2026 Volume: 01 Issue: 07 ISSN 1671-2838 Page No: 485-495

Pharmaceutical Care and Research

https://pcrjournal.com

Review Article

Volume: 01
Issue: 07

# DETAILED REVIEW ON MONOCLONAL ANTIBODIES IN MODERN THERAPY

**Arya K . Mali[1], Dr. Prasad V. Patrekar[2], Saurabh D. Joshi[3*], Poonam A. Mane- Patil[4], Shrirang V. Kharmate[5], Dipak R. Phalle[6], Satyajeet R. Jagdale[7]**

[1]Student, [2]Principal, [3]Assistant Professor, [4]Assistant Professor, [5]Assistant Professor, [6]Assistant Professor, [7]Assistant Professor.

Eklavya College Of Pharmacy, Tasgaon, Maharashtra, India.

**Article Received: 23 August 2026**
**Article Revised: 11 September 2026**
**Published on: 01 October 2026**

***Corresponding Author: Saurabh D. Joshi**
Assistant Professor, Eklavya College of Pharmacy, Tasgaon, Maharashtra, India.

DOI: https://doi-doi.org/101555/ijpcr.7135

## ABSTRACT

Monoclonal antibodies (mAbs) have evolved over five decades from being merely a scientific technique involving the fusion of antibody-producing B cells with myeloma cells into one of the fastest-growing and largest classes of therapeutics . This review will bring together results of analysis done through six recent review articles in connection with the relevant primary literature cited, providing an overview of antibody structure, mechanism of action, production techniques, clinical pharmacology, applications of mAbs for the treatment of oncological diseases, autoimmune conditions and infectious diseases including COVID-19, as well as emerging engineered antibodies such as bispecific antibodies, nanobodies , ADCs, and antibody mimetics . The efficacy of mAbs is achieved thanks to target specificity, prolonged half-life due to recycling by neonatal Fc receptor (FcRn) and diverse mechanisms of action including ADCC (antibody-dependent cellular cytotoxicity) and CDC (complement-dependent cytotoxicity) . Despite the existence of more than 100 approved products there are still a number of issues including expensive manufacturing, immunogenicity, lack of oral bioavailability and accessibility in low-resource areas facing mAb industry. This review will provide the synthesis of relevant historical, technical, pharmacological and clinical literature in order to orient researchers and clinicians to the current developments in the area of antibody therapies.

**KEYWORDS:** *Monoclonal Antibodies; Hybridoma Technology; Antibody–Drug Conjugates; Immunogenicity; Oncology; Autoimmune Disease.*

## 1. INTRODUCTION

Monoclonal antibodies (mAbs) represent engineered immunoglobulins specifically targeting one particular epitope with high affinity, replicating and enhancing specificity that is normally applied by the adaptive immune system for targeting of pathogens and aberrant cells [2,5]. Following the development of hybridoma technology by Köhler and Milstein in 1975 – work that was recognized by the Nobel Prize in Physiology or Medicine in 1984 [1,4] – mAbs have gone from being mere research tools into the mainstream of therapeutic products, having obtained FDA approval in oncology, autoimmune and inflammatory diseases, infectious diseases, cardiovascular diseases, and even rare conditions like paroxysmal nocturnal haemoglobinuria [2,5,6]. According to the 2018 statistics, mAbs made up for nearly 20% of all new FDA drug approvals [11], and by the early 2020s there were already more than 100 approved products with about 100 other mAbs currently undergoing development [6,10]. This review will combine information from six recent sources – general reviews of the mAb history and applications, clinical-pharmacology focused review, literature review dedicated to infectious diseases and COVID-19, and review of the future antibody engineering – along with the primary studies cited.

