The role of monoclonal antibodies in cancer treatment: Advances and challenges.

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Introduction

Monoclonal antibodies (mAbs) have emerged as a cornerstone in the treatment of various cancers, offering a more targeted and effective approach compared to traditional chemotherapy. By recognizing specific antigens expressed on tumor cells, mAbs can modulate immune responses, inhibit tumor growth, and deliver cytotoxic agents directly to cancer cells. This article explores how monoclonal antibodies function in cancer treatment, recent innovations, and the key obstacles facing their broader use [1].

Monoclonal antibodies combat cancer through multiple mechanisms: mAbs bind to tumor antigens and recruit immune cells such as natural killer (NK) cells to destroy the cancer cell. Some antibodies activate the complement cascade, leading to direct lysis of the target cell. Certain mAbs trigger signaling pathways that induce apoptosis in tumor cells [2].

Immune checkpoint inhibitors such as anti-PD-1 and anti-CTLA-4 block inhibitory signals, reactivating T cells to attack tumor cells. These combine mAbs with cytotoxic agents, delivering the drug directly to tumor cells while minimizing systemic toxicity. Rituximab targets CD20 on B cells and revolutionized the treatment of B-cell lymphomas [3].

Trastuzumab binds HER2/neu receptors in breast cancer, improving survival in HER2-positive patients. Bevacizumab inhibits VEGF, curbing tumor angiogenesis in colorectal and other cancers. Nivolumab and pembrolizumab, immune checkpoint inhibitors targeting PD-1, are now standard treatments for melanoma, lung, and other cancers [4].

Originally derived from mouse cells, early mAbs triggered immune reactions. Humanized and fully human antibodies now reduce immunogenicity, improving safety and efficacy. These are engineered to recognize two different antigens simultaneously. Blinatumomab, for example, connects CD19 on B cells and CD3 on T cells, bringing them into proximity to kill leukemia cells [5].

Recent FDA-approved ADCs like trastuzumab emtansine (T-DM1) combine tumor specificity with potent chemotherapy, enhancing therapeutic outcomes while limiting off-target effects. Tumor cells can mutate or downregulate target antigens, rendering antibodies ineffective. Resistance to trastuzumab, for example, can occur through alterations in the PI3K/AKT pathway [6].

The TME may impede antibody access, particularly in solid tumors. Dense stroma, abnormal vasculature, and immunosuppressive cells can all reduce mAb effectiveness. Checkpoint inhibitors can cause serious autoimmune side effects, including colitis, hepatitis, and myocarditis. These require careful monitoring and may necessitate discontinuation of therapy [7].

mAbs are expensive to produce, with some treatments costing thousands of dollars per dose. This limits access, particularly in low- and middle-income countries. Integrating genomics and proteomics can help tailor mAb therapies to individual tumor profiles. Biomarkers such as PD-L1 expression already guide treatment selection in immunotherapy [8].

Combining mAbs with chemotherapy, radiation, or other mAbs may enhance outcomes. Ongoing trials are investigating these synergies, especially for resistant cancers. AI tools are now being used to predict antigen-antibody interactions, optimize design, and accelerate the development of next-generation mAbs [9].

Since the approval of rituximab in 1997 for non-Hodgkin's lymphoma, the therapeutic landscape has expanded considerably. Despite these advances, challenges such as resistance, limited penetration in solid tumors, and high costs persist [10].

Conclusion

Monoclonal antibodies have significantly transformed cancer treatment, offering patients targeted, effective, and increasingly personalized therapies. Advances in antibody engineering continue to improve efficacy and reduce side effects. Nonetheless, challenges such as resistance, adverse events, and high costs need to be addressed. Through continued innovation, interdisciplinary research, and equitable healthcare strategies, monoclonal antibody therapy holds immense promise in the ongoing fight against cancer.

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***Received:** 03-Apr-2025, Manuscript No. AAJCIT-25-163920; **Editor assigned:** 04-Apr-2025, Pre QC No. AAJCIT-25-163920(PQ); **Reviewed:** 17-Apr-2025, QC No AAJCIT-25-163920; **Revised:** 21-Apr-2025, Manuscript No. AAJCIT-25-163920(R); **Published:** 28-Apr-2025, DOI:10.35841/aajcit-8.2.265*

***Citation:** Macholi E. The role of monoclonal antibodies in cancer treatment: Advances and challenges. J Cancer Immunol Ther. 2025;8(2):265*

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Citation: *Macholi E. The role of monoclonal antibodies in cancer treatment: Advances and challenges. J Cancer Immunol Ther. 2025;8(2):265*