Exploration of Immunology

Open Exploration

Open Access Review

Exploring immunotherapeutic strategies for bacterial and viral diseases

Ayodele Isaac Adedokun[1], Olaniyi Abideen Adigun[2], Adamu Muhammad Ibrahim[3], Ibrahim Idris[4], Paul Yiran Ntasin[5], Babatunde Ibrahim Olowu[6], Chinyere M. Ikele-Awaogu[7], Precious Kehinde Fadele[8], Ernesto Oluwafemi Dibia[9], Olalekan John Okesanya[10,11], Mohamed Mustaf Ahmed[12]*

[1]Department of Chemical Pathology, School of Medical Laboratory Science, Usmanu Danfodiyo University Sokoto, Sokoto 2346, Nigeria

[2]Department of Medical Laboratory Science, Nigerian Defence Academy, Kaduna 2109, Nigeria

[3]Department of Immunology, School of Medical Laboratory Science, Usmanu Danfodiyo University Sokoto, Sokoto 2346, Nigeria

[4]Faculty of Veterinary Medicine, Usmanu Danfodiyo University Sokoto, Sokoto 2346, Nigeria

[5]Interdisciplinary graduate program in Immunology, University of Iowa, Iowa, IA 52242, United States

[6]Faculty of Veterinary Medicine, University of Ibadan, Ibadan 200132, Nigeria

[7]Integrated Germline Biology Group Laboratory, Osaka University, Osaka 565-0871, Japan

[8]Department of Medicine and Surgery, Faculty of Medical Sciences, College of Medicine, University of Nigeria Enugu Campus, Enugu 400241, Nigeria

[9]Department of Medical Microbiology, University College Hospital, Ibadan 200212, Nigeria

[10]Department of Public Health and Maritime Transport, Faculty of Medicine, University of Thessaly, 38221 Volos, Greece

[11]Department of Medical Laboratory Science, Chrisland University, Abeokuta 110101, Nigeria

[12]Faculty of Medicine and Health Sciences, SIMAD University, Mogadishu 252, Somalia

***Correspondence:** Mohamed Mustaf Ahmed, Faculty of Medicine and Health Sciences, SIMAD University, Mogadishu 252, Somalia. momustafahmed@simad.edu.so

Academic Editor: Nitin Saksena, Victoria University, Australia

Received: January 20, 2025 **Accepted:** June 10, 2025 **Published:** July 11, 2025

Cite this article: Adedokun AI, Adigun OA, Ibrahim AM, Idris I, Ntasin PY, Olowu BI, et al. Exploring immunotherapeutic strategies for bacterial and viral diseases. Explor Immunol. 2025;5:1003202. https://doi.org/10.37349/ei.2025.1003202

Abstract

The global socioeconomic and health impacts of microbial diseases cannot be overemphasized. The emergence of the coronavirus in 2019 and the ongoing threat of infectious diseases, such as HIV/AIDS, tuberculosis, and hepatitis, remind us of the impact these infections have on economic stability and global health. Gaps in the treatment of microbial infections and their contribution to increased mortality necessitate holistic and long-term solutions, as opposed to antibiotics, which were previously relied upon. Immunotherapy is becoming increasingly promising for the treatment of microbial infections. This study reviews recent advances in immunotherapeutic strategies, particularly cytokine-based therapies, adoptive cell therapy, monoclonal antibodies, and immune checkpoint inhibitors, for the control of antimicrobial resistance. New inventive approaches, such as chimeric antigen receptor T cell therapy and mucosal-associated invariant T cells, have been discussed in the context of bacterial and viral infections, highlighting promising results from clinical trials and addressing the challenges of toxicity, immune evasion, and

therapy resistance that are inherent in these diseases. Future priorities include optimizing combination therapies and exploring new immunomodulatory targets to improve the effectiveness of these interventions in treating antimicrobial resistance and other infectious diseases.

Keywords

Coronavirus, immunotherapy, global health, microbial infections, diseases

Introduction

Antimicrobial resistance (AMR) is one of the most significant public health challenges of the twenty-first century, driven by genetic mutations that diminish the efficacy of antimicrobial drugs [1]. Emerging almost immediately after the introduction of antimicrobials, AMR has accelerated in recent years, posing a serious threat to modern medicine [2]. In 2019, bacterial AMR was directly responsible for approximately 1.27 million fatalities worldwide and contributed to over 5 million deaths [3, 4]. The number of deaths directly linked to AMR is expected to increase dramatically, with an estimated 39 million deaths between 2025 and 2050, corresponding to almost three deaths per minute [5]. The emergence of drug-resistant pathogens has spurred unwavering scientific interest in the development of new antimicrobials, leaving a dwindling arsenal against bacterial and viral diseases [6]. However, the misuse and overuse of these drugs have expedited the emergence of new resistant strains, rendering once-treatable infections increasingly untreatable. Resistance compromises treatment efficacy, necessitating the urgent development and implementation of novel strategies to counteract this global dilemma [1]. Clinically significant viral DNA and RNA diseases, such as HIV, hepatitis C, and SARS-CoV-2, and bacterial infections, such as gram-positive pathogens (e.g., *Staphylococcus* and *Streptococcus* spp., *Mycobacterium* spp.) and gram-negative bacteria (e.g., *Escherichia coli*, *Pseudomonas aeruginosa*, and *Actinobacter* spp.), exemplify the grave concerns posed by AMR. Diverse resistance patterns exhibited by viruses and bacteria to currently available antimicrobial agents have become a critical public health issue, complicating the diagnosis and treatment of an expanding range of diseases that were once treated with conventional therapies [2]. This underscores the need for robust preventive surveillance and control measures.

Antimicrobial compounds have been employed since ancient times, and natural extracts have been used historically for their therapeutic properties [7]. Numerous antibacterial drugs have been produced since Fleming discovered penicillin in 1929, which had a significant impact on global human mortality and health [8]. In recent decades, microbial pathogens such as HIV-1 and HIV-2, the 1918 influenza virus, the Middle East respiratory disease coronavirus, and SARS-CoV-2 have repeatedly emerged in human populations from domestic and wild animal reservoirs [9]. These emerging and re-emerging infectious diseases have exposed vulnerabilities in healthcare systems, particularly in underdeveloped regions, and emphasize the urgent need to develop innovative therapeutic strategies against them. In pursuit of universal health coverage and improved life expectancy, a novel treatment modality is revolutionizing healthcare. Immunotherapy offers an innovative solution, particularly for immunocompromised patients, by enhancing host defense against opportunistic infections. Recent advancements in immunotherapeutic strategies have proven instrumental in managing infectious diseases that affect humans. These approaches are pivotal in the broader context of disease prevention and control in humans, with a wider approach to One Health.

Immunotherapy is becoming increasingly popular for treating various diseases by efficiently modulating the host's innate and adaptive immune responses, thereby assisting in the management of several harmful microbial diseases [10]. These agents have diverse mechanisms of action, ranging from enhancing host immunity [cytokine therapy, immune checkpoint inhibitors (ICIs), and vaccines], targeting pathogenic determinants (monoclonal antibodies), and modifying immune cells [invariant killer T cells (iNKTs), mucosal-associated invariant T cells (MAITs), and adoptive T cell therapy], which shows a promising prospect in the fight against microbes. This review explores the recent advances, challenges, and future perspectives of immunotherapeutic strategies for clinically important bacterial and viral diseases. By

analyzing the current state of the field and identifying areas for further research, we hope to shed light on the role of immunotherapy in combating the growing threat of AMR and new infectious illnesses (Figure 1).

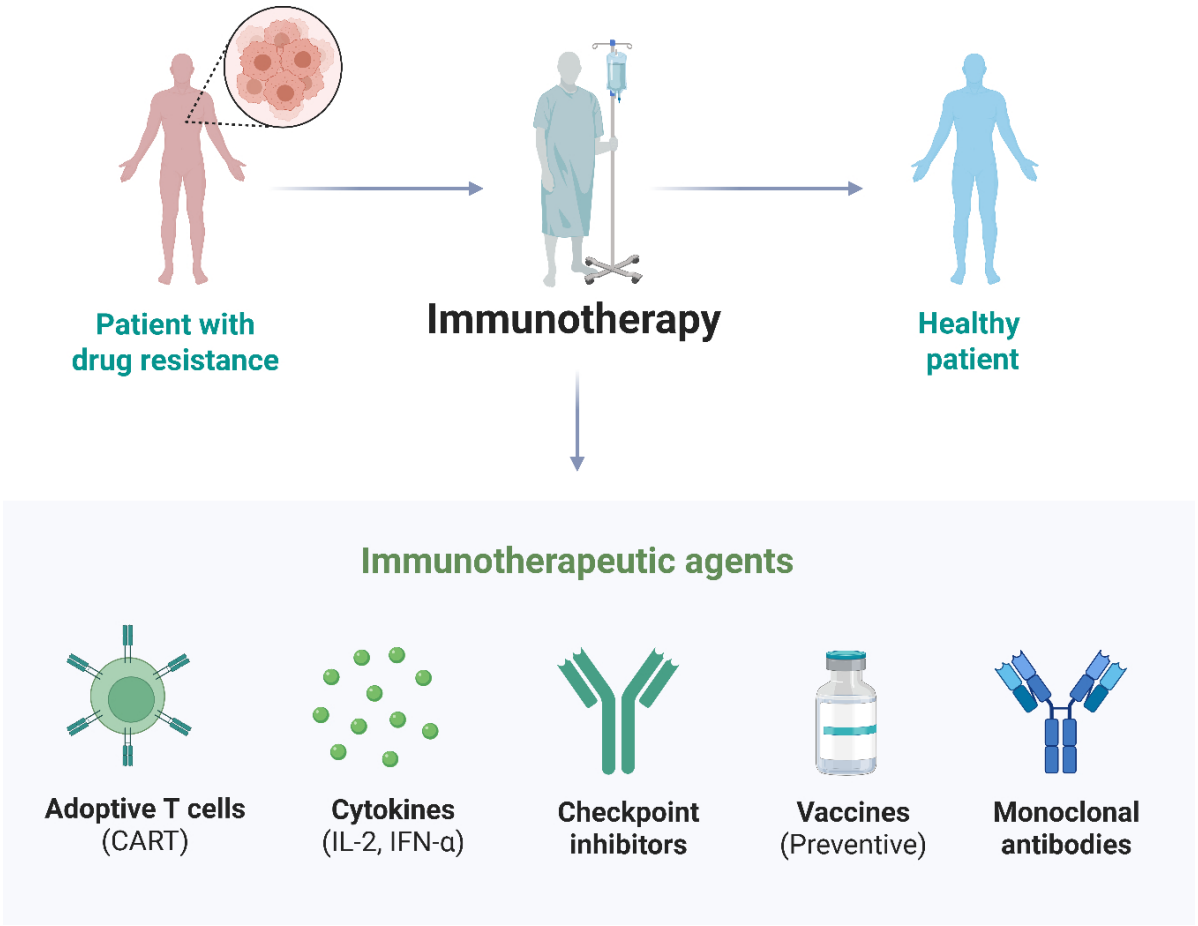

Figure 1. Conceptual pathway of immunotherapy. IFN-α: interferon-α. Created in BioRender. Ahmed, M. (2025) https://BioRender.com/5vsqipu

Cytokine-based therapies

Cytokines are small proteins that are essential for cell signaling within the immune system. These proteins play critical roles in the regulation of immune responses, inflammation, and hematopoiesis [11]. The primary cytokines used in these therapies include interleukins (ILs), interferons (IFNs), tumor necrosis factors (TNFs), and colony-stimulating factors (CSFs). Cytokine-based therapies are powerful tools for treating bacterial and viral diseases. Despite challenges such as toxicity and delivery issues, recent advances and combination strategies offer promising solutions. Granulocyte-macrophage colony-stimulating factor (GM-CSF) has been shown to be effective in stimulating the activation and proliferation of granulocytes and macrophages, thus boosting the immune response against bacterial pathogens. Currently, it is undergoing clinical trials for sepsis and bacterial pneumonia with promising initial outcomes [12]. For instance, an in vivo study revealed that a newly developed albumin-fused GM-CSF exhibited improved biostability and increased dendritic cell populations, which are key to initiating a strong immune response against *Mycobacterium tuberculosis* (MTB) [13]. Moreover, recombinant human interleukin-2 (rhIL-2) has been tested as adjunctive immunotherapy in patients with multidrug-resistant tuberculosis (MDR-TB) to improve treatment efficacy and shorten treatment duration [14]. Additionally, the cytokine IL-7, which supports immune hematopoiesis, has been evaluated in several clinical trials for treating lymphopenia in patients with sepsis suffering from excessive inflammation, known as cytokine storms [15].