## 2. Historical Development

The historical basis of the antibody therapy can be traced back to 1890, when Emil von Behring and Shibasaburo Kitasato discovered the ability of the serum from immunized animals to confer passive immunity against diphtheria – achievement that led not only to the establishment of serum therapy but also became a cornerstone of modern anti-infective antibody development [2,5]. The definition of "antibody" by Paul Ehrlich in 1897 and the understanding of immunoglobulin structure by Porter and Edelman, who won the Nobel Prize in 1972, set the physicochemical principles of the antibody engineering [2,3]. The key technological breakthrough happened in 1975, when Köhler and Milstein fused murine B lymphocytes secreting antibodies with immortal myeloma cells and obtained hybridomas capable of producing monoclonal antibodies infinitely [1,4,13]. The first therapeutic mAb, muromonab-CD3 (OKT3), received FDA approval in 1986 for preventing transplant rejection; however, its entirely murine origin made this product prone to human anti-mouse antibodies (HAMA) reaction and significantly reduced its half-life from 18 hours to several hours as well as causing occasional anaphylaxis in some patients [4,6]. Thus, the necessity to decrease the immunogenicity of mAbs drove the development of new waves of engineering: the chimeric antibodies, in which murine variable regions were spliced into human constant regions [14] (such as infliximab and rituximab); humanized antibodies with murine complementarity-determining regions spliced into human frameworks [15,16] (trastuzumab, daclizumab); and fully human antibodies generated either via transgenic mice or phage display [17,18].

## 3. Structure and Mechanisms of Action

### 3.1 Molecular Architecture

Monoclonal antibodies are large (approximately 150 kDa) heterodimeric Y-shaped glycoproteins comprised of two heavy chains and two light chains covalently bound via disulfide bonds [2,6]. The two legs of the Y represent antigen binding fragments (Fab), which consist of variable portions of heavy (VH) and light chains (VL), whose CDRs determine the specificity toward the particular epitope, while the stem portion represents crystallizable fragments (Fc) specifying isotype and responsible for effector function through Fc-gamma receptors (FcγR) expressed on immune cells [4,6]. The vast majority of marketed mAbs belong to IgG isotype, which can be further divided into IgG1–IgG4 subclasses, differing in complement and FcγR binding capacities; among them, IgG1 and IgG3 are the strongest classical complement and ADCC activators and thus the IgG1 subclass is considered to be the preferred backbone for cytotoxic indications in oncology; in turn, IgG2 and IgG4 are weak in effector function and therefore more suitable for cases when cytotoxic activity is undesirable [6].

### 3.2 Effector Mechanisms

The mechanisms of action for mAbs are numerous and overlapping: (i) signalling-induced apoptosis upon the cross-linking of surface antigens; (ii) inhibition of growth promoting interactions of ligands and receptors; (iii) ADCC, during which Fc domain binding to FcγRIII of natural killer cells triggers the lysis of opsonized cell; (iv) CDC, during which binding of C1q to the Fc region initiates formation of membrane attack complex; (v) ADCP and (vi) immunomodulation via agonistic or antagonistic activity against immune checkpoint receptors like CTLA-4 and PD-1/PD-L1 [2,19]. It should be emphasized that the high affinity to a target antigen does not necessarily mean the high specificity, as shown in a classic experiment of characterization of 52 antibodies directed against carcinoembryonic antigen (CEA), during which it was found that there is no direct correlation between affinity and cross-reactivity and antibodies with the highest affinity exhibited higher non-specific binding [2,20].

## 4. Production and Engineering Technologies

Apart from classical hybridoma technology, a variety of antibody discovery methods have been developed, each having its own advantages and limitations

1. Hybridoma technology is still the most commonly used method due to natural pairing of heavy and light chains and possibility of in vivo affinity maturation but it has low fusion efficiency and species immunogenicity issues [1,3,13].
2. Recombinant DNA technology allows isolation, restriction digestion, amplification via PCR and expression from vector of the antibody coding sequences [14,15].
3. The transgenic animals include the HuMAb Mouse and XenoMouse platforms, which contain human immunoglobulin loci in lieu of murine ones, allowing for the generation of full-length human antibodies with various, affinity-matured repertoires; the aforementioned platforms have been responsible for the creation of at least 18 FDA-approved mAbs [3,17].

4. Phage, yeast, bacterial, ribosome and mammalian cell display systems involve the surface presentation of antibody fragments (scFv, Fab) from the host organism or ribosomal complexes, thus facilitating iterative panning against a particular antigen using libraries with up to 10^11 – 10^15 members [3,21].

5. B-cell immortalization (by means of EBV transformation) and single B-cell antibodies involve the isolation of naturally paired, affinity-matured antibody genes from immune donors, offering a more efficient and cheaper alternative to hybridoma fusion [3].

6. Nucleic-acid based antibodies (DNA and RNA delivered) provide an ability for in vivo antibody production, eliminating the need for conventional manufacturing procedures while sacrificing speed of expression and causing doubts regarding potential immunogenicity of repeat doses [3].

