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Transformative Biotechnological Frontiers in Modern Therapeutic Discovery and Drug Development: A Scoping Review (2015–2025)

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Abstract

This scoping review examines major biotechnological innovations that transformed pharmaceutical research and development between 2015 and 2025. The review focuses on six rapidly advancing domains: CRISPR-based genome editing, RNA therapeutics, monoclonal antibody engineering, artificial intelligence (AI)-driven drug discovery, organ-on-chip (OoC) and organoid systems, and nanoparticle-mediated drug delivery. A systematic search following PRISMA-ScR guidelines identified 64 relevant studies from PubMed/MEDLINE, Scopus, and Web of Science databases.

The findings demonstrate that these technologies are advancing independently while also increasingly converging. CRISPR-Cas9 reached a major milestone, getting approved by the FDA for sickle cell anaemia in 2023, while newer genome-editing approaches, such as base and prime editing, are progressing through clinical trials. RNA therapeutics, especially mRNA-lipid nanoparticle platforms, gained global recognition through COVID-19 vaccines and are now being applied in cancer immunotherapy and rare disease treatment. Monoclonal antibody-based therapeutics, including bispecific variants and antibody-drug conjugates, maintain a dominant position in the global pharmaceutical market. Concurrently, the emergence of AI frameworks like AlphaFold 3 is significantly expediting drug development through precise biomolecular structure prediction and innovative molecular engineering Additionally, OoC systems and nanoparticle-based delivery platforms are improving disease modelling and targeted therapeutics. Despite remarkable progress, challenges, including regulatory issues, scalability, translational barriers, and algorithmic bias, remain significant concerns.

1. INTRODUCTION

Drug discovery is one of the most resource-intensive efforts in modern science, requiring more than a decade and over USD 2.6 billion for the development of a single new molecular entity. And clinical attrition rates are still above 90% [1,2]. This chronic inefficiency has been attributed to inadequate early-phase target validation, the poor translational fidelity of conventional animal and 2D cell-culture models, and the combinatorial complexity of human biology [3]. But in the last ten years, a convergence of biotechnological disciplines has begun to structurally reconfigure these parameters in ways that earlier generations of pharmaceutical scientists could not have foreseen.

Biotechnology defined broadly as the use of biological systems and living organisms to develop products, processes and therapeutic interventions has transformed from the production of recombinant proteins in the 1980s to include programmable genome editing, synthetic RNA therapeutics, AI-guided molecular design, precision immunotherapy and microfluidic tissue surrogates in the 2020s [4,5]. Importantly, these domains are not evolving independently – their convergence leads to compounding effects that accelerate the drug development cycle in several disease areas.

The speed and breadth of recent progress justify this scoping review. In late 2023, the global regulatory landscape achieved a historic milestone between 2020 and 2025 with the first-ever approval of a CRISPR-Cas9 gene-editing therapy. The large-scale clinical validation of mRNA-lipid nanoparticle (LNP) platforms; the release of AlphaFold 3, which can predict biomolecular interaction networks with near-experimental accuracy; and formal regulatory guidance that supports the use of organ-on-chip data as primary evidence for drug approval [6,7]. These developments are happening rapidly in different sub-disciplines and call for a consolidated analytical perspective.

This scoping review was conducted using the PRISMA for Scoping Reviews (PRISMA-ScR) guidelines [8] and encompasses six major biotechnological pillars, including: (i) CRISPR-based gene editing, (ii) RNA-based therapeutics such as mRNA and RNA interference (RNAi), (iii) monoclonal antibody engineering and cellular immunotherapy, (iv) AI and machine learning in drug discovery, (v) organ-on-chip and organoid drug-testing platforms, and (vi) nanotechnology-based drug delivery systems. For each domain, we discuss mechanistic foundations, landmark clinical evidence, translational status, and outstanding challenges.

2. METHODS

Study Design

This study is a scoping review that was carried out in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) [8] and the Joanna Briggs Institute (JBI) framework for scoping reviews [9]. A scoping review design was chosen over a systematic review due to the wide-ranging domains covered, heterogeneity of study designs in the primary literature, and desire to map evidence rather than synthesise quantitative outcomes.

