IJBPAS, December, 2026, 15(12): 6022-6035

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

# MONOCLONAL ANTIBODIES AS PRECISION TOOLS IN CANCER IMMUNOTHERAPY: A COMPREHENSIVE REVIEW

**CHAURE S, GAJBHIYE R, NIMGADE N AND RATNE N***

Nagpur College of Pharmacy, Wanadongri, Hingna Road, Nagpur (M.S.), India-441110

***Corresponding Author: Ms. Nandini Ratne: E Mail: nandini.ratne201@gmail.com**

**Received 29th May 2026; Revised 10th July 2026; Accepted 20th Sept. 2026; Available online 1st Dec. 2026**

https://doi.org/10.31032/IJBPAS/2026/15.12.10683

## ABSTRACT

Cancer remains one of the leading causes of morbidity and mortality worldwide, necessitating the development of innovative and targeted therapeutic strategies. Monoclonal antibodies (mAbs) have emerged as powerful precision tools in cancer immunotherapy due to their ability to selectively recognize tumor-associated antigens and modulate immune responses against malignant cells. This review comprehensively examines principles, mechanisms, therapeutic applications, and recent advancements of monoclonal antibody-based cancer immunotherapy. Monoclonal antibodies exert their antitumor effects through diverse mechanisms, including direct inhibition of oncogenic signaling pathways, induction of antibody-dependent cellular cytotoxicity (ADCC), complement-dependent cytotoxicity (CDC), and enhancement of immune-mediated tumor destruction. The review highlights the clinical significance of key therapeutic antibodies targeting receptors and immune checkpoints, such as programmed cell death protein-1 (PD-1), programmed death-ligand 1 (PD-L1), cytotoxic T-lymphocyte-associated protein-4 (CTLA-4), human epidermal growth factor receptor 2 (HER2), and CD20. Furthermore, emerging antibody-based platforms, including bispecific antibodies, antibody-drug conjugates (ADCs), and engineered antibody fragments, are discussed for their potential to improve therapeutic efficacy and overcome resistance mechanisms. Despite remarkable clinical success, challenges such as tumor heterogeneity, immune evasion, treatment resistance, adverse immune-related events, and high treatment costs continue to limit broader application. Recent advances in antibody engineering, biomarker-guided patient selection, and combination therapies are paving the way toward more personalized and effective cancer treatment approaches. By integrating current knowledge on the biological basis, clinical applications, and future prospects of monoclonal antibodies,

this review underscores their transformative role in precision oncology and their potential to further enhance cancer immunotherapy outcomes through continued innovation and translational research.

**Keywords: Monoclonal antibodies, Immunotherapy, Antibodies, Tumor cells, Oncology**

## 1. INTRODUCTION

Cancer is a complicated illness characterized by immunological evasion, genetic variety, and resistance to standard therapies **[1]**. Because monoclonal antibodies (mAbs) provide targeted, specific, and flexible therapeutic choices, they have completely changed cancer therapy **[2]**. MAbs minimize harm to healthy cells by selectively binding tumor-specific antigens, in contrast to chemotherapy **[3]**. Their methods include immunological activation (e.g., complement, ADCC) **[4]**, receptor inhibition **[5]**, and antibody-drug conjugate-based payload delivery **[6]**. The effectiveness is further increased by immune checkpoint inhibitors (such as anti-PD-1 and CTLA-4) **[7]** and next-generation formats like bispecifics and BiTEs **[8]**. Personalized treatment is supported by biomarker-driven diagnostics **[9]**. The development, mechanics, clinical application, difficulties, and prospects of monoclonal antibodies in cancer immunotherapy are described in this paper.

## 2. MONOCLONAL ANTIBODIES: OVERVIEW

Proteins created in a lab, monoclonal antibodies (mAbs) are effective tools for immune regulation and cancer treatment because they specifically target particular antigens **[3]**. Edward Jenner's vaccination efforts served as the foundation for their development, which culminated in 1975 with the development of the ground-breaking hybridoma technology by Milstein and Kohler **[11]**. The first clinical milestone was achieved by muromonabCD3 **[12]**, and trastuzumab, which targets HER2-positive breast cancer, marked the advent of customized therapy **[13]**.