IFN-based therapies have shown significant promise in the treatment of viral diseases. IFN-α has been extensively used to treat chronic viral infections such as hepatitis B and C [16]. Recent clinical studies have

demonstrated its effectiveness in significantly reducing viral load and improving liver function, thereby offering substantial therapeutic benefits. IFN-β, traditionally used in the management of multiple sclerosis, is currently being investigated for its potential use in treating COVID-19 [17]. Early clinical trials have indicated that IFN-β may reduce viral replication and modulate inflammatory responses, providing a promising therapeutic avenue for SARS-CoV-2 infections. Similarly, IL-7 has emerged as a potent therapeutic agent for viral infections, primarily because of its ability to enhance T cell recovery and function. Current clinical trials are evaluating its efficacy in treating HIV and post-viral fatigue syndromes, suggesting broader applications in viral immunotherapy [18].

The efficacy of cytokine therapies can be significantly enhanced by combining them with other therapeutic strategies. For example, the combination of IFN-α with ribavirin has substantially improved the treatment of hepatitis C, demonstrating the synergistic effects of cytokines and antiviral combinations [19]. Similarly, IFN-β combined with remdesivir has been investigated for its synergistic potential against SARS-CoV-2, presenting a promising therapeutic strategy for COVID-19 [20–22]. Furthermore, cytokines are paired with monoclonal antibodies or ICIs to amplify antitumor and anti-infective responses. These combinations are being examined in various clinical settings to optimize immunotherapy effectiveness. IL-6 inhibitors, such as tocilizumab, have also shown potential in managing severe bacterial infections by regulating inflammatory responses [23]. This highlights the therapeutic versatility of cytokine inhibitors in the treatment of complex bacterial diseases.

However, cytokine therapies present several challenges. High doses of cytokines can result in severe side effects, including systemic inflammation, cytokine release syndrome, and organ damage. Efficient delivery of cytokines to target tissues is challenging because of their rapid degradation and off-target effects. Additionally, prolonged cytokine use can lead to immune tolerance or resistance, diminishing their efficacy over time [24]. Possible solutions to these challenges include the development of nanoparticle-based delivery systems to protect cytokines from degradation and enhance their targeted delivery. These advanced delivery systems have the potential to significantly improve the efficacy of cytokine therapy. Efforts are also being made to design modified cytokines with enhanced stability and reduced toxicity. These engineered cytokines offer promising solutions to the challenges associated with cytokine therapies [25]. Ongoing research is aimed at determining the optimal dosing and timing of cytokine administration to maximize efficacy while minimizing the side effects. Optimizing these regimens is crucial for improving therapeutic outcomes. Additionally, combining cytokines with other immunomodulatory agents or therapies can enhance their efficacy and reduce the required dose, thereby mitigating side effects. This combination approach offers a promising strategy to overcome the limitations of current cytokine therapies [26]. Continued research and clinical trials are essential to fully harness the potential of cytokines for the treatment of infectious diseases.

ICIs

Over the years, ICIs have shown remarkable efficacy in treating hematological malignancies and solid tumors. Checkpoint inhibition therapy utilizes monoclonal antibodies to disrupt the interactions between immunosuppressive receptors and their ligands. They primarily target proteins such as cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), mucin domain-containing protein 3 (TIM3), and programmed cell death 1 ligand 1 (PD-L1) [27], thereby improving effector T cell activation. However, their use in the treatment of microbial diseases, including HIV, hepatitis B virus (HBV), and HCV, is poorly understood [28].

One of the unique features through which several chronic viral infections, such as HIV, hepatitis, and SARS-CoV-2, bypass immune responses is T cell exhaustion, resulting from the loss of T-cell effector function [29]. In addition, infectious agents possess pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs) [30]. Understanding the function of immune checkpoint molecules is crucial for reversing T cell exhaustion and mounting strong immune responses. Blockade of PD-1 has prompted T cell exhaustion to be redeemable via restoration of CD8+ T cell function by reducing the viral load in a murine model of induced chronic lymphocytic choriomeningitis viral infection [31]. Cao et al. [32] demonstrated that the activity of HBV-specific CD8+ T cells in the peripheral and intrahepatic

niches could be boosted by inhibiting the CTLA-4 checkpoint molecule in patients with chronic hepatitis B. Nonetheless, PD-1 inhibition can improve host immune alertness by promoting the production of IFN-γ in HIV- and HBV-specific cytotoxic T cells [33]. However, in preclinical studies, blocking PD-1 activity in vitro or ex vivo has been shown to potentiate latent HIV reversal [34, 35]. Another murine study indicated a potential adjuvant role for anti-CTLA-4, as CTLA-4 blockade during HIV immunization in mice led to increased CD4+ T cell activation, expansion of HIV-specific follicular helper T cells (Tfh), altered HIV-specific B-cell responses, and significantly increased anti-HIV antibodies with higher avidity and antibody-dependent cellular cytotoxicity [36]. In addition, only three published studies on checkpoint inhibitors have focused on people living with HIV in the absence of malignancy and antiretroviral therapy. Of these, two were abruptly dismissed owing to toxicities and complications in the study population [27]. These immune-related adverse effects pose a major setback to the clinical use of immune checkpoint blockade therapy. In the case of COVID-19, several studies have suggested the benefits of ICI therapy [37]. Clinical trials on the safety and efficacy of ICIs in COVID-19 patients are still being explored [38], with no published results validating ICIs' antiviral properties.

MTB remains a public health concern among all clinically important bacterial infections. ICIs have not been effective against tuberculosis (TB) in recent years. A group of researchers using a 3D microsphere model of human TB indicated that PD-1 inhibition promotes MTB growth and survival by enhancing cytokine production and TNF-α levels [39]. In a recent case report on a child, active TB development was correlated with an inherited PD-1 deficiency [40]. The emergence of TB has also been reported in patients with cancer who receive anti-PD-1/PD-L1 therapy [41]. To resolve this, combining ICIs with other treatment regimens could potentially curb TB pathogenesis and improve patient outcomes [29]. In a previous study, the combination of antibodies against LAG-3, CTLA-4, and TIGIT exhibited an additive effect on stimulating cytokine production by HIV-specific T cells. However, combinations with anti-PD-1 therapy did not yield the same outcomes [42]. In the treatment of Epstein-Barr virus (EBV)-associated tumors, different clinical trials have emphasized the clinical importance of PD-1/PD-L1 inhibitors. First, a phase Ib clinical trial (NCT02054806) of pembrolizumab documented a partial remission (PR) in seven of 27 patients and stable disease in 14 patients with recurrent or metastatic NPC after a 20-month follow-up, with an overall response rate (ORR) of 25.9% [43]. In another clinical trial, camrelizumab (NCT02721589 and NCT03121716) was used both as a mono and combination therapy with chemotherapeutic agents (gemcitabine + cisplatin) in similar patients, yielding an ORR of 34% in the monotherapy group and an impressive 91% in the combination therapy group [44]. Recent findings also indicate the significant impact of avelumab, an anti-PD-L1 agent, on EBV-positive cases (NCT02335411) [45].

Several limitations affect the clinical use of ICIs, including safety due to immune-related adverse events (irAEs) and immune checkpoint expression on other immune cell types, such as gamma delta T cells, Tregs, NK cells, and monocytes [27, 46]. Other immune checkpoint molecules, such as A2AR, B7-H4, BTLA, KIR, NOX2, HO-1, and SIGLEC7 [47], could be extensively explored for the treatment of acute and chronic microbial infections, in addition to the commonly explored immune checkpoints. Given the impact of microbial diseases on global health, exploring the interactions between gut microbiota and microbial infections is of utmost importance. Reports have shown that the gut microbiota also has specific characteristics that improve the therapeutic efficacy of immunotherapeutic drugs in various cancers [48]. Optimizing the usefulness of fecal microbiota transplantation can help enhance several immune-related limitations of ICI clinical use [49]. Therefore, exploring the beneficial role of gut microbiota in immunotherapy for bacterial and viral infections is crucial for achieving complete patient remission outcomes, especially as an adjunctive therapy to enhance the efficacy of ICIs [49]. Ongoing research is focused on the development of ICIs with higher immunity profiling using gut microbiota-assisted technology.

Vaccines (adjuvants)

Relevance of adjuvants in vaccine delivery for generating a long-lasting immunity

The effectiveness and efficacy of vaccines against viral and bacterial infections can be enhanced by adding adjuvants. Therefore, adjuvants are important in vaccine production. They are usually added to bolster immune responses and improve protection against disease. To achieve this, it is necessary to understand the different types of adjuvants and their mechanisms of action. Adjuvants are proteins or polysaccharides, such as tiny substances in vaccines, that facilitate the elicitation of robust immune responses in inactivated vaccines and may have lower immunogenicity than live-attenuated or whole-killed vaccines [50]. Adjuvants are classified into several classes based on their mode of action and composition. The most widely used adjuvant is aluminum salt, which has been used for more than seven decades. It functions by eliciting local immune responses that enhance antigen presentation [51]. Other classes of bacterial adjuvants, such as lipopolysaccharides and toxins, effectively stimulate immune responses. Bacterial toxins have been studied as effective adjuvants that can improve mucosal immune responses [52, 53]. Unlike traditional vaccines that rely on external adjuvants, mRNA vaccines function as self-adjuvants by stimulating innate immune receptors. The single-stranded RNA in these vaccines is recognized by pattern recognition receptors (PRRs), such as Toll-like receptor 7 (TLR7) and retinoic acid-inducible gene I (RIG-I), triggering a strong immune response [54]. This inherent adjuvant-like property enhances antigen presentation and cytokine production, leading to potent and durable immune responses. The success of mRNA vaccines, particularly in combating the COVID-19 pandemic, underscores their transformative role in vaccinology [55]. Moreover, advancements in lipid nanoparticle (LNP) formulations not only aid in mRNA delivery but also contribute to immunostimulatory effects, further optimizing the efficacy of vaccines.

Recent adjuvants, such as CpG motifs, precisely target immune cells to enhance the immune response by mimicking bacterial DNA. Matrix-M is included in the Novavax COVID-19 vaccine, which boosts the immune system by combining lipids and saponins [51]. Another special adjuvant, MF59, used in the influenza vaccine, boosts the immunological response using a distinctive formulation that enhances antigen delivery and immune cell absorption [56]. Adjuvants work by provoking immunological responses at the innate level, which then influence or steer the adaptive immune system. Antigen-presenting cells (APCs) are activated, and cytokines are produced by targeting PRRs on immune cells. This mechanism enhances vaccine antigen recognition and boosts a powerful, targeted, and focused immune response [52, 53]. The incorporation of adjuvants is vital in vaccine production, especially for certain diseases for which conventional vaccines do not offer effective and sufficient immunity. Adjuvants offer several benefits in vaccine production but must be used with caution to reduce potential side effects.

