The evolution of cancer immuno-oncology: Breakthroughs and challenges.

Michael Fuller*

Department of Radiology, University of California San Francisco, USA

Introduction

Cancer has long been one of the most formidable diseases to treat, largely due to its ability to evade the immune system, making traditional therapies such as chemotherapy and radiation less effective for many patients. However, over the past few decades, the field of cancer immuno-oncology has experienced revolutionary advancements, transforming cancer treatment by harnessing the body's own immune system to combat tumors. This shift has resulted in groundbreaking therapies that have significantly improved survival rates for certain cancers, although challenges remain in fully realizing the potential of immuno-oncology [1].

The concept of immuno-oncology dates back to the early 20th century, when William Coley, a surgeon, used bacterial toxins to treat cancer patients. Though his methods were not widely accepted at the time, Coley's work laid the foundation for understanding how the immune system could potentially be harnessed to fight cancer. Fast forward to the 1990s, when scientific discoveries regarding immune checkpoint inhibitors and the identification of tumor-specific antigens paved the way for more targeted approaches [2].

The understanding of immune checkpoints, particularly the role of molecules like PD-1 and CTLA-4, marked a pivotal moment in immuno-oncology. These checkpoints are regulatory pathways that prevent the immune system from attacking normal cells, but they can also allow cancer cells to escape detection. In the late 1990s, researchers began to investigate how blocking these checkpoints could unleash the immune system's ability to target and destroy cancer cells. This discovery would later lead to the development of immune checkpoint inhibitors, a class of drugs that has become the cornerstone of modern immuno-oncology [3].

The first major breakthrough came in 2011 with the approval of ipilimumab, a CTLA-4 inhibitor, for the treatment of melanoma. This was the first cancer immunotherapy to show significant survival benefits, marking a milestone in oncology. It was followed by the approval of nivolumab and pembrolizumab in 2014, both PD-1 inhibitors, which further confirmed the power of immune checkpoint blockade in treating cancers such as melanoma, non-small cell lung cancer, and more. These drugs demonstrated that inhibiting immune checkpoints could lead to long-lasting responses in a subset of patients, opening the door for a new era of cancer treatments [4].

In addition to checkpoint inhibitors, another major advancement in cancer immunotherapy has been the development of CAR-T cell therapy (Chimeric Antigen Receptor T-cell therapy). This involves genetically modifying a patient's own T cells to express a receptor that targets specific cancer antigens. Once reintroduced into the patient, these engineered T cells can recognize and attack cancer cells more effectively. The approval of Kymriah and Yescarta for certain types of blood cancers in 2017 marked another significant milestone in immuno-oncology, particularly for patients with relapsed or refractory leukemia and lymphoma [5].

Immuno-oncology has also contributed to the growing trend of personalized medicine. By understanding the specific molecular characteristics of a patient's tumor, oncologists can tailor immunotherapies to enhance effectiveness. The development of tumor mutational burden (TMB) as a biomarker is one example. TMB refers to the number of mutations in a tumor, and high TMB can predict better responses to immunotherapy. This move toward more individualized treatment plans is helping oncologists to optimize therapies for each patient, improving outcomes and reducing unnecessary side effects [6].

Despite the successes, cancer immuno-oncology faces several significant challenges. One of the main hurdles is the tumor microenvironment (TME), which can suppress immune activity. Tumors often create an environment that prevents immune cells from infiltrating and effectively attacking cancer cells. The TME can also promote the activity of immune-suppressive cells, such as regulatory T cells and myeloid-derived suppressor cells, which dampen immune responses. Understanding and overcoming these mechanisms is crucial for improving immunotherapy outcomes [7].

Additionally, resistance to immunotherapy is a growing concern. While some patients experience long-lasting remissions, others quickly relapse, with tumors either escaping immune surveillance or adapting to immune pressure. Research is ongoing to understand why certain tumors are resistant to immunotherapies, and strategies are being developed to combine immune checkpoint inhibitors with other therapies to overcome resistance [8].

To address the limitations of monotherapy, combination approaches are emerging as a promising solution. Combining immune checkpoint inhibitors with other immunotherapies, such as vaccines or oncolytic viruses, may enhance immune activation. Furthermore, combining immunotherapy with

***Correspondence to:** Michael Fuller, Department of Radiology, University of California San Francisco, USA. E-mail: michael.fuller@ucsf.edu

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traditional treatments like chemotherapy or targeted therapy could potentially create a synergistic effect that boosts overall efficacy. Clinical trials are actively investigating these combinations, with the goal of improving response rates and overcoming resistance [9].

While immunotherapy has proven highly effective for certain cancers like melanoma, non-small cell lung cancer, and bladder cancer, its efficacy in other types of cancer, such as pancreatic, ovarian, and colorectal cancers, remains limited. Researchers are focusing on identifying the biomarkers and molecular characteristics that predict better responses in these harder-to-treat cancers. The hope is that, with time, immuno-oncology will be able to benefit a broader range of cancer patients, expanding the treatment's reach [10].

Conclusion

The evolution of cancer immuno-oncology has been nothing short of transformative, bringing about breakthroughs that have already saved countless lives. While challenges such as resistance, the tumor microenvironment, and expanding immunotherapy to all cancer types remain, the field is progressing at an unprecedented rate. As new therapies emerge and more patients benefit from immuno-oncology, the future of cancer treatment appears brighter than ever. With continued innovation, the dream of making cancer a manageable chronic condition or even a curable disease could soon become a reality.

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