### 2.1 Classification of Monoclonal Antibodies:

MAbs are classified based on their origin and the extent of humanization **[14]**:

**a. Murine (-omab):**

Antibodies that are entirely sourced from mice, produced by combining myeloma cells with mouse B cells. Although they work well in experiments, their short half-life and high immunogenicity restrict their application in humans since they weakly activate the immune system and cause the development of anti-drug antibodies (ADAs) **[15]**.

**b. Chimeric (-ximab):**

These antibodies have about 65% human structure by combining human constant regions with murine variable regions. Although they have a longer half-life and are

less immunogenic, they nonetheless run the risk of causing ADA **[16]**.

**c. Humanized (-zumab):**

Although their manufacture is complicated, these mAbs further lower immunogenicity by incorporating only the murine antigen-binding (CDR) regions into a human framework (~95% human) **[17]**.

**d. Fully Human (-umab):**

These mAbs, which are made from transgenic animals that include human immunoglobulin genes, exhibit low immunogenicity and improved biological compatibility, which makes them perfect for long-term therapeutic use **[18]**.

**2.2 Types of mAbs:**

Based on application and composition, mAbs are categorized into:

**a. Unconjugated (Naked) mAbs:**

These mAbs are commonly employed in cancer treatment and function independently. They stop tumor growth by blocking growth signals, inducing immunological responses, or targeting immune checkpoints **[3]**.

**b. Conjugated mAbs:**

These are chemically bonded to radioactive isotopes or cytotoxic medications, which serve as delivery systems to target cancer cells precisely while avoiding harm to healthy organs **[6]**.

**c. Bispecific mAbs:**

These mAbs physically connect immune and cancer cells, increasing targeted cytotoxicity by binding two different antigens at the same time—one on an immune cell and the other on a cancer cell **[21]**.

**2.3 Mechanism of action:**

Knowing how these antibodies attack cancer cells has revolutionized cancer treatment and led to a more manageable toxicity profile than traditional chemotherapy **[14]**. There are multiple ways that mAbs work to kill cancer cells when used in oncology. These techniques include avoiding immunological checkpoints **[7]**, preventing tumor growth by interfering with tumor angiogenesis **[24]**, preventing tumor cell survival cascades **[2]**, and avoiding programmed cell death **[5]**. The following are a few of the several mechanisms of action:

**a. Direct tumor cell killing:**

Receptor agonist activity, such as an antibody attaching to a tumor cell surface receptor and activating it, which results in cell death, stimulates this function **[3]**. Additionally, it can be triggered by receptor antagonist activity, "for example, an antibody binding to a cell surface receptor and preventing downstream signaling, dimerization, and kinase activation, which results in decreased proliferation and apoptosis **[28]**. Nine Conjugated antibodies can be utilized to transfer a payload, like a

medication, to the tumor cel **[6]**. whereas monoclonal antibodies can neutralize an enzyme and cause death **[30]**.

**b. Immune-mediated tumor cell killing:**

The immune system will look for and eliminate cancer cells in this environment. One of numerous pathways may be initiated to cause this kind of cell death **[3]**. Among these mechanisms are:

a) Phagocytosis **[32]**;
b) Complement activation **[33]**;
c) Antibody-dependent cellular cytotoxicity (ADCC) **[34]**;
d) Genetically altered T lymphocytes that use a single chain variable segment to target the tumor **[35]**;
e) Antibody-mediated cross-presentation of antigen to dendritic cells activates T cells **[36]**; or
f) Inhibition of T-cell inhibitory receptors **[7]**.

**c. Vascular and stromal cell ablation:**

One of the numerous possibilities also starts this action. These consist of:

a) vasculature receptor antagonism or ligand trapping **[24]**;
b) stromal cell inhibition **[39]**;
c) administration of toxic substances to stromal cells **[40]**; or
d) delivery of a toxin to the vasculature **[30]**.

**3. Mab production technology:**

**a. Antibody Phage Display:**

Phage display is a molecular method that uses antibody fragments (or ligands) on the surface of bacteriophages to connect antibody genotype to phenotype [42]. Phage genomes are modified to incorporate DNA encoding various antibody variants, which fuse with coat protein genes (usually pIII) **[43]**. Phage assembly and surface presentation of the encoded antibodies occur when bacteria are infected. By screening these displayed antibodies against immobilized antigens, high-affinity binders can be selectively enriched. Binding, washing, elution, and amplification are iterative processes that improve specificity **[44]**. Finding uncommon, high-affinity binders without immunization is made possible by phage display's capacity to quickly screen large combinatorial libraries **[45]**.