Current developments in adjuvants have substantially improved the prevention of infectious diseases and led to the production of efficient vaccines that offer robust and long-lasting immune responses. For example, TLR agonists, such as monophosphoryl lipid A (MPL), are a potential class of adjuvants that activate innate immunity, thereby enhancing the immune response against viral antigens [57]. They have been used in hepatitis B and SARS-CoV-2 vaccines, substantially improving both antibody and T cell responses [57]. Similarly, TLR7/8 agonists, such as imiquimod, are promising adjuvants in HIV and influenza vaccines that evoke a strong cellular immune response, thereby making them efficient in producing a powerful and long-lasting immune response [57].

Recent developments in vaccine design for bacterial/viral infections

Vaccines against infections such as diphtheria, whooping cough, TB, meningitis, tetanus, and other microbial infections are already in clinical use; however, their effectiveness does not cover all age groups and disease stages (Table 1). The promising nature of mRNA vaccines in cancer treatment has prompted research into the design of mRNA vaccines against bacterial and viral infections (Figure 2). Nonetheless, the biology of microbes and their interactions with host immunity require further investigation [58]. Unlike live-attenuated or inactivated vaccines, mRNA vaccines offer the flexibility of selecting antigen types that can achieve a well-balanced interaction between humoral and cellular immunity [58]. In addition to classic adjuvants, genetic adjuvants have shown effectiveness in disease prevention and treatment [59], alongside

multi-epitope vaccines that encode only individual epitopes of target antigens, thereby minimizing potential adverse effects [60].

Table 1. Summary of mRNA vaccines for the prevention and therapy of bacterial and viral infections

mRNA vaccine	Infection type	References
M72/AS01	Tuberculosis	[61]
BNT162b2 (Comirnaty)	COVID-19	[62]
mRNA-1215	Nipah virus	[63]
ID91*	Tuberculosis	[64]
19ISP	Lyme disease	[65]
mRNA-1273 (Spikevax)	COVID-19	[66–68]
VAL-506440	Influenza	[69]

* Tested in animal models

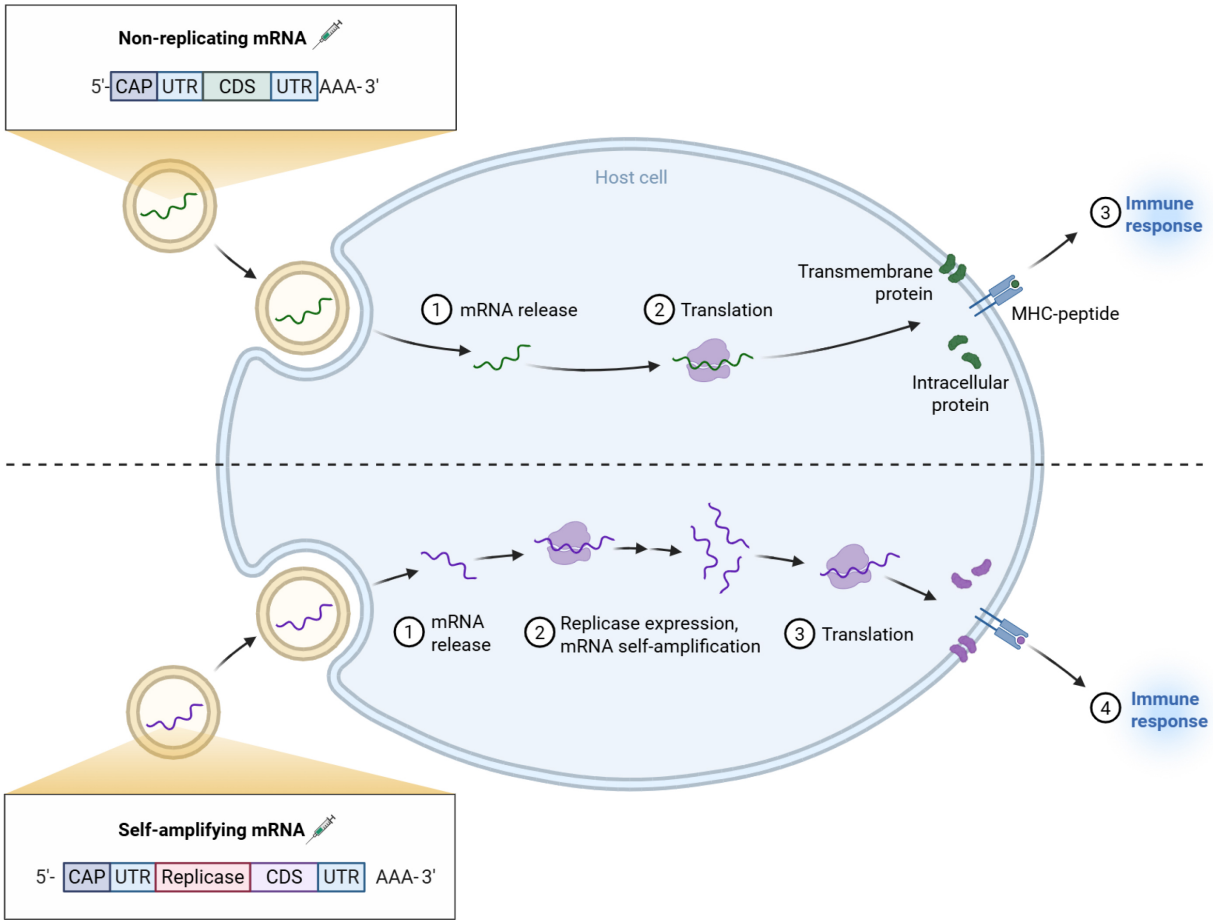

Figure 2. Mechanism of non-replicating versus self-amplifying mRNA vaccines. Created in BioRender. Ahmed, M. (2025) https://BioRender.com/89asvgv

In the development of bacterial vaccines, the WHO has listed virulent multidrug-resistant (MDR) pathogens as top-priority threats, collectively known as ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species). MTB remains a major public health concern that requires novel therapeutic approaches [58]. Before 2023, research on mRNA vaccines for MTB was conducted without the use of delivery systems, administering the vaccine in an unmodified form [58]. However, vaccination with ID91 saRNA encapsulated in a nanostructured lipid carrier elicited both cellular and humoral immune responses [64]. The vaccine also provided prophylactic protection by reducing the bacterial load in the lungs of immunized mice infected with a low dose of MTB H37Rv. Moreover, using an mRNA vaccine in a prime-protein boost format significantly reduced bacterial load in the lungs [64].

Another study by Wang et al. [70] investigated mRNA vaccine variants against *Pseudomonas aeruginosa*: (i) PcrV antigen, a component of the type III secretion system (TSS3), and (ii) a fusion protein OprF-I, composed of outer membrane proteins OprF and OprI. Their findings showed that the PcrV antigen vaccine stimulated adaptive immune responses more effectively than OprF-I. Furthermore, immunization with both mRNA vaccine types generated a more pronounced immune response, exhibited fewer side effects, and increased survival rates [70]. The efficacy of PcrV as an antigen in mRNA vaccines has been further validated in subsequent studies [71]. Other studies have focused on mRNA vaccines against bacterial infections of public health significance. One study formulated mRNA into cationic LNPs combined with the glycolipid α-GC as an adjuvant. This mRNA delivery system, tested in animal models, improved both innate and adaptive immune responses against Listeria monocytogenes [72].

The COVID-19 pandemic accelerated mRNA vaccine development, demonstrating their potential for infectious disease control. A study on mRNA-1273 revealed a robust type 1 helper T cell (Th1)-biased CD4 T cell response but weak Th2 and CD8 T cell responses. The efficient neutralizing antibodies produced indicate strong protection against SARS-CoV-2 [67, 73]. mRNA vaccines are typically administered intramuscularly, intradermally, or subcutaneously, facilitating antigen presentation to immune cells. This process induces CD8+ T cell responses, polyfunctional Th1 cells, and antibodies that inhibit viral replication [74]. Similarly, an mRNA vaccine against chikungunya virus (CHIKV) encoded a potent neutralizing human monoclonal antibody, proving effective for CHIKV treatment [75].

In the treatment of EBV infection, a vaccine amalgamating the glycoprotein 350 and a multi-epitope vaccine antigen (EBVpoly) with an amphiphilic (AMP)-modified CpG DNA adjuvant (AMP-CpG) augmentation was developed to promote a continuing antibody and cell-mediated immunity, assessed in different human leukocyte antigen-typed multiple sclerosis mouse models [76]. This approach was vital in eliciting lasting EBV-specific neutralizing antibodies and multifunctional CD4+ and CD8+ T cell responses in the models [77]. In addition, an mRNA-1189 vaccine that encodes four EBV proteins: gp350, gH/gL, gB, and gp42, is currently undergoing phase I clinical trials at Moderna in an attempt to avert EBV infection. At the West China Hospital of Sichuan University, a similar study is being performed by improving an mRNA vaccine that encodes EBV-LMP2 integrated with the MHC-I molecule's intracellular sequence to optimize immune presentation and processing (NCT05714748) [78]. Furthermore, a novel multimeric EBV gp350-ferritin nanoparticle vaccine with a saponin-based Matrix-M adjuvant (NCT04645147) has been evaluated by the National Institute of Health, demonstrating an attempt to utilize mRNA vaccine technology to combat infections and illnesses linked to EBV [79].

Immunoinformatic has also revolutionized mRNA vaccine design [80]. Advances in artificial intelligence and bioinformatics have facilitated the development of machine learning tools and neural network platforms for antigen prediction and analysis [81, 82]. These in silico approaches enable the selection of epitopes that elicit optimal cytotoxic T lymphocyte (CTL), helper T lymphocyte (HTL), and B-cell responses [80, 83]. However, designing mRNA vaccines for viral infections remains more challenging than for bacterial infections because of the complexity of selecting appropriate target antigens.

Monoclonal antibodies

Antibodies are naturally present in human blood and cells. Another type of immunity is invasive immunity, which is imposed using synthetically manufactured antibodies that mimic the body system, known as monoclonal antibodies (Figure 3). Some monoclonal antibodies are used as immunotherapeutic agents that function synchronously with cells to attack foreign bodies and treat diseases (Table 2). They can equally target and block signals that cause abnormal multiplication or division of cells, as observed in cancer [84]. Several monoclonal antibodies effective against viral or bacterial infections have been developed, although only a few have been approved for clinical practice [85], while others are progressing through clinical trials with great prospects, particularly those with altered structures to provide optimal advantages [86]. This approach can help overcome the limitations of serum-derived immunoglobulin G (IgG) preparations [85]. Monoclonal antibodies are more effective than polyclonal antibodies because of their consistent characteristics and immunity profile, which relates to the ease of production in large quantities in most

immunotherapeutic remedies [87]. This result was attributed to their affinity for specific antigens. Based on the structure (composition), monoclonal antibodies are classified as murine (fully mouse-derived), chimeric (mouse variable regions fused to human constant regions), humanized [only the mouse monoclonal antibody complementarity-determining regions (CDRs) are grafted onto a human framework], and human (entirely human-derived antibody) [88]. Although antibodies have been used to treat a wide variety of diseases, only a few can be used to treat viral and bacterial infections [89]. The repeated use of mouse monoclonal antibodies as therapeutics in humans leads to the generation of anti-mouse antibodies, thereby reducing the therapeutic window of these immunotherapeutic agents. To address this issue, a chimeric antibody was developed to suppress the immunogenicity of monoclonal antibodies in humans [90].