7. Artificial intelligence and machine learning have become widely employed in predicting the CDR structure, antibody-antigen binding affinity and various "developability" factors, including aggregation propensity and immunogenicity [3].

**5. Clinical Pharmacology: mAbs versus Small Molecules**

Monoclonal antibodies are fundamentally different from small-molecule therapeutics in terms of structure, pharmacokinetics and safety profile [6,9]. Due to their relatively large size (~150 kDa), polarity, and propensity to digestion in the digestive tract, mAbs lack oral bioavailability (<1%) and are predominantly delivered intravenously or subcutaneously [5,6]. Their most characteristic pharmacokinetic property is a long half-life in circulation (11–30 days) resulting from the binding of IgG by the neonatal Fc receptor (FcRn) located on the surface of vascular endothelial cells at mildly acidic pH of endosomes followed by recycling and release of the mAb molecule back to circulation at physiological pH [6,8]. Such a mechanism is hard to saturate at therapeutic doses and has intentionally been engineered to further prolong half-life [6,8]. Since mAbs are not substrates of cytochrome P450 enzymes, they are free from drug–drug interactions common for small molecules (except rare cases such as CYP modulation caused by tocilizumab through IL-6 receptor blockade) [6]. Mainly, they are eliminated through intracellular uptake and lysosomal degradation, not metabolism in liver and kidneys [6,9]. Attempts to increase bioavailability of orally delivered antibodies through coating of capsules and engineering of IgG2 isotypes resistant to hinge region proteolysis with use of FcRn receptors in the intestine demonstrated some degree of success in non-human primates [6]. Table 1 demonstrates the main differences between small molecules and mAbs.

*Table 1. Comparison of pharmacology of small-molecule drugs and monoclonal antibodies [6].*

| Property | Small Molecule | Monoclonal Antibodies |
|---|---|---|
| Molecular weight | < 700 Da | ~150,000 Da |
| Production | Chemical synthesis | Mammalian cell culture (e.g., CHO, HEK293) |
| Target affinity | Moderate (nmol/L–µmol/L) | High (fmol/L–pmol/L) |
| Route of administration | Oral, IV, SC, inhaled | IV or SC; oral bioavailability <1% |
| Half-life | 4–24 hours | 11–30 days (FcRn-mediated recycling) |
| Clearance | Hepatic (CYP450), biliary, renal | Intracellular lysosomal degradation |
| Main safety concern | Off-target chemical effects | Immunogenicity; injection-site/infusion reactions |

## 6. Therapeutic Applications

### 6.1 Oncology

Oncology is the leading indication for mAbs [7,22]. Therapeutic antibodies exert their antitumour effect by: (i) opsonizing tumor cells and activating ADCC/CDC as it is the case for rituximab targeting CD20-positive B-cell tumors; (ii) blocking growth-factor receptor signaling (such as trastuzumab for HER2-overexpressing breast and gastric cancer or cetuximab and panitumumab for EGFR-driven colorectal and head-and-neck cancer); (iii) blocking angiogenesis as with bevacizumab targeting VEGF; (iv) delivering cytotoxic payloads via antibody-drug conjugates (e.g., trastuzumab emtansine, Kadcyla, and brentuximab vedotin) [23]; and (v) blocking immune checkpoints, as exemplified by CTLA-4-blocking anti-CTLA-4 antibody ipilimumab and anti-PD-1/PD-L1 antibodies (e.g., nivolumab, pembrolizumab and atezolizumab) [2,7,19]. Development of trastuzumab is the classic example of rational biomarker-driven antibody discovery: preclinical studies revealed association of HER2/neu oncogene overexpression with aggressive breast and ovarian cancer [24], and humanization of murine anti-p185HER2 antibody led to creation of recombinant antibody with ~95% human sequence and reduced immunogenicity [16] – this approach set the paradigm for immunohistochemistry/FISH-based patient selection in drug development [4]. Another achievement is the creation of bispecific T-cell engagers (BiTEs), e.g., blinatumomab that binds simultaneously two molecules, a tumour antigen (e.g., CD19) and CD3 on cytotoxic T cell and triggers immune response against the malignant cell [2,25].