**b. Hybridoma Technology:**

Hybridoma technology, created in 1975 by Kohler and Milstein, is still a fundamental technique for producing monoclonal antibodies **[11]**. It entails combining immortal myeloma cells with B cells that make antibodies to produce hybridomas, which are cells that continuously manufacture a single antibody. Following antigen vaccination, B-cell collection, cell fusion, selection (usually in HAT medium), and screening are the next steps in the procedure. Clones that produce antibodies

with the required specificity and activity are found using methods such as flow cytometry and ELISA **[47]**. Hybridomas are prized for their durability, isotype constancy, and potential for the generation of therapeutic antibodies, even in the face of more recent techniques. This platform has been improved by innovations such as humanized mice, which allow for the creation of fully human mAb for clinical use **[48, 49]**.

## 4. MECHANISM OF ANTICANCER ACTION

### a. Antibody Dependent Cell-Mediated (ADCC):

In ADCC, mAbs bind to tumor antigens and engage immune effector cells like natural killer (NK) cells, macrophages, and γδ T cells through their Fc receptors **[50]**. This triggers the direct killing or phagocytosis of cancer cells. The efficiency of ADCC depends on receptor types and genetic variants **[51, 52]**. Drugs like rituximab and trastuzumab rely heavily on this mechanism for therapeutic success **[53]**.

### b. Complement-Dependent Cytotoxicity (CDC):

CDC begins when mAbs activate the complement system after attaching to tumor cells, starting with C1q binding **[54]**. This leads to a cascade resulting in membrane attack and cell death. The strength of CDC is influenced by the antibody's ability to cluster and recruit complement proteins effectively, with IgG1 being particularly efficient **[55]**.

### c. Antibody-Drug Conjugates (ADCs):

ADCs are cutting-edge treatments in which mAbs are connected by specific linkers to potent cytotoxic medications. By delivering the medication straight to cancer cells, these antibodies reduce harm to healthy tissue **[56]**. T-DM1 and trastuzumab deruxtecan are two examples. The way and timing of the drug's release can be influenced by the cleavability of the linkers **[57]**. ADCs are accurate, but because of their possible toxicity, they must be carefully controlled **[58]**.

i. CTLA-4 inhibitors
ii. PD-1/PD-L1 inhibitors
iii. Combination therapies

### i.CTLA-4 inhibitors:

CTLA-4, discovered in 1987, is an immune checkpoint receptor that down regulates T cell activity by competing with CD28 for CD80/CD86 binding. Its role in cancer was established when blocking it with antibodies triggered tumor rejection. Ipilimumab, approved in 2011, was the first FDA-approved CTLA-4 inhibitor **[59]**.

### ii. PD-L1/PD-1 inhibitors:

PD-1 is another checkpoint that suppresses T cell activity mainly in peripheral tissues. Its ligands PD-L1 and PDL2 are often overexpressed in tumors, leading to immune

evasion. Anti-PD-1/PD-L1 antibodies like nivolumab and pembrolizumab restore immune function and are approved for various cancers **[60]**.

**iii.Combination therapy:**

Checkpoint inhibitors may be less effective when tumors lack T cell infiltration. To enhance response, combinations with chemotherapy, radiotherapy, vaccines, cytokines, or CAR-T therapy are being explored. These strategies aim to boost immune activation and overcome tumor resistance **[61, 62]**.