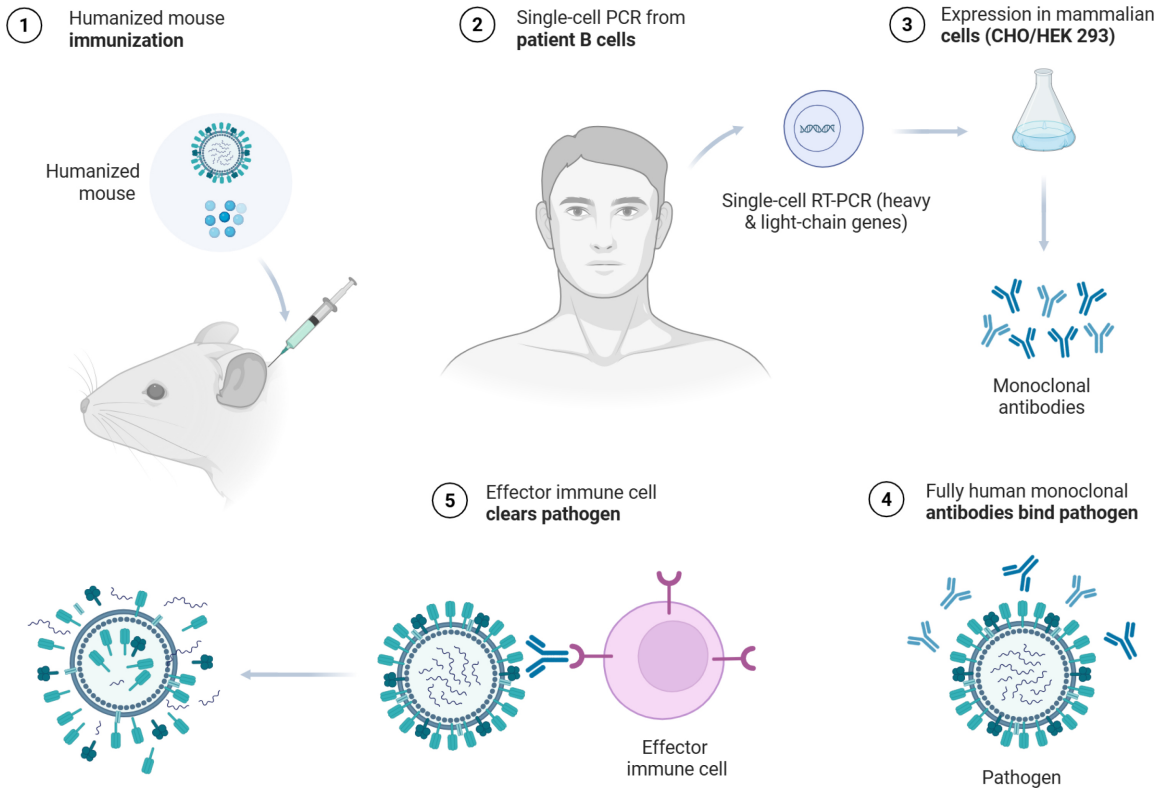

Figure 3. Workflow for fully human monoclonal antibodies. Created in BioRender. Ahmed, M. (2025) https://BioRender.com/f6460ol

Table 2. Summary of monoclonal antibodies for the prevention and treatment of bacterial and viral infections

mAbs	Infection type	References
Palivizumab	Respiratory syncytial virus	[91]
Anti-PhtD	*Streptococcus pneumoniae*	[92]
MEDI3902 (Gremubamab)	*Pseudomonas aeruginosa*	[93]
AR-301 (Salvecin)	Bacterial infection	[94]
514G3	*Staphylococcus aureus*	[95]
Nirsevimab	Respiratory syncytial virus	[96]
Clesrovimab	Respiratory syncytial virus	[97]
Bebtelovimab	COVID-19 Omicron variant	[98]
Raxibacumab	Anthrax	[99]
Bezlotoxumab	*Clostridium difficile*	[100]
Oblitoxaximab	Anthrax	[101]
Twinrab™	Rabies	[102]
Rabishield	Rabies	[103]
Ibalizumab	HIV	[104, 105]

mAbs: monoclonal antibodies

The curbing of SARS-CoV-2 entry was remedied through an immunotherapeutic mechanism to identify the interaction between angiotensin-converting enzyme (ACE) and viral spike glycoprotein, which could be blocked by antibodies targeting the spike viral domain, thereby inhibiting viral infection [89]. Monoclonal antibody-based immunotherapy effectively targets tumor cells and promotes long-lasting antitumor immune responses, thereby improving cancer treatment strategies [106]. These protective effects can be employed against bacterial and viral pathogens, as observed in tumor cells. A previous study demonstrated that evaluating antibody-coated bacteria (ACB) in endotracheal aspirate samples significantly improves the specificity of ventilator-associated pneumonia (VAP) diagnosis by ensuring a clear distinction between viral colonization and non-infectious conditions, thereby reducing overtreatment and resulting in antibody resistance [107].

Monoclonal antibodies offer several advantages over traditional serum-derived immunoglobulin treatments, including greater specificity and potency by targeting specific epitopes, reduced risk of pathogen transmission, more consistent antibody content between batches, and the ability to engineer an extended half-life. Human antibodies with unprecedented activities could become the principal tools for managing future viral and bacterial epidemics, with potential applications in preventing and treating severe human infections [108].

Adoptive cell therapies

Adoptive cell therapy involves boosting the number of immune cells or modifying their function to treat disease conditions. This is achieved by expanding autologous or allogeneic immune cell numbers and infusing genetically engineered immune cells to enhance their function [109]. Adoptive cell therapy, particularly chimeric antigen receptor (CAR) T cell therapy, has gained popularity in the treatment of hematological malignancies. To date, six CAR T cell therapies have been approved by the US FDA [39]. The relative success of adoptive cell therapy in hematological malignancies has prompted the feasibility of adopting this strategy for chronic infectious diseases, infections due to a dysfunctional or suppressed immune system, and MDR infections [110]. Hematopoietic stem cell transplantation is used as a treatment option for various disorders, but it comes at the cost of an immune-deficient phase in which the patient is susceptible to opportunistic viral infections, such as cytomegalovirus, EBV, and adenovirus infections [111]. Transfusion of virus-specific T cells (VSTs) is effective in treating these infections, as evidenced by approximately 20 completed phase I/II clinical trials and over 30 ongoing clinical trials [111, 112]. VSTs are currently in clinical use against post-transplantation viral infections on a compassionate use basis; posoleucel was expected to receive FDA approval; however, it failed to satisfy the primary endpoints of a phase III clinical trial [113]. Tabelecleucel for patients with EBV-associated post-transplant lymphoproliferative disease is another VST in phase III clinical trials (NCT03394365), and its enthusiasts hope to obtain FDA approval [114]. Genetic engineering of VSTs with CAR to increase their lifespan and efficacy is already underway in studies targeting the HIV, HBV, HCV, and coronaviruses [115]. CAR T cell strategies have gained more prominence in HIV studies than in studies of other viruses, considering the formidable challenge of developing a cure for HIV [116]. Preclinical and clinical trials (NCT04648046 and NCT03240328) targeting viral proteins, mainly gp-120, employing CD4 and/or CD8 CAR T cells showed significant suppression of HIV replication and destruction of HIV-infected cells; however, total elimination of HIV-infected cells has not yet been achieved with this approach because of low surface HIV antigen expression on the infected cell membrane and poor CAR T cell infiltration [117, 118]. Intermittent co-administration with vaccine peptides or APCs has been shown to sustain CAR T cell expansion and boost immune responses, considering their poor persistence in tissues [119]. Schreiber et al. [120] reported the efficacy of CAR T cells transduced with HBV-specific antibody fragments in murine studies, demonstrating the potential of CAR T cell therapy for treating infectious diseases. Kalinina et al. [121] transduced naïve T cells with a TCR targeting *S. typhimurium* antigen; the T cells demonstrated a higher capacity for bacterial elimination after transfer into infected mice when compared to normal T cells. Similar outcomes were observed when monocyte-derived macrophages were used to treat MDR bacterial infections in murine models [122] and when macrophages were loaded with photosensitizers to treat MDR *Staphylococcus*

aureus and *Acinetobacter baumannii* in mice [123]. CAR T cell therapy for MTB infections is currently being evaluated, considering the increased number of cases of drug resistance and chronic proclivities [110]. Adoptive T cell therapy has been widely explored, and scientists have begun to pay more attention to the adoptive transfer of other immune cell types as a treatment option in the past few years. Chung et al. [124] showed an increase in the antibody population and a decrease in viral load when virus-specific B cells targeting lymphocytic choriomeningitis virus were infused into mice. The variety of microbial antigens and their potential for mutation, which dampens CAR efficacy, the cost of CAR T cell production, and safety concerns, are some drawbacks of this strategy that are being addressed with better sequencing tools and gene editing technologies [119]. The increase in superbugs, chronic infections, and therapy-induced immunosuppression makes adoptive cell therapy a viable alternative to other less effective therapeutic strategies [39].

iNKT

Immune system cells are conventionally cells of innate or adaptive immunity [125], although some cells are better prepared to switch between the two functions of innate and adaptive immunity, and one of the best-equipped cells is the iNKT [126]. iNKTs, also known as cytotoxic innate lymphoid cells (ILCs), are a subset of cells endowed with molecular memory of surface markers [127]. An invariant αβ TCR associated with the class I major histocompatibility complex, class I-related protein CD1d, reacts with glycolipid antigens on the surface of APCs [128]. They are activated in many infectious diseases and inflammatory conditions and rapidly produce large amounts of cytokines that influence other immune cells [129].

iNKTs recognize lipid-derived determinants on the cell surface, supporting their weaponization for antitumor, viral, and bacterial therapies [130]. They are also explicitly equipped with compact exosomes that package and express eomesodermin (Eomes) [131]. These Eomes-containing exosomes exhibit antitumor properties comparable to those of NK cells and respond to various intracellular pathogens such as bacteria and viruses [132, 133]. Exosomes found in iNKTs are also rich in cytotoxic proteins, such as perforin and granzymes, as well as death receptor ligands, such as FasL and TRAIL [134], which enable exosomes to induce apoptosis in cancer cells and cells infected by viral or bacterial pathogens, such as MTB [135] and SARS-CoV-2 [136], effectively mimicking the cytotoxic and cell-dissolving effects of NK cells, but without requiring direct cell-to-cell contact [137]. Advantageously, the use of NK cell-derived exosomes in immunotherapy helps generate a broader network of immune responses that can penetrate tissues and dissipate deep tumor cells or tissue-invading pathogens with systemic effects [138, 139]. Therefore, more giant cells cannot reach this area without the risk of an autoimmune reaction [140]. This property is a revolutionary point for the use of iNKT cells in immunotherapy and allows pre-administration, re-administration, and re-dosing of cellular components in clinical trials until therapeutic interventions are achieved [141].

Previously, the effector cells that mediated antitumor, viral, and bacterial therapy immunity were αβ T cells and iNKTs [142]. Recently, it has been shown that γδ T cells are the complementary element by which tumor cells are rejected and adapted to defend against the invasion of highly pathogenic organisms into cells and tissue systems [143]. The limitations of iNKTs are due to their inability to enhance the ability of γδ T cells in antigen presentation, regulatory functions, and induction of antitumor responses to excessively malignant tumors, as well as in the treatment of inflammatory conditions caused mainly by pathogen invasion [144]. The weaponization of iNKTs by molecular mechanisms allows them to express the functions of γδ T cells by switching intracellularly and producing compact cytokines that enable them to express the functions of both iNKTs and γδ T cells, demonstrating their potential use in immunotherapy, molecular immunology, and vaccinology [145].