### 6.2 Autoimmune and Chronic Inflammatory Disease

Monoclonal antibodies have revolutionized treatment of rheumatoid arthritis, inflammatory bowel disease, psoriasis, multiple sclerosis, and other autoimmune diseases through blocking pro-inflammatory cytokines or depletion of pathogenic lymphocytes [6,7]. First major achievements in this field were anti-TNF-α antibodies (infliximab, adalimumab, golimumab, certolizumab pegol) and TNF

receptor-Fc fusion protein etanercept, created on the basis of laboratory observations that blocking TNF-α in culture of rheumatoid synovial tissue suppresses "TNF-dependent cytokine cascade" including IL-1, IL-6, GM-CSF and IL-8 [26,27]; used early in combination with methotrexate, anti-TNF therapy allows to render over half of rheumatoid arthritis patients drug-free or disease-free [4]. Anti-CD20 (rituximab) and anti-CD52 (alemtuzumab) antibodies deplete B- or T/B lymphocytes, respectively, while more recently developed agents block IL-6 (tocilizumab, sarilumab), IL-17 (secukinumab, ixekizumab), IL-12/23 (ustekinumab) or BAFF (belimumab, approved for systemic lupus erythematosus) [6,28]. Such therapies are not completely risk-free as anti-TNF agents may reactivate latent tuberculosis, and immunomodulatory mAbs may cause autoantibodies formation, lupus-like syndrome, vasculitis, or thyroid autoimmune disease [2,5,12].

**6.3 Infectious Disease, Including COVID-19**

Use of antibodies in treatment of infections is quite recent area: only about 8% of FDA-approved mAbs are directed to infectious agents because of high costs, poor stability and large size of conventional IgG [5]. Currently, there are palivizumab which reduces severity of respiratory syncytial virus infection in infants [29]; ibalizumab which is a CD4 post-attachment inhibitor for multidrug-resistant HIV-1 infection [30]; and raxibacumab, obiltoxaximab and analogues of rabies immunoglobulin which are used in post-exposure prophylaxis from anthrax and rabies [6]. The COVID-19 pandemic significantly contributed to the development of antibodies for treatment of this infection [2,31]. Antibody cocktails that are designed to bind non-overlapping epitopes of SARS-CoV-2 spike RBD thus preventing interaction with ACE2 (such as casirivimab plus imdevimab) and preventing rapid mutation escape in preclinical studies [32] were found to reduce hospitalization, mortality and viral load in high-risk seronegative patients [33]. However, appearance of new variants of concern (especially Omicron which contains more than 15 mutations in RBD compared with average 3 mutations in other variants) decreased neutralizing activity of first-generation cocktails and made broad neutralizing antibodies necessary in order to overcome antigenic shift – several mAbs were withdrawn or had usage restrictions due to this problem [5,34]. It was found that application of antibodies in immunocompromised or persistently infected patients accelerates mutations of viral spike and suggests that both neutralizing activity of antibodies and host T-cell immunity play role in viral evolution [35]. In addition to direct neutralizing activity, another type of COVID-19 mAbs targets hyperinflammatory "cytokine storm"; tocilizumab reduced mortality by about 13% in hospitalized patients with severe pneumonia [36] and baricitinib increased 28-day survival in patients with severe COVID-19 in COV-BARRIER study [37]. New evidence suggests that treatment with antiviral mAbs results in generation of immune complexes taken up by antigen-presenting cells and inducing vaccine-like immune priming.

**6.4 Other Indications**

Besides cancers, autoimmune and infectious diseases, mAbs have been approved for use in platelet inhibition (abciximab, which targets glycoprotein GPIIb/IIIa), migraine prophylaxis (erenumab,

fremanezumab and galcanezumab, targeting the calcitonin gene-related peptide pathway), hypercholesterolaemia (evolocumab and alirocumab, targeting PCSK9), osteoporosis (denosumab, targeting RANKL), asthma and atopic dermatitis, and paroxysmal nocturnal haemoglobinuria (eculizumab, targeting complement C5) [2,4,5,6].

**7. Next-Generation Antibody Formats**

Apart from the conventional IgG mAbs, there are many types of engineered antibody variants that extend the applicability of antibodies in therapy and diagnostics [3,7]:

1. The bispecific antibodies (bsAbs) bind to two antigens or epitopes at once, e.g. targeting a tumour antigen and CD3 on T cells. By doing so, they increase the specificity and potency of treatment while reducing the risk of side effects. There are over 50 different recombinant bsAb formats such as CrossMab, HexaBody and DuoBody formats, as well as catumaxomab and blinatumomab, which were the first bsAbs to be clinically approved [3,7,25].
2. The nanobodies (single-domain VHH antibodies) are the fragments of antibodies isolated from heavy-chain only antibodies of camelids [38] and possess high antigen-binding affinity despite their smaller structure (12-15 kDa, i.e. 1/10th of a typical IgG). Due to their unique properties, such as better tissue penetration, the ability to target cryptic epitopes, and stability in extreme pH and temperatures [39], they are used not only in diagnostics, but also in treatment. The caplacizumab, used for treating acquired thrombotic thrombocytopenic purpura, became the first approved nanobody drug. There are currently more than a dozen other nanobody drugs in clinical trials, including those targeting the SARS-CoV-2 Omicron strain [3,5].
3. The scFv (single-chain variable fragments) consist of VH and VL domains linked with a flexible peptide chain, thus improving their tissue penetration and renal clearance, although having a relatively
4. Engineered-Fc antibodies use mutations or glycoengineering (for instance, afucosylation) at the Fc domain of the antibody to increase or suppress the activity of ADCC, CDC or FcRn recycling depending on what therapeutic application an antibody needs to fulfill [3,6].
5. Antibody-drug conjugates (ADCs) join a targeting antibody to a small molecule that carries out the toxic effect, thus concentrating chemotherapy only on cancer cells and spares healthy tissue; brentuximab vedotin and trastuzumab emtansine represent some of the pioneering clinically valuable examples [4,23].
6. Antibody biosimilars are highly similar, though not necessarily identical, to an original mAb made from different cell lines and provide affordable access to the drugs like infliximab, rituximab, trastuzumab and bevacizumab under stricter comparison rules compared to small-molecule generics [3].
7. Antibody mimetics (affibodies, DARPins, adnectins, aptamers, and other frameworks) mimic the antigen binding activity in absence of the Fc domain, having the advantages of low price, enhanced

chemical stability, reduced immunogenicity at the cost of shorter half-life and lack of Fc effector functions [3].

## 8. Challenges and Limitations

Despite the incredible therapeutic value, monoclonal antibodies still suffer from four overlapping problems [5,12]:

1. Manufacturing cost and scalability: higher costs associated with cell-culture manufacturing, cumbersome purification steps and strict quality control standards make monoclonal antibodies (mAbs) much more costly to manufacture than small molecules, limiting patient access, especially in developing countries; continuous bioprocess manufacturing could potentially reduce costs of goods by 20–40% compared to batch manufacturing [2,7].
2. Immunogenicity: even fully human and humanized antibodies may elicit anti-drug antibodies, reducing efficacy or causing infusion reactions; a classification system has been developed based on the types of reactions: alpha – cytokine-release, beta – allergic reaction, gamma – immune imbalance, delta – cross-reactivity and epsilon – non-immunological [5,7,12].
3. Pharmacokinetics and delivery challenges: poor oral bioavailability, inability to cross intact blood-brain barrier and limited volumes of distribution restrict access to intracellular and CNS targets, spurring development of intranasal administration, brain shuttling via transferrin receptors, and FcRn-mediated oral targeting [5,6].
4. Regulatory and ethical frameworks and biosimilar comparability standards: organizations like the FDA and EMA need to assess increasingly complicated antibodies (bispecifics, ADCs, biosimilars), while initiatives such as EU 2010/63/EU drive the field towards animal-free discovery platforms [7].

## 9. Future Directions

Some trends that seem to be defining the future decade for antibody-based drugs include [5,7]: first, combination of mAbs with genetic and cell therapies – such as expression of antibodies in vivo or combination with chimeric antigen receptor (CAR) T-cell platforms – will allow more durable and personalized treatment options [3,7]; second, advancement in artificial intelligence and machine learning will speed up the drug discovery by predicting paratope-epitope interactions, optimizing developability and humanization with reduced need for iterative wet lab screening [3]; third, moving beyond cancer treatment into neurodegenerative diseases, chronic pain and infectious targets (Ebola, hepatitis B/C and antibiotic-resistant bacteria) due to overcoming the obstacles with the blood-brain barrier and stability fourth, development of stereospecific and conformationally recognizing antibodies in combination with nanobodies and multivalency technology may resolve the viral "escape" from the first generation of neutralizing mAbs – the case in point being the Omicron wave of SARS-CoV-2 infection [5,34]; and finally, innovations in biomanufacturing and biosimilar pathway may eventually reduce the cost burden [3,7].