## 5. FDA-APPROVED MONOCLONAL ANTIBODIES IN CANCER THERAPY

**Table 1: Selected FDA-Approved Monoclonal Antibodies in Cancer Therapy**

| Monoclonal Antibody | Target | Indications | Mechanism of Action |
|---|---|---|---|
| Rituximab [63] | CD20 | Non-Hodgkin lymphoma (NHL), chronic lymphocytic leukemia | ADCC, CDC, direct apoptosis |
| Trastuzumab [13] | HER2 | HER2+ breast, gastric cancers | Inhibits HER2 signaling, ADCC |
| Bevacizumab [24] | VEGF | Colorectal, NSCLC, glioblastoma | Anti-angiogenesis |
| Cetuximab [66] | EGFR | Colorectal, head & neck cancers | EGFR inhibition, ADCC |
| Pembrolizumab [67] | PD-1 | Melanoma, NSCLC, bladder cancer | Immune checkpoint blockade |
| Atezolizumab [68] | PD-L1 | NSCLC, urothelial carcinoma | Immune checkpoint blockade |
| Brentuximab vedotin [69] | CD30 | Hodgkin lymphoma, ALCL | ADC (delivers MMAE cytotoxin) |
| Daratumumab [70] | CD38 | Multiple myeloma | ADCC, CDC, complement activation Emerging Targets and Next-Generation mAbs |

**Table 2: Successes and Challenges of Monoclonal Antibody Therapy**

| Success Stories | Limitations/Challenges |
|---|---|
| Durable responses with PD-1/PD-L1 inhibitors [71] | Immune-related adverse events (IrAEs) [72] |
| HER2-targeted therapy improves survival in breast cancer [13] | Development of acquired resistance (e.g., EGFR mutations) [74] |
| ADCs offer targeted delivery of cytotoxic agents [65] | High cost and limited accessibility in developing regions [66] |
| Combination of checkpoint inhibitors improves outcomes [67] | Limited predictive biomarkers for patient selection [68] |

## 6. EMERGING TARGETS AND NEXT GENERATION MAbs

### a. Bispecific antibodies

Bispecific antibodies (bsAbs) represent a pivotal advancement in immunotherapy, with the ability to bind simultaneously to two distinct epitopes or antigens. This dual specificity enables precise redirection of immune cells—particularly T-cells—toward malignant targets. A prominent example is Blinatumomab, a BiTE (Bispecific T-cell Engager) approved for acute lymphoblastic leukemia (ALL), which links CD3 on T-cells with CD19 on Bcells to stimulate immune

destruction. Unlike traditional mAbs, bsAbs offer enhanced tumor cell lysis, improved immunological synapse formation, and bypass the need for major histocompatibility complex (MHC) presentation **[69]**.

**b. Nanobodies and engineered fragments**

Nanobodies are the variable domains of heavy-chain antibodies derived from camelids. Their compact structure (≈15 kDa) makes them ideal for deep tissue penetration, blood-brain barrier crossing, and rapid clearance. They maintain high affinity and specificity while exhibiting excellent thermal and chemical stability **[70]**. Engineered antibody fragments, such as single-chain variable fragments (scFv), diabodies, and minibodies, also offer flexible pharmacokinetics, reduced immunogenicity, and greater tumor infiltration **[71]**.

**c. T-cell engaging antibodies (BiTEs)**

BiTEs represent a major innovation in cancer immunotherapy. They are designed to link CD3+ T-cells with tumor-specific antigens, resulting in T-cell activation and subsequent tumor cell lysis. BiTEs do not require costimulatory signals or MHC presentation, making them effective even against tumors with immune escape mechanisms. The modular design of BiTEs is being adapted for solid tumors, offering broader clinical applications beyond hematological malignancies **[72]**.

## 7. CHALLENGES IN MONOCLONAL ANTIBODY THERAPY

**a. Tumour Resistance Mechanisms:**

Cancer cells can evade mAb therapy by altering or losing the target antigen, mutating it, or shedding it from their surface. Tumors may also activate alternative survival pathways or create an immunosuppressive microenvironment that weakens the immune response. These adaptations reduce treatment effectiveness over time, requiring combination therapies to maintain clinical benefit **[3]**.

**b. Immune-Related Adverse Events:**

mAbs that modulate the immune system, especially checkpoint inhibitors or T-cell engaging antibodies, can provoke serious immune side effects. These may include cytokine release syndrome (CRS), neurological toxicity, and autoimmune-like reactions affecting organs such as the lungs, liver, or intestines. Effective management involves close monitoring, timely immunosuppressive treatment, and, when necessary, stopping therapy **[74]**. **c. Cost and Accessibility:**

Monoclonal antibody treatments are highly costly due to complex production and strict regulatory standards. This limits their availability, particularly in low- and middle-income countries. Developing biosimilars, improving manufacturing efficiency, and promoting policy reforms are essential steps

to enhance global access and affordability **[5]**.