MAITs

MAITs represent a significant subset of unconventional T lymphocytes, forming the largest cadre of innate-like T cells in humans [146]. They are uniquely positioned at the nexus of innate and adaptive immunity,

largely due to their semi-invariant TCR, primarily Vα7.2-Jα33 in humans, which enables them to recognize vitamin B metabolites, such as 5-OP-RU, produced via the riboflavin (vitamin B2) biosynthetic pathway in bacteria, viruses, and fungi [147, 148]. Unlike conventional T cells, which rely on the presentation of peptide antigens by highly polymorphic MHC molecules, MAITs interact with antigens via the evolutionarily conserved MHC class I-related protein, MR1, found on diverse APC [146]. While early investigations suggested that the conserved nature of both MR1 and semi-invariant TCR might limit the scope of antigen recognition, emerging research has revealed a surprising degree of TCR diversity within the MAIT population [148]. This broader repertoire enables the detection of a wider array of microbial metabolites and the mounting of clonotype-dependent responses against various pathogens [146]. Upon activation, MAITs rapidly unleash robust effector functions, marked by the secretion of pro-inflammatory cytokines, such as IFN-γ, TNF-α, and IL-17, and the deployment of potent cytotoxic mediators, such as granzyme B and granulysin [149, 150]. Their abundant distribution across mucosal tissues, including the skin, gastrointestinal tract, and respiratory tract, underscores their essential role as vigilant sentinels, orchestrating localized immune responses against drug-resistant bacteria, fungi, and emerging viral threats [151].

As immunotherapeutic strategies continue to evolve in response to AMR and complex infectious challenges, the potential of MAITs as therapeutic targets is increasingly recognized [152]. Their rapid responsiveness to microbial antigens, coupled with their extraordinary capacity to mobilize both innate and adaptive immune mechanisms, renders them particularly attractive for novel treatment strategies [146]. A pivotal advance in MAIT research was the development of MR1 tetramers, which allow for the precise identification and characterization of these cells across diverse tissues and disease states [153]. Promising approaches, such as ex vivo expansion, antibody opsonization, IL-7 treatment, and the use of artificial APCs (aAPCs), have demonstrated the feasibility of enhancing MAIT responses, while synthetic MR1 ligands and engineered MAIT populations offer innovative avenues to enhance antimicrobial efficacy [154–157]. These strategies are particularly compelling given the cells' ability to recognize conserved microbial metabolic signatures, an attribute that may circumvent the limitations of conventional antibiotic therapies against resistant strains, such as MTB and antibiotic-resistant *Escherichia coli* [152].

In parallel, the emerging field of immuno-antibiotics, which integrates direct antimicrobial actions with the targeted modulation of MAIT responses, represents a promising avenue for overcoming the limitations of traditional antibiotics, particularly against drug-resistant bacteria [152]. However, translating these findings into clinical practice requires overcoming challenges, such as MAIT exhaustion observed in chronic infections, managing potential off-target effects, and unraveling the complex interplay between MAITs and other immune components [146, 158]. Future research is poised to optimize combination therapies by integrating MAIT modulation with monoclonal antibodies, cytokine-based interventions, and even CAR T cell approaches to enhance overall immune responsiveness [159]. Ultimately, a deeper understanding of MAIT biology, their interactions within the tissue microenvironment, and the sophisticated strategies some microbes employ to evade immune detection will be pivotal in realizing their full therapeutic potential, offering a transformative strategy against the escalating threat of infectious diseases and AMR.

Conclusions

Immunotherapeutic strategies offer promising alternatives to address the growing threat of AMR and other infectious diseases in humans. Advances in cytokine-based therapies, adoptive cell therapy, monoclonal antibodies, and ICIs have shown significant potential for modulating immune responses and improving patient outcomes. However, challenges such as toxicity, delivery mechanisms, and immune resistance remain. Leveraging novel technologies, such as nanoparticle-based delivery systems and genetic modifications, can enhance the therapeutic efficacy of these approaches. Future research should focus on optimizing combination therapies and exploring novel immunomodulatory targets to develop more effective and durable treatments for AMR and emerging infectious diseases.

Abbreviations

AMR: antimicrobial resistance

APCs: antigen-presenting cells

CAR: chimeric antigen receptor

CHIKV: chikungunya virus

CSFs: colony-stimulating factors

CTLA-4: cytotoxic T-lymphocyte-associated protein 4

EBV: Epstein-Barr virus

Eomes: eomesodermin

GM-CSF: granulocyte-macrophage colony-stimulating factor

HBV: hepatitis B virus

ICIs: immune checkpoint inhibitors

IFNs: interferons

ILs: interleukins

iNKTs: invariant killer T cells

LNP: lipid nanoparticle

MAITs: mucosal-associated invariant T cells

MDR: multidrug-resistant

MTB: *Mycobacterium tuberculosis*

ORR: overall response rate

PD-L1: programmed cell death 1 ligand 1

PRRs: pattern recognition receptors

TB: tuberculosis

TLR7: Toll-like receptor 7

TNFs: tumor necrosis factors

VSTs: virus-specific T cells

Declarations

Author contributions

AIA and OAA: Conceptualization, Visualization, Investigation, Writing—original draft, Writing—review & editing, Validation. AMI, CMIA, and PKF: Investigation, Validation, Writing—original draft. II, BIO, and EOD: Investigation, Writing—original draft. PYN: Conceptualization, Validation, Writing—original draft, Investigation. OJO: Writing—review & editing, Validation, Supervision. MMA: Writing—review & editing, Validation, Supervision, Visualization. All authors read and approved the submitted version.

Conflicts of interest

All authors declare that they have no conflicts of interest.

Ethical approval

Not applicable.

Consent to participate

Not applicable.

Consent to publication

Not applicable.

Availability of data and materials

Not applicable.

Funding

Not applicable.

Publisher's note

References

1. Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 2022;399:629–55. [DOI] [PubMed] [PMC]
2. Haldar J. Confronting the Rising Threat of Antimicrobial Resistance: A Global Health Imperative. ACS Infect Dis. 2024;10:1–2. [DOI] [PubMed]
3. World Health Organization. Antimicrobial resistance [Internet]. World Health Organization; c2025 [cited 2025 Mar 25]. Available from: https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance
4. Antimicrobial Resistance Facts and Stats [Internet]. U.S. Centers for Disease Control and Prevention; [cited 2025 May 9]. Available from: https://www.cdc.gov/antimicrobial-resistance/data-research/facts-stats/
5. New forecasts reveal that 39 million deaths will be directly attributable to bacterial antimicrobial resistance (AMR) between 2025-2050 [Internet]. Welcome; [cited 2025 May 9]. Available from: https://wellcome.org/news/new-forecasts-reveal-39-million-deaths-will-be-directly-attributable-bacterial-antimicrobial#top
6. Antimicrobial Resistance Threats in the United States, 2021–2022 [Internet]. U.S. Centers for Disease Control and Prevention; [cited 2024 Dec 30]. Available from: https://www.cdc.gov/antimicrobial-resistance/data-research/threats/update-2022.html
7. Muteeb G, Rehman MT, Shahwan M, Aatif M. Origin of Antibiotics and Antibiotic Resistance, and Their Impacts on Drug Development: A Narrative Review. Pharmaceuticals (Basel). 2023;16:1615. [DOI] [PubMed] [PMC]
8. Lobanovska M, Pilla G. Penicillin's Discovery and Antibiotic Resistance: Lessons for the Future? Yale J Biol Med. 2017;90:135–45. [PubMed] [PMC]
9. Baker RE, Mahmud AS, Miller IF, Rajeev M, Rasambainarivo F, Rice BL, et al. Infectious disease in an era of global change. Nat Rev Microbiol. 2022;20:193–205. [DOI] [PubMed] [PMC]
10. Mir MA, Hamdani SS, Qadri H. Significance of immunotherapy for human bacterial diseases and antibacterial drug discovery. In: Mir MA, editor. Human Pathogenic Microbes. Academic Press; 2022. pp. 129–61. [DOI]

11. cytokine [Internet]. Encyclopædia Britannica, Inc.; c2025 [cited 2024 Nov 20]. Available from: https://www.britannica.com/science/cytokine
12. Petrina M, Martin J, Basta S. Granulocyte macrophage colony-stimulating factor has come of age: From a vaccine adjuvant to antiviral immunotherapy. Cytokine Growth Factor Rev. 2021;59:101–10. [DOI] [PubMed] [PMC]
13. Chuang Y, He L, Pinn ML, Tsai Y, Cheng MA, Farmer E, et al. Albumin fusion with granulocyte-macrophage colony-stimulating factor acts as an immunotherapy against chronic tuberculosis. Cell Mol Immunol. 2021;18:2393–401. [DOI] [PubMed] [PMC]
14. Sheng L, Li X, Weng F, Wu S, Chen Y, Lou L. Efficacy and Safety of Adjunctive Recombinant Human Interleukin-2 for Patients with Pulmonary Tuberculosis: A Meta-Analysis. J Trop Med. 2022;2022: 5071816. [DOI] [PubMed] [PMC]
15. Karki R, Kanneganti T. The 'cytokine storm': molecular mechanisms and therapeutic prospects. Trends Immunol. 2021;42:681–705. [DOI] [PubMed] [PMC]
16. Khanna NR, Gerriets V. Interferon. Treasure Island (FL): StatPearls Publishing; 2025. [PubMed]
17. Calabrese LH, Lenfant T, Calabrese C. Interferon therapy for COVID-19 and emerging infections: Prospects and concerns. Cleve Clin J Med. 2020. [DOI] [PubMed]
18. Gunst JD, Goonetilleke N, Rasmussen TA, Søgaard OS. Immunomodulation with IL-7 and IL-15 in HIV-1 infection. J Virus Erad. 2023;9:100347. [DOI] [PubMed] [PMC]
19. Morillas RM, Masnou H, Ardévol M, López D. Role of ribavirin in interferon-free therapy for the treatment of hepatitisC virus. Gastroenterol Hepatol. 2017;40:699–708. [DOI] [PubMed]
20. Wagoner J, Herring S, Hsiang T, Ianevski A, Biering SB, Xu S, et al. Combinations of Host- and Virus-Targeting Antiviral Drugs Confer Synergistic Suppression of SARS-CoV-2. Microbiol Spectr. 2022;10: e0333122. [DOI] [PubMed] [PMC]
21. Bojkova D, Stack R, Rothenburger T, Kandler JD, Ciesek S, Wass MN, et al. Synergism of interferon-beta with antiviral drugs against SARS-CoV-2 variants. J Infect. 2022;85:573–607. [DOI] [PubMed] [PMC]
22. Choi MH, Wan EYF, Wong ICK, Chan EWY, Chu WM, Tam AR, et al. Comparative effectiveness of combination therapy with nirmatrelvir-ritonavir and remdesivir versus monotherapy with remdesivir or nirmatrelvir-ritonavir in patients hospitalised with COVID-19: a target trial emulation study. Lancet Infect Dis. 2024;24:1213–24. [DOI] [PubMed]
23. Aliyu M, Zohora FT, Anka AU, Ali K, Maleknia S, Saffarioun M, et al. Interleukin-6 cytokine: An overview of the immune regulation, immune dysregulation, and therapeutic approach. Int Immunopharmacol. 2022;111:109130. [DOI] [PubMed]
24. Cytokine Release Syndrome [Internet]. WebMD LLC; c1994-2025 [cited 2024 Dec 10]. Available from: https://emedicine.medscape.com/article/2500111-overview
25. Deckers J, Anbergen T, Hokke AM, de Dreu A, Schrijver DP, de Bruin K, et al. Engineering cytokine therapeutics. Nat Rev Bioeng. 2023;1:286–303. [DOI] [PubMed] [PMC]
26. Pires IS, Hammond PT, Irvine DJ. Engineering Strategies for Immunomodulatory Cytokine Therapies - Challenges and Clinical Progress. Adv Ther (Weinh). 2021;4:2100035. [DOI] [PubMed] [PMC]
27. Gubser C, Chiu C, Lewin SR, Rasmussen TA. Immune checkpoint blockade in HIV. EBioMedicine. 2022;76:103840. [DOI] [PubMed] [PMC]
28. Shah NJ, Pia AD, Wu T, Williams A, Weber M, Sinclaire B, et al. Clinical Outcomes of Immune Checkpoint Inhibitors in Unique Cohorts Underrepresented in Clinical Trials. Cancers (Basel). 2024; 16:2223. [DOI] [PubMed] [PMC]
29. Wykes MN, Lewin SR. Immune checkpoint blockade in infectious diseases. Nat Rev Immunol. 2018; 18:91–104. [DOI] [PubMed] [PMC]
30. Vance RE, Eichberg MJ, Portnoy DA, Raulet DH. Listening to each other: Infectious disease and cancer immunology. Sci Immunol. 2017;2:eaai9339. [DOI] [PubMed] [PMC]