## 10. CONCLUSION

Since their first application as laboratory tools in 1975 , monoclonal antibodies have become a therapeutic class whose importance spans oncology, autoimmune disorders, infectious diseases, and other conditions, both common and rare. While the pharmacologic strengths of this class of drugs include exceptional target specificity, enhanced effector function, and extended plasma half-life via the FcRn pathway, their high production costs, potential for immunogenicity and restricted route of administration due to the above characteristics confine their use exclusively to injection. Newer formats of biologics such as bispecific antibodies, nanobodies, antibody-drug conjugates, biosimilars, and antibody mimics, along with AI-enabled discovery and combination with gene and cell therapies, will further the scope and efficacy of this therapeutic class while reducing its costs, making antibodies one of the major therapeutic modalities of the twenty-first century.

## REFERENCES


1. Köhler G, Milstein C. Derivation of specific antibody-producing tissue culture and tumor lines by cell fusion. Eur J Immunol. 1976; 6:511-519.
2. Kothari M, Wanjari A, Acharya S, Karwa V, Chavhan R, Kumar S, Kadu A, Patil R. A comprehensive review of monoclonal antibodies in modern medicine: tracing the evolution of a revolutionary therapeutic approach. Cureus. 2024; 16(6):e61983. doi:10.7759/cureus.61983.
3. Singh R, Chandley P, Rohatgi S. Recent advances in the development of monoclonal antibodies and next-generation antibodies. ImmunoHorizons. 2023;7(12):886-897. doi:10.4049/immunohorizons.2300102.
4. Shepard HM, Phillips GL, Thanos CD, Feldmann M. Developments in therapy with monoclonal antibodies and related proteins. Clin Med (Lond). 2017;17(3):220-232. doi:10.7861/clinmedicine.17-3-220.
5. Atanasov PY, Moneva-Sakelarieva MG, Kobakova YA, et al. Monoclonal antibodies: their place in applied medicine and their role in the newest infectious disease — history, present, and future. Pharmacia. 2025;72:1-18. doi:10.3897/pharmacia.72.e159772.
6. Castelli MS, McGonigle P, Hornby PJ. The pharmacology and therapeutic applications of monoclonal antibodies. Pharmacol Res Perspect. 2019;7(6):e00535. doi:10.1002/prp2.535.
7. Udeabor SE. Monoclonal antibodies in modern medicine: their therapeutic potential and future directions. Trends Pharm Biotechnol. 2024;2(2):12-20. doi:10.57238/tpb.2024.153196.1019.
8. Roopenian DC, Akilesh S. FcRn: the neonatal Fc receptor comes of age. Nat Rev Immunol. 2007;7:715-725.
9. Ryman JT, Meibohm B. Pharmacokinetics of monoclonal antibodies. CPT Pharmacometrics Syst Pharmacol. 2017;6(9):576-588. doi:10.1002/psp4.12224.
10. Kaplon H, Reichert JM. Antibodies to watch in 2019. MAbs. 2019;11(2):219-238. doi:10.1080/19420862.2018.1556465.