## 8. PERSONALIZED MEDICINE AND BIOMARKER-DRIVEN THERAPY

### a. Role of predictive biomarkers:

Predictive biomarkers have become essential tools for guiding monoclonal antibody use. For example, HER2 amplification predicts responsiveness to trastuzumab in breast cancer, while EGFR mutations indicate eligibility for cetuximab in colorectal cancer **[56]**. These biomarkers enable tailored therapies, reduce exposure to ineffective drugs, and improve overall outcomes **[47]**.

### b. Companion diagnostics:

Laboratory tests known as companion diagnostics (CDx) are used to determine which patients are most likely to benefit from a particular treatment. Through the confirmation of biomarker expression, they are essential in guaranteeing therapy precision. For example, in non-small cell lung cancer (NSCLC), PD-L1 testing is frequently necessary prior to the prescription of checkpoint inhibitors. Nowadays, mAb drug development and regulatory approval depend heavily on FDA-approved CDx tests **[58]**.

### c. Patient stratification for mAb therapy:

Stratification involves dividing patients into subgroups based on molecular, genetic, or immunological characteristics. This is particularly vital in oncology, where tumors exhibit high heterogeneity. Using highthroughput omics technologies, clinicians can classify patients into responders, partial responders, or nonresponders—thereby optimizing treatment selection and minimizing toxicity **[59]**.

## 9. FUTURE PROSPECTS AND INNOVATIONS

The future of monoclonal antibody (mAb) therapy is rapidly evolving, with breakthroughs across technology, immunotherapy, and precision medicine.

### a. MAbs in Combination with CAR-T, Vaccines, or Radiation:

Combining mAbs with CAR-T cells, cancer vaccines, or radiation therapy holds great promise. mAbs can enhance CAR-T cell infiltration or make tumors more responsive to radiation. Similarly, radiation and vaccines can trigger immunogenic cell death, which works synergistically with mAb-induced ADCC to boost antitumor immunity **[60]**.

### b. Role of AI in mAb Design:

Artificial Intelligence is revolutionizing antibody development. AI algorithms can model antibody-antigen interactions, improve binding affinity, and predict immunogenic responses. These tools are accelerating discovery timelines and

enabling the creation of smarter, more effective antibodies tailored to tumor targets **[61]**.

**c. Trends in Personalized and Precision Oncology:**

With advancements in single-cell technologies and immune profiling, mAb therapies are becoming more individualized. Future treatments will likely adapt in real time to tumor evolution and immune resistance, offering dynamic, feedback-based cancer management tailored to each patient's unique biology **[62]**.

## CONCLUSION

Monoclonal antibodies (mAbs) offer precise, targeted cancer therapy with reduced toxicity. Breakthroughs like bispecifics, ADCs, and checkpoint inhibitors have expanded their impact. Biomarker-based approaches enhance personalization and treatment outcomes. Challenges include resistance, immune side effects, and high costs. Future directions involve AI-designed mAbs and combinational immunotherapies. mAbs remain central to the evolution of precision medicine and next-generation oncology.

## REFERENCES

**[1]** Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell. 2011;144(5):646–74.

**[2]** Scott AM, Wolchok JD, Old LJ. Antibody therapy of cancer. Nat Rev Cancer. 2012;12(4):278–87.

**[3]** Weiner LM, Surana R, Wang S. Monoclonal antibodies: versatile platforms for cancer immunotherapy. Nat Rev Immunol. 2010;10(5):317–27.

**[4]** Nimmerjahn F, Ravetch JV. Antibody-mediated modulation of immune responses. Nat Rev Immunol. 2008;8(1):34–47.

**[5]** Hudis CA. Trastuzumab — mechanism of action and use in clinical practice. N Engl J Med. 2007;357(1):39– 51.

**[6]** Lambert JM, Berkenblit A. Antibody–drug conjugates for cancer treatment. Annu Rev Med. 2018;69:191–207.

**[7]** Ribas A, Wolchok JD. Cancer immunotherapy using checkpoint blockade. Science. 2018;359(6382):1350–55.

**[8]** Labrijn AF, Janmaat ML, Reichert JM, Parren PWHI. Bispecific antibodies: a mechanistic review of the pipeline. Nat Rev Drug Discov. 2019;18(8):585–608.

