11)

CHALLENGES IN IMMUNOTHERAPY

While immunotherapy has transformed cancer care, several challenges remain:

1. **Tumor Heterogeneity**: Genetic and phenotypic variability within tumors can limit the effectiveness of therapies targeting specific antigens.
2. **Immunosuppressive Microenvironment**: Tumor-associated factors, such as regulatory T cells (Tregs) and myeloid-derived suppressor cells (MDSCs), dampen immune responses. (12)
3. **Toxicity**: Immune-related adverse events (irAEs), such as colitis, pneumonitis, and endocrinopathies, pose significant management challenges.

Cost and Accessibility: High costs of treatments like CAR-T therapy and checkpoint inhibitors limit global accessibility. (13)

FUTURE DIRECTIONS

To address these challenges, research is exploring several promising avenues:

- **Combination Therapies**: Combining ICIs with CAR-T therapy, oncolytic viruses, or targeted therapies may enhance efficacy.
- **Biomarkers**: Identifying predictive biomarkers, such as tumor mutational burden (TMB) and PD-L1 expression, can guide patient selection for immunotherapy.
- **Gene Editing**: Techniques like CRISPR are being used to engineer more effective immune cells and overcome resistance mechanisms.

Affordable Solutions: Developing cost-effective manufacturing processes for cell-based therapies will improve accessibility worldwide.

CONCLUSION

Immunotherapy represents a paradigm shift in cancer treatment, offering hope for durable responses and improved survival rates. The rapid evolution of technologies, from checkpoint inhibitors to CAR-T cells and emerging modalities, underscores the potential for even greater advances in the fight against cancer. Collaborative efforts in research, clinical practice, and policy-making will ensure these innovations benefit patients globally.

REFERENCES

1. Swaika A, Hammond WA, Joseph RW. Current state of anti-PD-L1 and anti-PD-1 agents in cancer therapy. Molecular immunology. 2015 Oct 1;67(2):4-17.
2. Philips GK, Atkins M. Therapeutic uses of anti-PD-1 and anti-PD-L1 antibodies. International immunology. 2015 Jan 1;27(1):39-46.
3. Gupta A, De Felice KM, Loftus Jr EV, Khanna S. Systematic review: colitis associated with anti-CTLA-4 therapy. Alimentary pharmacology & therapeutics. 2015 Aug;42(4):406-17.
4. Seidel JA, Otsuka A, Kabashima K. Anti-PD-1 and anti-CTLA-4 therapies in cancer: mechanisms of action, efficacy, and limitations. Frontiers in oncology. 2018 Mar 28;8:86.
5. Rafiq S, Hackett CS, Brentjens RJ. Engineering strategies to overcome the current roadblocks in CAR T cell therapy. Nature reviews Clinical oncology. 2020 Mar;17(3):147-67.
6. Sadelain M, Rivière I, Riddell S. Therapeutic T cell engineering. Nature. 2017 May 25;545(7655):423-31.
7. Milone MC, Xu J, Chen SJ, Collins MA, Zhou J, Powell Jr DJ, Melenhorst JJ. Engineering-enhanced CAR T cells for improved cancer therapy. Nature cancer. 2021 Aug;2(8):780-93.
8. Drake CG. Immunotherapy for prostate cancer: an

emerging treatment modality. Urologic Clinics. 2010 Feb 1;37(1):121-9.

9. Muthukutty P, Woo HY, Ragothaman M, Yoo SY. Recent Advances in Cancer Immunotherapy Delivery Modalities. Pharmaceutics. 2023 Feb;15(2):504.
10. Sambi M, Bagheri L, Szewczuk MR. Current challenges in cancer immunotherapy: multimodal approaches to improve efficacy and patient response rates. Journal of oncology. 2019;2019(1):4508794.
11. Wang C, Ye Y, Hu Q, Bellotti A, Gu Z. Tailoring biomaterials for cancer immunotherapy: emerging trends and future outlook. Advanced materials. 2017 Aug;29 (29):1606036.
12. Taefehshokr S, Parhizkar A, Hayati S, Mousapour M, Mahmoudpour A, Eleid L, Rahmanpour D, Fattahi S, Shabani H, Taefehshokr N. Cancer immunotherapy: Challenges and limitations. Pathology-Research and Practice. 2022 Jan 1;229:153723.
13. Mediratta K, El-Sahli S, D'Costa V, Wang L. Current progresses and challenges of immunotherapy in triple-negative breast cancer. Cancers. 2020 Nov 26;12 (12):3529.