31. Saeidi A, Zandi K, Cheok YY, Saeidi H, Wong WF, Lee CYQ, et al. T-Cell Exhaustion in Chronic Infections: Reversing the State of Exhaustion and Reinvigorating Optimal Protective Immune Responses. Front Immunol. 2018;9:2569. [DOI] [PubMed] [PMC]
32. Cao H, Zhang R, Zhang W. CTLA4 interferes with the HBV-specific T cell immune response (Review). Int J Mol Med. 2018;42:703–12. [DOI] [PubMed] [PMC]
33. Jubel JM, Barbati ZR, Burger C, Wirtz DC, Schildberg FA. The Role of PD-1 in Acute and Chronic Infection. Front Immunol. 2020;11:487. [DOI] [PubMed] [PMC]
34. Fromentin R, DaFonseca S, Costiniuk CT, El-Far M, Procopio FA, Hecht FM, et al. PD-1 blockade potentiates HIV latency reversal ex vivo in $CD4^+$ T cells from ART-suppressed individuals. Nat Commun. 2019;10:814. [DOI] [PubMed] [PMC]
35. Van der Sluis RM, Kumar NA, Pascoe RD, Zerbato JM, Evans VA, Dantanarayana AI, et al. Combination Immune Checkpoint Blockade to Reverse HIV Latency. J Immunol. 2020;204:1242–54. [DOI] [PubMed] [PMC]
36. Lewis PE, Poteet EC, Liu D, Chen C, LaBranche CC, Stanfield-Oakley SA, et al. CTLA-4 Blockade, during HIV Virus-Like Particles Immunization, Alters HIV-Specific B-Cell Responses. Vaccines (Basel). 2020; 8:284. [DOI] [PubMed] [PMC]
37. Mellinghoff SC, Vanshylla K, Dahlke C, Addo MM, Cornely OA, Klein F, et al. Case Report: Clinical Management of a Patient With Metastatic Non-Small Cell Lung Cancer Newly Receiving Immune Checkpoint Inhibition During Symptomatic COVID-19. Front Immunol. 2021;12:798276. [DOI] [PubMed] [PMC]
38. Pan Y, Tan J, Li J, Li T, Li J, Cao Y, et al. Immune checkpoint inhibitors in cancer patients with COVID-19. Open Life Sci. 2023;18:20220641. [DOI] [PubMed] [PMC]
39. Karsten H, Matrisch L, Cichutek S, Fiedler W, Alsdorf W, Block A. Broadening the horizon: potential applications of CAR-T cells beyond current indications. Front Immunol. 2023;14:1285406. [DOI] [PubMed] [PMC]
40. Ogishi M, Yang R, Aytekin C, Langlais D, Bourgey M, Khan T, et al. Inherited PD-1 deficiency underlies tuberculosis and autoimmunity in a child. Nat Med. 2021;27:1646–54. [DOI] [PubMed] [PMC]
41. Barber DL, Sakai S, Kudchadkar RR, Fling SP, Day TA, Vergara JA, et al. Tuberculosis following PD-1 blockade for cancer immunotherapy. Sci Transl Med. 2019;11:eaat2702. [DOI] [PubMed] [PMC]
42. Chiu CY, Chang JJ, Dantanarayana AI, Solomon A, Evans VA, Pascoe R, et al. Combination Immune Checkpoint Blockade Enhances IL-2 and CD107a Production from HIV-Specific T Cells Ex Vivo in People Living with HIV on Antiretroviral Therapy. J Immunol. 2022;208:54–62. [DOI] [PubMed] [PMC]
43. Hsu C, Lee S, Ejadi S, Even C, Cohen RB, Tourneau CL, et al. Safety and Antitumor Activity of Pembrolizumab in Patients With Programmed Death-Ligand 1-Positive Nasopharyngeal Carcinoma: Results of the KEYNOTE-028 Study. J Clin Oncol. 2017;35:4050–6. [DOI] [PubMed]
44. Fang W, Yang Y, Ma Y, Hong S, Lin L, He X, et al. Camrelizumab (SHR-1210) alone or in combination with gemcitabine plus cisplatin for nasopharyngeal carcinoma: results from two single-arm, phase 1 trials. Lancet Oncol. 2018;19:1338–50. [DOI] [PubMed]
45. Fuchs CS, Doi T, Jang RW, Muro K, Satoh T, Machado M, et al. Safety and Efficacy of Pembrolizumab Monotherapy in Patients With Previously Treated Advanced Gastric and Gastroesophageal Junction Cancer: Phase 2 Clinical KEYNOTE-059 Trial. JAMA Oncol. 2018;4:e180013. [DOI] [PubMed] [PMC]
46. Gay CL, Bosch RJ, McKhann A, Moseley KF, Wimbish CL, Hendrickx SM, et al. Suspected Immune-Related Adverse Events With an Anti-PD-1 Inhibitor in Otherwise Healthy People With HIV. J Acquir Immune Defic Syndr. 2021;87:e234–6. [DOI] [PubMed] [PMC]
47. Cai X, Zhan H, Ye Y, Yang J, Zhang M, Li J, et al. Current Progress and Future Perspectives of Immune Checkpoint in Cancer and Infectious Diseases. Front Genet. 2021;12:785153. [DOI] [PubMed] [PMC]
48. Yan J, Yang L, Ren Q, Zhu C, Du H, Wang Z, et al. Gut microbiota as a biomarker and modulator of anti-tumor immunotherapy outcomes. Front Immunol. 2024;15:1471273. [DOI] [PubMed] [PMC]

49. Lin A, Jiang A, Huang L, Li Y, Zhang C, Zhu L, et al. From chaos to order: optimizing fecal microbiota transplantation for enhanced immune checkpoint inhibitors efficacy. Gut Microbes. 2025;17: 2452277. [DOI] [PubMed]
50. Fan J, Jin S, Gilmartin L, Toth I, Hussein WM, Stephenson RJ. Advances in Infectious Disease Vaccine Adjuvants. Vaccines (Basel). 2022;10:1120. [DOI] [PubMed] [PMC]
51. Zhao T, Cai Y, Jiang Y, He X, Wei Y, Yu Y, et al. Vaccine adjuvants: mechanisms and platforms. Signal Transduct Target Ther. 2023;8:283. [DOI] [PubMed] [PMC]
52. Manriquez GGG, Tuero I. Adjuvants: friends in vaccine formulations against infectious diseases. Hum Vaccin Immunother. 2021;17:3539–50. [DOI] [PubMed] [PMC]
53. Crothers JW, Norton EB. Recent advances in enterotoxin vaccine adjuvants. Curr Opin Immunol. 2023;85:102398. [DOI] [PubMed] [PMC]
54. Verbeke R, Hogan MJ, Loré K, Pardi N. Innate immune mechanisms of mRNA vaccines. Immunity. 2022;55:1993–2005. [DOI] [PubMed] [PMC]
55. Kutikuppala LVS, Kourampi I, Kanagala RSD, Bhattacharjee P, Boppana SH. Prospects and Challenges in Developing mRNA Vaccines for Infectious Diseases and Oncogenic Viruses. Med Sci (Basel). 2024; 12:28. [DOI] [PubMed] [PMC]
56. Adjuvants and Vaccines [Internet]. U.S. Centers for Disease Control and Prevention; [cited 2025 Feb 25]. Available from: https://www.cdc.gov/vaccine-safety/about/adjuvants.html?CDC_AAref_Val=https://www.cdc.gov/vaccinesafety/concerns/adjuvants.html
57. Kayesh MEH, Kohara M, Tsukiyama-Kohara K. TLR agonists as vaccine adjuvants in the prevention of viral infections: an overview. Front Microbiol. 2023;14:1249718. [DOI] [PubMed] [PMC]
58. Khlebnikova A, Kirshina A, Zakharova N, Ivanov R, Reshetnikov V. Current Progress in the Development of mRNA Vaccines Against Bacterial Infections. Int J Mol Sci. 2024;25:13139. [DOI] [PubMed] [PMC]
59. Muslimov A, Tereshchenko V, Shevyrev D, Rogova A, Lepik K, Reshetnikov V, et al. The Dual Role of the Innate Immune System in the Effectiveness of mRNA Therapeutics. Int J Mol Sci. 2023;24:14820. [DOI] [PubMed] [PMC]
60. Vasileva OO, Tereschenko VP, Krapivin BN, Muslimov AR, Kukushkin IS, Pateev II, et al. Immunogenicity of full-length and multi-epitope mRNA vaccines for *M. Tuberculosis* as demonstrated by the intensity of T-cell response: a comparative study in mice. Bull Russ State Med Univ. 2023: 42–8. [DOI]
61. van den Berg RA, De Mot L, Leroux-Roels G, Bechtold V, Clement F, Coccia M, et al. Adjuvant-Associated Peripheral Blood mRNA Profiles and Kinetics Induced by the Adjuvanted Recombinant Protein Candidate Tuberculosis Vaccine M72/AS01 in Bacillus Calmette-Guérin-Vaccinated Adults. Front Immunol. 2018;9:564. [DOI] [PubMed] [PMC]
62. World Health Organization. Pfizer-BioNTech COVID-19 Vaccine, COMIRNATY® (Tozinameran). World Health Organization; 2022.
63. Loomis RJ, DiPiazza AT, Falcone S, Ruckwardt TJ, Morabito KM, Abiona OM, et al. Chimeric Fusion (F) and Attachment (G) Glycoprotein Antigen Delivery by mRNA as a Candidate Nipah Vaccine. Front Immunol. 2021;12:772864. [DOI] [PubMed] [PMC]
64. Larsen SE, Erasmus JH, Reese VA, Pecor T, Archer J, Kandahar A, et al. An RNA-Based Vaccine Platform for Use against *Mycobacterium tuberculosis*. Vaccines (Basel). 2023;11:130. [DOI] [PubMed] [PMC]
65. Sajid A, Matias J, Arora G, Kurokawa C, DePonte K, Tang X, et al. mRNA vaccination induces tick resistance and prevents transmission of the Lyme disease agent. Sci Transl Med. 2021;13:eabj9827. [DOI] [PubMed]
66. SPIKEVAX [Internet]. U.S. Food and Drug Administration; [cited 2025 May 7]. Available from: https://www.fda.gov/vaccines-blood-biologics/spikevax

67. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med. 2021;384:403–16. [DOI] [PubMed] [PMC]
68. Wilson B, Geetha KM. Lipid nanoparticles in the development of mRNA vaccines for COVID-19. J Drug Deliv Sci Technol. 2022;74:103553. [DOI] [PubMed] [PMC]
69. Feldman RA, Fuhr R, Smolenov I, Ribeiro AM, Panther L, Watson M, et al. mRNA vaccines against H10N8 and H7N9 influenza viruses of pandemic potential are immunogenic and well tolerated in healthy adults in phase 1 randomized clinical trials. Vaccine. 2019;37:3326–34. [DOI] [PubMed]
70. Wang X, Liu C, Rcheulishvili N, Papukashvili D, Xie F, Zhao J, et al. Strong immune responses and protection of PcrV and OprF-I mRNA vaccine candidates against *Pseudomonas aeruginosa*. NPJ Vaccines. 2023;8:76. [DOI] [PubMed] [PMC]
71. Kawaguchi K, Kinoshita M, Sudo K, Inoue K, Naito Y, Oba M, et al. mRNA vaccine induces protective immunity against the type III secretory virulence of *Pseudomonas aeruginosa*. bioRxiv 2023.06.09.544431 [Preprint]. 2023 [cited 2024 Nov 20]. Available from: https://doi.org/10.1101/2023.06.09.544431
72. Verbeke R, Lentacker I, Breckpot K, Janssens J, Calenbergh SV, Smedt SCD, et al. Broadening the Message: A Nanovaccine Co-loaded with Messenger RNA and α-GalCer Induces Antitumor Immunity through Conventional and Natural Killer T Cells. ACS Nano. 2019;13:1655–69. [DOI] [PubMed]
73. Corbett KS, Flynn B, Foulds KE, Francica JR, Boyoglu-Barnum S, Werner AP, et al. Evaluation of the mRNA-1273 Vaccine against SARS-CoV-2 in Nonhuman Primates. N Engl J Med. 2020;383:1544–55. [DOI] [PubMed] [PMC]
74. Chaudhary N, Weissman D, Whitehead KA. mRNA vaccines for infectious diseases: principles, delivery and clinical translation. Nat Rev Drug Discov. 2021;20:817–38. [DOI] [PubMed] [PMC]
75. Kose N, Fox JM, Sapparapu G, Bombardi R, Tennekoon RN, de Silva AD, et al. A lipid-encapsulated mRNA encoding a potently neutralizing human monoclonal antibody protects against chikungunya infection. Sci Immunol. 2019;4:eaaw6647. [DOI] [PubMed] [PMC]
76. Dasari V, McNeil LK, Beckett K, Solomon M, Ambalathingal G, Thuy TL, et al. Lymph node targeted multi-epitope subunit vaccine promotes effective immunity to EBV in HLA-expressing mice. Nat Commun. 2023;14:4371. [DOI] [PubMed] [PMC]
77. Wang J, Wang R, Wang M, Ge J, Wang Y, Li Y, et al. Cutting-Edge Therapy and Immune Escape Mechanisms in EBV-Associated Tumors. Med Res Rev. 2025;45:1184–210. [DOI] [PubMed]
78. Guo X, Liu D, Huang Y, Deng Y, Wang Y, Mao J, et al. Revolutionizing viral disease vaccination: the promising clinical advancements of non-replicating mRNA vaccines. Virol J. 2023;20:64. [DOI] [PubMed] [PMC]
79. Bu W, Joyce MG, Nguyen H, Banh DV, Aguilar F, Tariq Z, et al. Immunization with Components of the Viral Fusion Apparatus Elicits Antibodies That Neutralize Epstein-Barr Virus in B Cells and Epithelial Cells. Immunity. 2019;50:1305–16.e6. [DOI] [PubMed] [PMC]
80. Mortazavi B, Molaei A, Fard NA. Multi-epitopevaccines, from design to expression; an in silico approach. Hum Immunol. 2024;85:110804. [DOI] [PubMed]
81. Thrift WJ, Perera J, Cohen S, Lounsbury NW, Gurung HR, Rose CM, et al. Graph-pMHC: graph neural network approach to MHC class II peptide presentation and antibody immunogenicity. Brief Bioinform. 2024;25:bbae123. [DOI] [PubMed] [PMC]
82. Albert BA, Yang Y, Shao XM, Singh D, Smit KN, Anagnostou V, et al. Deep neural networks predict class I major histocompatibility complex epitope presentation and transfer learn neoepitope immunogenicity. Nat Mach Intell. 2023;5:861–72. [DOI] [PubMed] [PMC]
83. Parvizpour S, Pourseif MM, Razmara J, Rafi MA, Omidi Y. Epitope-based vaccine design: a comprehensive overview of bioinformatics approaches. Drug Discov Today. 2020;25:1034–42. [DOI] [PubMed]

84. Monoclonal antibodies (mAbs) [Internet]. Cancer Research UK; [cited 2025 Feb 20]. Available from: https://www.cancerresearchuk.org/about-cancer/treatment/targeted-cancer-drugs-immunotherapy/monoclonal-antibodies
85. Esposito S, Amirthalingam G, Bassetti M, Blasi F, Rosa FGD, Halasa NB, et al. Monoclonal antibodies for prophylaxis and therapy of respiratory syncytial virus, SARS-CoV-2, human immunodeficiency virus, rabies and bacterial infections: an update from the World Association of Infectious Diseases and Immunological Disorders and the Italian Society of Antinfective Therapy. Front Immunol. 2023; 14:1162342. [DOI] [PubMed] [PMC]
86. Motley MP, Banerjee K, Fries BC. Monoclonal antibody-based therapies for bacterial infections. Curr Opin Infect Dis. 2019;32:210–6. [DOI] [PubMed] [PMC]
87. Iqbal T, Choudhary P, Raza K. Monoclonal Antibodies in Cancer Therapy. Int J Multidiscip Res. 2023; 5. [DOI]
88. Monoclonal Antibodies and Their Side Effects [Internet]. American Cancer Society, Inc.; c2025 [cited 2025 May 5]. Available from: https://www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy/monoclonal-antibodies.html
89. Pantaleo G, Correia B, Fenwick C, Joo VS, Perez L. Antibodies to combat viral infections: development strategies and progress. Nat Rev Drug Discov. 2022;21:676–96. [DOI] [PubMed] [PMC]
90. Otsubo R, Yasui T. Monoclonal antibody therapeutics for infectious diseases: Beyond normal human immunoglobulin. Pharmacol Ther. 2022;240:108233. [DOI] [PubMed] [PMC]
91. Makari D, Jensen KM, Harris B, Jafri HS. Randomized, Double-Blind Study of the Safety of the Liquid Versus Lyophilized Formulation of Palivizumab in Premature Infants and Children with Chronic Lung Disease of Prematurity. Infect Dis Ther. 2014;3:339–47. [DOI] [PubMed] [PMC]
92. Brookes RH, Ming M, Williams K, Hopfer R, Gurunathan S, Gallichan S, et al. Passive protection of mice against Streptococcus pneumoniae challenge by naturally occurring and vaccine-induced human anti-PhtD antibodies. Hum Vaccin Immunother. 2015;11:1836–9. [DOI] [PubMed] [PMC]
93. Ali SO, Yu XQ, Robbie GJ, Wu Y, Shoemaker K, Yu L, et al. Phase 1 study of MEDI3902, an investigational anti-*Pseudomonas aeruginosa* PcrV and Psl bispecific human monoclonal antibody, in healthy adults. Clin Microbiol Infect. 2019;25:629.e1–6. [DOI] [PubMed]
94. François B, Mercier E, Gonzalez C, Asehnoune K, Nseir S, Fiancette M, et al. Safety and tolerability of a single administration of AR-301, a human monoclonal antibody, in ICU patients with severe pneumonia caused by *Staphylococcus aureus*: first-in-human trial. Intensive Care Med. 2018;44: 1787–96. [DOI] [PubMed]
95. Varshney AK, Kuzmicheva GA, Lin J, Sunley KM, Bowling RA Jr, Kwan T, et al. A natural human monoclonal antibody targeting Staphylococcus Protein A protects against *Staphylococcus aureus* bacteremia. PLoS One. 2018;13:e0190537. [DOI] [PubMed] [PMC]
96. Esposito S, Abu-Raya B, Bonanni P, Cahn-Sellem F, Flanagan KL, Torres FM, et al. Coadministration of Anti-Viral Monoclonal Antibodies With Routine Pediatric Vaccines and Implications for Nirsevimab Use: A White Paper. Front Immunol. 2021;12:708939. [DOI] [PubMed] [PMC]
97. Clesrovimab in Infants and Children at Increased Risk for Severe Respiratory Syncytial Virus Disease [Internet]. Rahway: Merck & Co., Inc.; c2025 [cited 2025 May 8]. Available from: https://www.merckclinicaltrials.com/trial/nct04938830/
98. Coronavirus (COVID-19) Update: FDA Authorizes Additional Monoclonal Antibody for Treatment of COVID-19 2021 [Internet]. U.S. Food and Drug Administration; [cited 2024 Oct 10]. Available from: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-additional-monoclonal-antibody-treatment-covid-19#:~:text=Today%2C%20the%20U.S.%20Food%20and,about%2088%20pounds%5D)%20with
99. Mazumdar S. Raxibacumab. MAbs. 2009;1:531–8. [DOI] [PubMed] [PMC]
100. Johnson S, Gerding DN. Bezlotoxumab. Clin Infect Dis. 2019;68:699–704. [DOI] [PubMed]

101. Greig SL. Obiltoxaximab: First Global Approval. Drugs. 2016;76:823–30. [DOI] [PubMed]
102. Kansagra K, Parmar D, Mendiratta SK, Patel J, Joshi S, Sharma N, et al. A Phase 3, Randomized, Open-label, Noninferiority Trial Evaluating Anti-Rabies Monoclonal Antibody Cocktail (Twinrab™) Against Human Rabies Immunoglobulin (HRIG). Clin Infect Dis. 2021;73:e2722–8. [DOI] [PubMed]
103. Fan L, Zhang L, Li J, Zhu F. Advances in the progress of monoclonal antibodies for rabies. Hum Vaccin Immunother. 2022;18:2026713. [DOI] [PubMed] [PMC]
104. 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:e00110–19. [DOI] [PubMed] [PMC]
105. FDA approves new HIV treatment for patients who have limited treatment options [Internet]. U.S. Food and Drug Administration; [cited 2025 May 9]. Available from: https://www.natap.org/2018/CROI/croi_36.htm#:~:text=%22Trogarzo%20is%20the%20first%20drug%20in%20a,have%20run%20out%20of%20HIV%20treatment%20options.&text=A%20significant%20decrease%20in%20viral%20load%20after,to%20their%20failing%20ART%20(or%20no%20therapy)
106. Zahavi D, Weiner L. Monoclonal Antibodies in Cancer Therapy. Antibodies (Basel). 2020;9:34. [DOI] [PubMed] [PMC]
107. Ranzani OT, Forte DN, Forte AC, Mimica I, Forte WCN. The value of antibody-coated bacteria in tracheal aspirates for the diagnosis of ventilator-associated pneumonia: a case-control study. J Bras Pneumol. 2016;42:203–10. [DOI] [PubMed] [PMC]
108. Crowe JE Jr. Human Antibodies for Viral Infections. Annu Rev Immunol. 2022;40:349–86. [DOI] [PubMed]
109. Walti CS, Stuehler C, Palianina D, Khanna N. Immunocompromised host section: Adoptive T-cell therapy for dsDNA viruses in allogeneic hematopoietic cell transplant recipients. Curr Opin Infect Dis. 2022;35:302–11. [DOI] [PubMed]
110. Morte-Romea E, Pesini C, Pellejero-Sagastizábal G, Letona-Giménez S, Martínez-Lostao L, Aranda SL, et al. CAR Immunotherapy for the treatment of infectious diseases: a systematic review. Front Immunol. 2024;15:1289303. [DOI] [PubMed] [PMC]
111. Koukoulias K, Papayanni PG, Leen AM, Vasileiou S. Virus-Specific T-Cell Therapy for the Management of Viral Infections in the Immunocompromised. Transfus Med Hemother. 2024;52:5–26. [DOI] [PubMed] [PMC]
112. Keller MD, Hanley PJ, Chi Y, Aguayo-Hiraldo P, Dvorak CC, Verneris MR, et al. Antiviral cellular therapy for enhancing T-cell reconstitution before or after hematopoietic stem cell transplantation (ACES): a two-arm, open label phase II interventional trial of pediatric patients with risk factor assessment. Nat Commun. 2024;15:3258. [DOI] [PubMed] [PMC]
113. Pfeiffer T, Tzannou I, Wu M, Ramos C, Sasa G, Martinez C, et al. Posoleucel, an Allogeneic, Off-the-Shelf Multivirus-Specific T-Cell Therapy, for the Treatment of Refractory Viral Infections in the Post-HCT Setting. Clin Cancer Res. 2023;29:324–30. [DOI] [PubMed] [PMC]
114. Mahadeo KM, Baiocchi R, Beitinjaneh A, Chaganti S, Choquet S, Dierickx D, et al. Tabelecleucel for allogeneic haematopoietic stem-cell or solid organ transplant recipients with Epstein-Barr virus-positive post-transplant lymphoproliferative disease after failure of rituximab or rituximab and chemotherapy (ALLELE): a phase 3, multicentre, open-label trial. Lancet Oncol. 2024;25:376–87. [DOI] [PubMed]
115. Seif M, Einsele H, Löffler J. CAR T Cells Beyond Cancer: Hope for Immunomodulatory Therapy of Infectious Diseases. Front Immunol. 2019;10:2711. [DOI] [PubMed] [PMC]
116. Rothemejer FH, Lauritsen NP, Søgaard OS, Tolstrup M. Strategies for enhancing CAR T cell expansion and persistence in HIV infection. Front Immunol. 2023;14:1253395. [DOI] [PubMed] [PMC]
117. Mazzi MT, Hajdu KL, Ribeiro PR, Bonamino MH. CAR-T cells leave the comfort zone: current and future applications beyond cancer. Immunother Adv. 2020;1:ltaa006. [DOI] [PubMed] [PMC]