**[9]** Topalian SL, Taube JM, Anders RA, Pardoll DM. Mechanism-driven biomarkers to guide immune checkpoint blockade in cancer therapy. Nat Rev Cancer. 2016;16(5):275–87.

**[10]** Kohler G, Milstein C. Continuous cultures of fused cells secreting

antibody of predefined specificity. Nature. 1975;256(5517):495–97.

**[11]** Orthner CL, Krakauer RS, Bongiovanni KF, *et al*. Muromonab-CD3: a monoclonal antibody with a critical role in transplantation. Pharmacotherapy. 1993;13(2):166–77.

**[12]** Slamon DJ, Leyland-Jones B, Shak S, *et al*. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. N Engl J Med. 2001;344(11):783–92.

**[13]** Chames P, Van Regenmortel M, Weiss E, Baty D. Therapeutic antibodies: successes, limitations and hopes for the future. Br J Pharmacol. 2009;157(2):220–33.

**[14]** Nelson AL, Dhimolea E, Reichert JM. Development trends for human monoclonal antibody therapeutics. Nat Rev Drug Discov. 2010;9(10):767–74.

**[15]** Presta LG. Engineering of therapeutic antibodies to minimize immunogenicity and optimize function. Adv Drug Deliv Rev. 2006;58(5–6):640–56.

**[16]** Harding FA, Stickler MM, Razo J, DuBridge RB. The immunogenicity of humanized and fully human antibodies. mAbs. 2010;2(3):256–65.

**[17]** Lonberg N. Fully human antibodies from transgenic mouse and phage display platforms. Curr Opin Immunol. 2008;20(4):450–59.

**[18]** Labrijn AF, Janmaat ML, Reichert JM, Parren PWHI. Bispecific antibodies: a mechanistic review of the pipeline. Nat Rev Drug Discov. 2019;18(8):585–608.

**[19]** Ferrara N, Hillan KJ, Gerber H-P, Novotny W. Discovery and development of bevacizumab, an anti-VEGF antibody for treating cancer. Nat Rev Drug Discov. 2004;3(5):391–400.

**[20]** Adams GP, Weiner LM. Monoclonal antibody therapy of cancer. Nat Biotechnol. 2005;23(9):1147–57.

**[21]** Beck A, Wurch T, Bailly C, Corvaïa N. Strategies and challenges for the next generation of therapeutic antibodies. Nat Rev Immunol. 2010;10(5):345–52.

**[22]** Clynes RA, Towers TL, Presta LG, Ravetch JV. Inhibitory Fc receptors modulate in vivo cytotoxicity against tumor targets. Nat Med. 2000;6(4):443–46.

**[23]** Golay J, Taylor RP. The role of complement in the immune response against cancer. Semin Immunol. 2021;53:101529.

**[24]** Nimmerjahn F, Ravetch JV. Fcγ receptors as regulators of immune responses. Nat Rev Immunol. 2008;8(1):34–47.

**[25]** June CH, O'Connor RS, Kawalekar OU, Ghassemi S, Milone MC. CAR T

cell immunotherapy for human cancer. Science. 2018;359(6382):1361–65.

**[26]** Amigorena S, Bonnerot C. Fc receptor signaling and trafficking: a connection with antigen processing. Immunol Rev. 1999;172(1):279–84.

**[27]** Pietras K, Ostman A. Hallmarks of cancer: interactions with the tumor stroma. Exp Cell Res. 2010;316(8):1324–31.

**[28]** Goldenberg DM, Sharkey RM. Antibody-targeted therapy of cancer using radiolabeled antibodies. J Nucl Med. 2017;58(4):617–22.

**[29]** Zhang Y. Evolution of phage display libraries for therapeutic antibody discovery. MAbs. 2023;15(1):2213793.

**[30]** McCafferty J, *et al*. Phage antibodies: filamentous phage displaying antibody variable domains. Nature. 1990;348(6301):552–4.

**[31]** Hoogenboom HR. Selecting and screening recombinant antibody libraries. Nat Biotechnol. 2005;23(9):1105–
16.

**[32]** Bradbury AR, Sidhu S, Dübel S, McCafferty J. Beyond natural antibodies: display technologies. Nat Biotechnol. 2011;29(3):245–54.