11. Mullard A. 2018 FDA drug approvals. Nat Rev Drug Discov. 2019;18:85-89. doi:10.1038/d41573-019-00014-x.
12. Samaranayake H, Wirth T, Schenkwein D, Räty JK, Ylä-Herttuala S. Challenges in monoclonal antibody-based therapies. Ann Med. 2009;41:322-331. doi:10.1080/07853890802698842.
13. Mitra S, Tomar PC. Hybridoma technology; advancements, clinical significance, and future aspects. J Genet Eng Biotechnol. 2021;19:159. doi:10.1186/s43141-021-00264-6.
14. Morrison SL, Johnson MJ, Herzenberg LA, Oi VT. Chimeric human antibody molecules: mouse antigen-binding domains with human constant region domains. Proc Natl Acad Sci USA. 1984;81:6851-6855.
15. Jones PT, Dear PH, Foote J, Neuberger MS, Winter G. Replacing the complementarity-determining regions in a human antibody with those from a mouse. Nature. 1986;321:522-525.
16. Carter P, Presta L, Gorman CM, et al. Humanization of an anti-p185HER2 antibody for human cancer therapy. Proc Natl Acad Sci USA. 1992;89:4285-4289.
17. Lonberg N. Human antibodies from transgenic animals. Nat Biotechnol. 2005;23:1117-1125.
18. Smith GP. Filamentous fusion phage: novel expression vectors that display cloned antigens on the virion surface. Science. 1985;228:1315-1317.
19. 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):275-287. doi:10.1038/nrc.2016.36.
20. Nap M, Hammarström ML, Börmer O, et al. Specificity and affinity of monoclonal antibodies against carcinoembryonic antigen. Cancer Res. 1992;52:2329-2339.
21. Boder ET, Wittrup KD. Yeast surface display for screening combinatorial polypeptide libraries. Nat Biotechnol. 1997;15:553-557.
22. Scott AM, Allison JP, Wolchok JD. Monoclonal antibodies in cancer therapy. Cancer Immun. 2012;12:14.
23. Tsuchikama K, An Z. Antibody-drug conjugates: recent advances in conjugation and linker chemistries. Protein Cell. 2018;9(1):33-46. doi:10.1007/s13238-016-0323-0.
24. Slamon DJ, Clark GM, Wong SG, et al. Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene. Science. 1987;235:177-182.
25. Brinkmann U, Kontermann RE. The making of bispecific antibodies. MAbs. 2017;9:182-212.
26. Brennan FM, Chantry D, Jackson A, Maini RN, Feldmann M. Inhibitory effect of TNF antibodies on synovial cell interleukin-1 production in rheumatoid arthritis. Lancet. 1989;2:244-247.
27. Feldmann M, Maini RN. Lasker Clinical Medical Research Award. TNF defined as a therapeutic target for rheumatoid arthritis and other autoimmune diseases. Nat Med. 2003;9:1245-1250.
28. Hahn BH. Belimumab for systemic lupus erythematosus. N Engl J Med. 2013;368:1528-1535.

29. Boivin G, Caouette G, Frenette L, Carbonneau J, Ouakki M, De Serres G. Human respiratory syncytial virus and other viral infections in infants receiving palivizumab. J Clin Virol. 2008;42(1):52-57. doi:10.1016/j.jcv.2007.11.012.
30. Beccari MV, Mogle BT, Sidman EF, Mastro KA, Asiago-Reddy E, Kufel WD. Ibalizumab, a novel monoclonal antibody for the management of multidrug-resistant HIV-1 infection. Antimicrob Agents Chemother. 2019;63(6):e00110-19. doi:10.1128/aac.00110-19.
31. McCreary EK, Escobar ZK, Justo JA. Monoclonal antibodies for the treatment of COVID-19 — every day you fight like you're running out of time. JAMA Netw Open. 2023;6:e239702. doi:10.1001/jamanetworkopen.2023.9702.
32. Baum A, Fulton BO, Wloga E, et al. Antibody cocktail to SARS-CoV-2 spike protein prevents rapid mutational escape seen with individual antibodies. Science. 2020;369(6506):1014-1018. doi:10.1126/science.abd0831.
33. Weinreich DM, Sivapalasingam S, Norton T, et al. REGN-COV2, a neutralizing antibody cocktail, in outpatients with Covid-19. N Engl J Med. 2021;384(3):238-251. doi:10.1056/NEJMoa2035002.
34. Cameroni E, Bowen JE, Rosen LE, et al. Broadly neutralizing antibodies overcome SARS-CoV-2 Omicron antigenic shift. Nature. 2022;602(7898):664-670. doi:10.1038/s41586-021-04386-2.
35. Gupta A, Konnova A, Smet M, et al. Host immunological responses facilitate development of SARS-CoV-2 mutations in patients receiving monoclonal antibody treatments. J Clin Invest. 2023;133(6):e166032. doi:10.1172/JCI166032.
36. Rosas IO, Bräu N, Waters M, et al. Tocilizumab in hospitalized patients with severe Covid-19 pneumonia. N Engl J Med. 2021;384(16):1503-1516. doi:10.1056/NEJMoa2028700.
37. Marconi VC, Ramanan AV, de Bono S, et al. Efficacy and safety of baricitinib for the treatment of hospitalised adults with COVID-19 (COV-BARRIER): a randomised, double-blind, parallel-group, placebo-controlled phase 3 trial. Lancet Respir Med. 2021;9(12):1407-1418. doi:10.1016/S2213-2600(21)00331-3.
38. Hamers-Casterman C, Atarhouch T, Muyldermans S, et al. Naturally occurring antibodies devoid of light chains. Nature. 1993;363:446-448.
39. Muyldermans S. A guide to: generation and design of nanobodies. FEBS J. 2021;288:2084-2102.