118. Zmievskaya E, Valiullina A, Ganeeva I, Petukhov A, Rizvanov A, Bulatov E. Application of CAR-T Cell Therapy beyond Oncology: Autoimmune Diseases and Viral Infections. Biomedicines. 2021;9:59. [DOI] [PubMed] [PMC]
119. Maldini CR, Ellis GI, Riley JL. CAR T cells for infection, autoimmunity and allotransplantation. Nat Rev Immunol. 2018;18:605–16. [DOI] [PubMed] [PMC]
120. Schreiber S, Dressler LS, Loffredo-Verde E, Asen T, Färber S, Wang W, et al. CARs derived from broadly neutralizing, human monoclonal antibodies identified by single B cell sorting target hepatitis B virus-positive cells. Front Immunol. 2024;15:1340619. [DOI] [PubMed] [PMC]
121. Kalinina AA, Nesterenko LN, Bruter AV, Balunets DV, Chudakov DM, Izraelson M, et al. Adoptive Immunotherapy Based on Chain-Centric TCRs in Treatment of Infectious Diseases. iScience. 2020;23:101854. [DOI] [PubMed] [PMC]
122. Tacke R, Sun J, Uchiyama S, Polovina A, Nguyen DG, Nizet V. Protection Against Lethal Multidrug-Resistant Bacterial Infections Using Macrophage Cell Therapy. Infect Microbes Dis. 2019;1:61–9. [DOI]
123. Wang Z, Wu A, Cheng W, Li Y, Li D, Wang L, et al. Adoptive macrophage directed photodynamic therapy of multidrug-resistant bacterial infection. Nat Commun. 2023;14:7251. [DOI] [PubMed] [PMC]
124. Chung YR, Dangi T, Palacio N, Sanchez S, Penaloza-MacMaster P. Adoptive B cell therapy for chronic viral infection. Front Immunol. 2022;13:908707. [DOI] [PubMed] [PMC]
125. Institute for Quality and Efficiency in Health Care: Executive Summaries. Cologne: Institute for Quality and Efficiency in Health Care (IQWiG); 2005. [PubMed]
126. Kaer LV, Parekh VV, Wu L. Invariant natural killer T cells: bridging innate and adaptive immunity. Cell Tissue Res. 2011;343:43–55. [DOI] [PubMed] [PMC]
127. Jeong D, Woo YD, Chung DH. Invariant natural killer T cells in lung diseases. Exp Mol Med. 2023;55:1885–94. [DOI] [PubMed] [PMC]
128. Wu L, Kaer LV. Natural killer T cells in health and disease. Front Biosci (Schol Ed). 2011;3:236–51. [DOI] [PubMed] [PMC]
129. Al-Qahtani AA, Alhamlan FS, Al-Qahtani AA. Pro-Inflammatory and Anti-Inflammatory Interleukins in Infectious Diseases: A Comprehensive Review. Trop Med Infect Dis. 2024;9:13. [DOI] [PubMed] [PMC]
130. Jin Y, Tan Y, Wu J, Ren Z. Lipid droplets: a cellular organelle vital in cancer cells. Cell Death Discov. 2023;9:254. [DOI] [PubMed] [PMC]
131. Zhang P, Lee JS, Gartlan KH, Schuster IS, Comerford I, Varelias A, et al. Eomesodermin promotes the development of type 1 regulatory T (T_R1) cells. Sci Immunol. 2017;2:eaah7152. [DOI] [PubMed] [PMC]
132. Batista IA, Quintas ST, Melo SA. The Interplay of Exosomes and NK Cells in Cancer Biology. Cancers (Basel). 2021;13:473. [DOI] [PubMed] [PMC]
133. Razizadeh MH, Zafarani A, Taghavi-Farahabadi M, Khorramdelazad H, Minaeian S, Mahmoudi M. Natural killer cells and their exosomes in viral infections and related therapeutic approaches: where are we? Cell Commun Signal. 2023;21:261. [DOI] [PubMed] [PMC]
134. Wen C, Seeger RC, Fabbri M, Wang L, Wayne AS, Jong AY. Biological roles and potential applications of immune cell-derived extracellular vesicles. J Extracell Vesicles. 2017;6:1400370. [DOI] [PubMed] [PMC]
135. Sada-Ovalle I, Chiba A, Gonzales A, Brenner MB, Behar SM. Innate invariant NKT cells recognize Mycobacterium tuberculosis-infected macrophages, produce interferon-gamma, and kill intracellular bacteria. PLoS Pathog. 2008;4:e1000239. [DOI] [PubMed] [PMC]
136. Chaudhari P, Ghate V, Nampoothiri M, Lewis S. Multifunctional role of exosomes in viral diseases: From transmission to diagnosis and therapy. Cell Signal. 2022;94:110325. [DOI] [PubMed] [PMC]

137. Fiore PF, Pace ALD, Conti LA, Tumino N, Besi F, Scaglione S, et al. Different effects of NK cells and NK-derived soluble factors on cell lines derived from primary or metastatic pancreatic cancers. Cancer Immunol Immunother. 2023;72:1417–28. [DOI] [PubMed] [PMC]
138. Hatami Z, Hashemi ZS, Eftekhary M, Amiri A, Karpisheh V, Nasrollahi K, et al. Natural killer cell-derived exosomes for cancer immunotherapy: innovative therapeutics art. Cancer Cell Int. 2023;23:157. [DOI] [PubMed] [PMC]
139. Prokopeva AE, Emene CC, Gomzikova MO. Antitumor Immunity: Role of NK Cells and Extracellular Vesicles in Cancer Immunotherapy. Curr Issues Mol Biol. 2023;46:140–52. [DOI] [PubMed] [PMC]
140. Wang MM, Coupland SE, Aittokallio T, Figueiredo CR. Resistance to immune checkpoint therapies by tumour-induced T-cell desertification and exclusion: key mechanisms, prognostication and new therapeutic opportunities. Br J Cancer. 2023;129:1212–24. [DOI] [PubMed] [PMC]
141. Liu Y, Wang G, Chai D, Dang Y, Zheng J, Li H. iNKT: A new avenue for CAR-based cancer immunotherapy. Transl Oncol. 2022;17:101342. [DOI] [PubMed] [PMC]
142. Tognarelli EI, Gutiérrez-Vera C, Palacios PA, Pasten-Ferrada IA, Aguirre-Muñoz F, Cornejo DA, et al. Natural Killer T Cell Diversity and Immunotherapy. Cancers (Basel). 2023;15:5737. [DOI] [PubMed] [PMC]
143. Hu Y, Hu Q, Li Y, Lu L, Xiang Z, Yin Z, et al. γδ T cells: origin and fate, subsets, diseases and immunotherapy. Signal Transduct Target Ther. 2023;8:434. [DOI] [PubMed] [PMC]
144. Wang Y, Xu Y, Chen H, Zhang J, He W. Novel insights based on the plasticity of γδ T cells in the tumor microenvironment. Explor Immunol. 2022;2:98–132. [DOI]
145. Revesz IA, Joyce P, Ebert LM, Prestidge CA. Effective γδ T-cell clinical therapies: current limitations and future perspectives for cancer immunotherapy. Clin Transl Immunology. 2024;13:e1492. [DOI] [PubMed] [PMC]
146. Godfrey DI, Koay H, McCluskey J, Gherardin NA. The biology and functional importance of MAIT cells. Nat Immunol. 2019;20:1110–28. [DOI] [PubMed]
147. Rouxel O, Lehuen A. Mucosal-associated invariant T cells in autoimmune and immune-mediated diseases. Immunol Cell Biol. 2018;96:618–29. [DOI] [PubMed]
148. Corbett AJ, Awad W, Wang H, Chen Z. Antigen Recognition by MR1-Reactive T Cells; MAIT Cells, Metabolites, and Remaining Mysteries. Front Immunol. 2020;11:1961. [DOI] [PubMed] [PMC]
149. Hinks TSC, Zhang X. MAIT Cell Activation and Functions. Front Immunol. 2020;11:1014. [DOI] [PubMed] [PMC]
150. Aboagye EO, Bhujwalla ZM. Malignant transformation alters membrane choline phospholipid metabolism of human mammary epithelial cells. Cancer Res. 1999;59:80–4. [PubMed]
151. Nel I, Bertrand L, Toubal A, Lehuen A. MAIT cells, guardians of skin and mucosa? Mucosal Immunol. 2021;14:803–14. [DOI] [PubMed] [PMC]
152. Leeansyah E, Boulouis C, Kwa ALH, Sandberg JK. Emerging Role for MAIT Cells in Control of Antimicrobial Resistance. Trends Microbiol. 2021;29:504–16. [DOI] [PubMed]
153. Gherardin NA, Souter MN, Koay H, Mangas KM, Seemann T, Stinear TP, et al. Human blood MAIT cell subsets defined using MR1 tetramers. Immunol Cell Biol. 2018;96:507–25. [DOI] [PubMed] [PMC]
154. Liu Y, Wang W, Wu X, Weng X. Detection, Expansion, and Isolation of Human MAIT Cells. Methods Mol Biol. 2020;2111:285–93. [DOI] [PubMed]
155. Sortino O, Richards E, Dias J, Leeansyah E, Sandberg JK, Sereti I. IL-7 treatment supports CD8+ mucosa-associated invariant T-cell restoration in HIV-1-infected patients on antiretroviral therapy. AIDS. 2018;32:825–8. [DOI] [PubMed] [PMC]
156. Siefert AL, Fahmy TM, Kim D. Artificial Antigen-Presenting Cells for Immunotherapies. Methods Mol Biol. 2017;1530:343–53. [DOI] [PubMed]

157. Krawic JR, Ladd NA, Cansler M, McMurtrey C, Devereaux J, Worley A, et al. Multiple Isomers of Photolumazine V Bind MR1 and Differentially Activate MAIT Cells. J Immunol. 2024;212:933–40. [DOI] [PubMed] [PMC]
158. Leeansyah E, Ganesh A, Quigley MF, Sönnerborg A, Andersson J, Hunt PW, et al. Activation, exhaustion, and persistent decline of the antimicrobial MR1-restricted MAIT-cell population in chronic HIV-1 infection. Blood. 2013;121:1124–35. [DOI] [PubMed] [PMC]
159. Bohineust A, Tourret M, Derivry L, Caillat-Zucman S. Mucosal-associated invariant T (MAIT) cells, a new source of universal immune cells for chimeric antigen receptor (CAR)-cell therapy. Bull Cancer. 2021;108:S92–5. [DOI] [PubMed]