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Emerging Therapeutic Targets of Bispecific Antibody Immune-cell Engagers in Cancer Immunotherapy

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Introduction

Bispecific antibody-based immune-cell engagers have emerged as a groundbreaking approach in cancer immunotherapy, offering a novel means to harness the body's immune system to selectively target and eliminate cancer cells. These engineered antibodies possess the ability to bind two different antigens simultaneously, facilitating interactions between immune effector cells and tumor cells to enhance antitumor activity. The development of bispecific antibodies (BsAbs) has led to a new class of immunotherapeutics that bridge T cells or Natural Killer (NK) cells with cancer cells, thereby promoting targeted immune responses and reducing off-target effects associated with traditional therapies. One of the primary mechanisms by which bispecific antibodies function is through T cell redirection. These agents are designed to engage CD3, a key component of the T cell receptor complex, on one arm, while the other arm binds to a Tumor-Associated Antigen (TAA) expressed on cancer cells. This dual specificity enables the formation of an immunological synapse between T cells and tumor cells, leading to direct T cell-mediated cytotoxicity. Unlike conventional monoclonal antibodies, which rely on natural immune effector functions such as Antibody-Dependent Cellular Cytotoxicity (ADCC) or Complement-Dependent Cytotoxicity (CDC), bispecific T cell engagers (BiTEs) actively recruit and activate T cells in a major histocompatibility complex (MHC)-independent manner, making them effective even in tumors with low antigen presentation.

Description

The clinical success of blinatumomab, the first FDA-approved BiTE, has paved the way for further development of bispecific antibody-based therapies. Blinatumomab targets CD19, a surface antigen commonly expressed in B-cell malignancies, and has demonstrated remarkable efficacy in treating relapsed or refractory B-cell acute lymphoblastic leukemia (B-ALL). Its success has led to the expansion of bispecific antibody research into other hematologic malignancies, with several promising candidates targeting antigens such as BCMA in multiple myeloma and CD20 in B-cell lymphomas. These agents have shown significant potential in clinical trials, offering new hope for patients with limited treatment options. Beyond hematologic malignancies, bispecific antibodies are being actively developed for the treatment of solid tumors, which present additional challenges due to the complexity of the tumor microenvironment. Unlike blood cancers, solid tumors are often characterized by an immunosuppressive milieu, physical barriers, and heterogeneous antigen expression, which can hinder the effectiveness of immune-based therapies. Nevertheless, researchers have identified promising TAAs for bispecific antibody targeting in solid tumors, including HER2, EGFR, PSMA, and MUC16. By leveraging bispecific antibodies to recruit and activate immune cells within the tumor microenvironment, scientists aim to overcome these obstacles and enhance antitumor responses [1,2].

In addition to T cell engagers, bispecific antibodies targeting NK cells have gained traction as an alternative immunotherapeutic approach. NK cell engagers typically bind to CD16, a key activating receptor on NK cells, while simultaneously targeting TAAs on cancer cells. Unlike T cell engagers, which require antigen presentation and immune synapse formation, NK cell engagers rely on innate immune recognition and cytotoxic mechanisms to eliminate tumor cells. This approach offers several advantages, including a lower risk of Cytokine Release Syndrome (CRS) and the ability to target tumors that may evade T cell-mediated immunity. Furthermore, the combination of NK cell engagers with immune checkpoint inhibitors or cytokine therapies holds promise for enhancing their therapeutic efficacy. The engineering of bispecific antibodies has also evolved to improve their pharmacokinetic properties, stability, and safety profiles. Early-generation bispecific antibodies faced challenges related to short half-life, immunogenicity, and off-target toxicity. Advances in antibody engineering have led to the development of more stable formats, such as full-length IgG-like bispecifics and Fc-modified constructs, which exhibit improved half-life and reduced immunogenicity. Additionally, the incorporation of conditional activation mechanisms, such as protease-sensitive linkers or masked epitopes, has enabled greater tumor specificity while minimizing toxicity to normal tissues [3-5].

Conclusion

Another promising avenue in bispecific antibody development involves targeting immune checkpoint pathways. The blockade of immune checkpoints, such as PD-1/PD-L1 and CTLA-4, has revolutionized cancer therapy, leading to durable responses in certain malignancies. By designing bispecific antibodies that simultaneously block immune checkpoints and engage tumor-specific antigens, researchers aim to enhance the therapeutic potential of immune checkpoint inhibitors. These dual-function bispecifics can promote T cell activation while preventing immune exhaustion, thereby boosting antitumor immune responses in tumors that are resistant to conventional checkpoint blockade therapy.

Acknowledgement

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Conflict of Interest

None.

References

1. Arruebo, Manuel, Nuria Vilaboa, Berta Sáez-Gutierrez and Julio Lambea, et al. "Assessment of the evolution of cancer treatment therapies." *Cancers* 3 (2011): 3279-3330.
2. Basak, Debasish, Scott Arrighi, Yasenya Darwiche and Subrata Deb. "Comparison of anticancer drug toxicities: Paradigm shift in adverse effect profile." *Life* 12 (2021): 48.
3. Baldo, Brian A. "Immune-and non-immune-mediated adverse effects of monoclonal antibody therapy: A survey of 110 approved antibodies." *Antibodies* 11 (2022): 17.
4. Vidarsson, Gestur, Gillian Dekkers and Theo Rispens. "IgG subclasses and allotypes: From structure to effector functions." *Front immunol* 5 (2014): 520.

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5. Ruf, Peter, Hartwig W. Bauer, Alexandra Schoberth and Claudia Kellermann, et al. "First time intravesically administered trifunctional antibody catumaxomab in patients with recurrent non-muscle invasive bladder cancer indicates high tolerability and local immunological activity." *Cancer Immunol Immunother* 70 (2021): 2727-2735.

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