**[33]** Danve A, Khalasi Y, Vettom EJ. Hybridoma technology: an overview. Int J Immunol Res. 2024;3(6):200– 202.

**[34]** Mogibullah RS, Chandra P. Recent Advances in Monoclonal Antibodies and Next-Generation Antibodies. ImmunoHorizons. 2023;7(12):886–97.

**[35]** Van der Mark C, Aarts A, van den Brink A, Hoeben RC, Wijnen B, Evers M, *et al*. Functional diversification of hybridoma-produced antibodies by CRISPR/HDR genomic engineering. Sci Adv. 2021;7(5):eabe1822.

**[36]** Nimmerjahn F, Ravetch JV. Fcγ receptors as regulators of antibody functions. Nat Rev Immunol. 2022;22(5):282–94.

**[37]** Smith NL, Patel RK, Selby MJ, Ritchey JK, Pulido I, Menon S, *et al*. Harnessing ADCC in monoclonal antibody cancer therapy. Front Immunol. 2023;14:1124569.

**[38]** Lux A, Yu X, Scanlan CN, Nimmerjahn F. Impact of immune effector mechanisms of IgG antibodies on clinical efficacy. Immunol Rev. 2021;302(1):114–32.

**[39]** Sicheneder E, Gruber T, Kirchner M, *et al*. FcγR polymorphisms affect ADCC activity and clinical responses to rituximab in B-cell malignancies. J Hematol Oncol. 2022;15(1):74.

**[40]** Melis JP, Strumane K, Ruuls SR, Beurskens FJ, Schuurman J, Parren PW. Complement in antibody therapy of

cancer: Friend or foe? Trends Immunol. 2023;44(1):10–23.

**[41]** Wang G, Zhou D, Chen Y, Qin S, Liu Y, *et al*. Enhancing complement-dependent cytotoxicity of therapeutic antibodies through Fc engineering. Cancer Immunol Immunother. 2023;72(2):359–72.

**[42]** Beck A, Goetsch L, Dumontet C, Corvaïa N. Strategies and challenges for next-generation antibody–drug conjugates. Nat Rev Drug Discov. 2022;21(11):763–89.

**[43]** Modi S, Park YH, Kim SB, *et al*. Updated results from DESTINY-Breast03: Trastuzumab deruxtecan vs TDM1 in HER2-positive breast cancer. Lancet. 2023;401(10381):105–17.

**[44]** Dhal PK, Kaila N, Tang Y, Vrudhula VM. Linker design strategies for antibody–drug conjugates to enhance efficacy and safety. J Med Chem. 2021;64(5):2333–57.

**[45]** Sharma P, Allison JP. The future of immune checkpoint therapy. Science. 2021;371(6531):eabf6732.

**[46]** Darvin P, Toor SM, Sasidharan Nair V, Elkord E. Immune checkpoint inhibitors: recent progress and potential biomarkers. Exp Mol Med. 2023;55(1):1–16.

**[47]** Kalbasi A, Ribas A. Tumor-intrinsic resistance to immune checkpoint blockade. Nat Rev Immunol. 2020;20(1):25–39.

**[48]** Hegde PS, Chen DS. Top 10 challenges in cancer immunotherapy. Immunity. 2020;52(1):17–35.

**[49]** Maloney DG, Grillo-López AJ, White CA, *et al*. IDEC-C2B8 (Rituximab): a monoclonal antibody for the treatment of B-cell non-Hodgkin's lymphoma. J Clin Oncol. 1997;15(8):3266–74.

**[50]** Van Cutsem E, Köhne CH, Hitre E, *et al*. Cetuximab and chemotherapy as initial treatment for metastatic colorectal cancer. N Engl J Med. 2009;360(14):1408–17.

**[51]** Robert C, Ribas A, Wolchok JD, *et al*. Anti–programmed-death-receptor-1 treatment with pembrolizumab in patients with advanced melanoma: a phase 1 trial. Lancet. 2014;384(9948):1109–17.

**[52]** Fehrenbacher L, Spira A, Ballinger M, *et al*. Atezolizumab versus docetaxel for patients with previously treated non-small-cell lung cancer (POPLAR): a multicentre, open-label, phase 2 randomised controlled trial. Lancet. 2016;387(10030):1837–46.

**[53]** Younes A, Gopal AK, Smith SE, *et al*. Results of a pivotal phase II study of brentuximab vedotin for patients with relapsed or refractory Hodgkin's

lymphoma. J Clin Oncol. 2012;30(18):2183–89.

**[54]** Lokhorst HM, Plesner T, Laubach JP, *et al*. Targeting CD38 with daratumumab monotherapy in multiple myeloma. N Engl J Med. 2015;373(13):1207–19.

**[55]** Topalian SL, Hodi FS, Brahmer JR, *et al*. Safety, activity, and immune correlates of anti–PD-1 antibody in cancer. N Engl J Med. 2012;366(26):2443–54.

**[56]** Postow MA, Sidlow R, Hellmann MD. Immune-related adverse events associated with immune checkpoint blockade. N Engl J Med. 2018;378(2):158–68.

**[57]** Kobayashi S, Boggon TJ, Dayaram T, *et al*. EGFR mutation and resistance of non–small-cell lung cancer to gefitinib. N Engl J Med. 2005;352(8):786–92.

**[58]** Lambert JM, Morris CQ. Antibody–drug conjugates (ADCs) for personalized treatment of solid tumors: a review. Adv Ther. 2017;34(5):1015–35.

**[59]** Aggarwal A. What's fueling the biotech boom? Challenges in global access to cancer biologics. Nat Rev Drug Discov. 2020;19(6):367–68.

**[60]** Wolchok JD, Chiarion-Sileni V, Gonzalez R, *et al*. Overall survival with combined nivolumab and ipilimumab in advanced melanoma. N Engl J Med. 2017;377(14):1345–56.

**[61]** McDermott DF, Atkins MB. PD-1 as a potential target in cancer therapy. Cancer Med. 2013;2(5):662–73.

**[62]** Mack M, Riethmüller G, Kufer P. A small bispecific antibody construct expressed as a functional single-chain molecule with high tumor cell cytotoxicity. Proc Natl Acad Sci U S A. 1995;92(15):7021–5.

**[63]** Muyldermans S. Nanobodies: natural single-domain antibodies. Annu Rev Biochem. 2013;82:775–97.

**[64]** Holliger P, Hudson PJ. Engineered antibody fragments and the rise of single domains. Nat Biotechnol. 2005;23(9):1126–36.

**[65]** Bargou R, Leo E, Zugmaier G, Klinger M, Goebeler M, Knop S, *et al*. Tumor regression in cancer patients by very low doses of a T cell–engaging antibody. Science. 2008;321(5891):974–7.

**[66]** Postow MA, Sidlow R, Hellmann MD. Immune-related adverse events associated with immune checkpoint blockade. N Engl J Med. 2018;378(2):158–68.

**[67]** Aggarwal SR. What's fueling the biotech engine—2012 to 2013. Nat Biotechnol. 2014;32(1):32–9.

**[68]** Ross JS, Slodkowska EA, Symmans WF, Pusztai L, Ravdin PM, Hortobagyi GN. The HER-2 receptor and breast cancer: ten years of targeted anti–HER-2 therapy and personalized medicine. Oncologist. 2009;14(4):320– 68.

**[69]** Dienstmann R, Mason MJ, Sinicrope FA, *et al*. Prediction of response to anti-EGFR therapy in colorectal cancer: clinical biomarkers and tumor models. Nat Rev Clin Oncol. 2013;10(8):467–77.

**[70]** Frueh FW, Quinn B. Biomarkers and personalized medicine: current regulatory perspective. Biomark Med. 2014;8(3):317–20.

**[71]** Hood L, Friend SH. Predictive, personalized, preventive, participatory (P4) cancer medicine. Nat Rev Clin Oncol. 2011;8(3):184–7.

**[72]** Galluzzi L, Vacchelli E, Bravo-San Pedro JM, Buqué A, Senovilla L, Baracco EE, *et al*. Classification of current anticancer immunotherapies. Oncotarget. 2014;5(24):12472–508.

**[73]** Krawczyk K, Liu X, Baker T, Shi J, Deane CM. Improving B-cell epitope prediction and antibody-antigen docking using machine learning. Brief Bioinform. 2014;15(3):408–20.

**[74]** Bedard PL, Hansen AR, Ratain MJ, Siu LL. Tumour heterogeneity in the clinic. Nature. 2013;501(7467):355–64.