Search Strategy

Four electronic databases were searched from January 2015 to May 2025: PubMed/MEDLINE, Scopus, Web of Science Core Collection, and ClinicalTrials.gov. Two independent reviewers conducted all searches; results were merged and deduplicated using Rayyan. Database-specific search strings and record yields were as follows:

Table 1. Database-Specific Search Strings and Record Yields

Database	Search String	Records Retrieved
PubMed/MEDLINE	("biotechnology" [MeSH] OR "biotech"[tiab]) AND ("drug discovery"[MeSH] OR "drug development"[tiab] OR "therapeutics"[MeSH]) AND ("CRISPR-Cas Systems"[MeSH] OR "RNA, Messenger"[MeSH] OR "Receptors, Chimeric Antigen"[MeSH] OR "Antibodies, Monoclonal"[MeSH] OR "artificial intelligence"[MeSH] OR "organ-on-chip"[tiab] OR "organoid"[tiab] OR "nanoparticle"[tiab]) Filters: 2015–2025, English	743
Scopus	TITLE-ABS-KEY(biotechnology OR biotech) AND TITLE-ABS-KEY("drug discovery" OR "drug development" OR therapeutics) AND TITLE-ABS-KEY	681

	(CRISPR OR "gene editing" OR mRNA OR "RNA therapeutics" OR "CAR-T" OR "monoclonal antibody" OR "artificial intelligence" OR "machine learning" OR "organ-on-chip" OR organoid OR nanoparticle OR "lipid nanoparticle") AND PUBYEAR > 2014 AND LANGUAGE(English)	
Web of Science Core Collection	TS=(biotechnology OR biotech) AND TS=("drug discovery" OR "drug development" OR therapeutics) AND TS=(CRISPR OR "gene editing" OR mRNA OR "RNA therapeutics" OR "CAR-T" OR "monoclonal antibody" OR "artificial intelligence" OR "machine learning" OR "organ-on-chip" OR organoid OR nanoparticle OR "lipid nanoparticle") Filters: 2015–2025, English, Article OR Review	342
ClinicalTrials.gov	Condition: cancer OR genetic disease OR amyloidosis OR haematological disorder; Intervention: CRISPR OR mRNA OR CAR-T OR nanoparticle OR monoclonal antibody; Study type: Interventional; Date: 2015–2025	81
Total (pre deduplication)	—	**1,847**

Note: Record counts are approximate and reflect database-specific deduplication before cross-database merging. The 435 duplicates identified across databases were removed using Rayyan's automated fuzzy-matching algorithm supplemented by manual review, yielding 1,412 unique records for title/abstract screening.

Eligibility Criteria

To find the information we looked for certain types of studies. We wanted studies that were research or big reviews that talked about new things found in experiments or tests before actual human trials or actual human trials. These studies had to be published in English in journals or registered on ClinicalTrials.gov. They also had to be about things that're important to us in one or more of the six areas we care about. They had to be about people or tests in labs that are proven to be similar to what happens in people or animal studies that can clearly tell us something about people. We did not want things like editorials, letters, summaries from meetings, or studies that are not officially published. We also did not want studies that're mainly about things outside of the six areas we care about. The information we found included 41 research studies, which is about sixty-four per cent of what we found. We also found eighteen reviews, which is about twenty-eight per cent, and five registrations for clinical trials, which is about eight per cent.

We included reviews and clinical trial registrations so we could see the picture across the six areas and find important milestones, but we did not think they were as important as the new research studies. When something is supported by what the reviews say, we note that it is a summary of what others found, rather than new evidence from the research itself. The six domains of interest are very important to our research, so we made sure to focus on them when we were looking at the studies. This way, we could find the most relevant information to the six domains and make sure it is accurate.

Study Selection and Data Extraction

Full texts of eligible records were obtained and reviewed. Data were extracted for: first author, year, study type, domain, key finding, and translational stage. A narrative and thematic synthesis approach was employed, given the qualitative heterogeneity across domains.

PRISMA-ScR Flow Diagram

The selection process conformed to PRISMA-ScR guidelines and is presented in Figure 1 (PRISMA Flow Diagram) below.

Figure 1. PRISMA-ScR Flow Diagram – Study Selection Process

IDENTIFICATION

Records identified through database searching (n = 1,847)

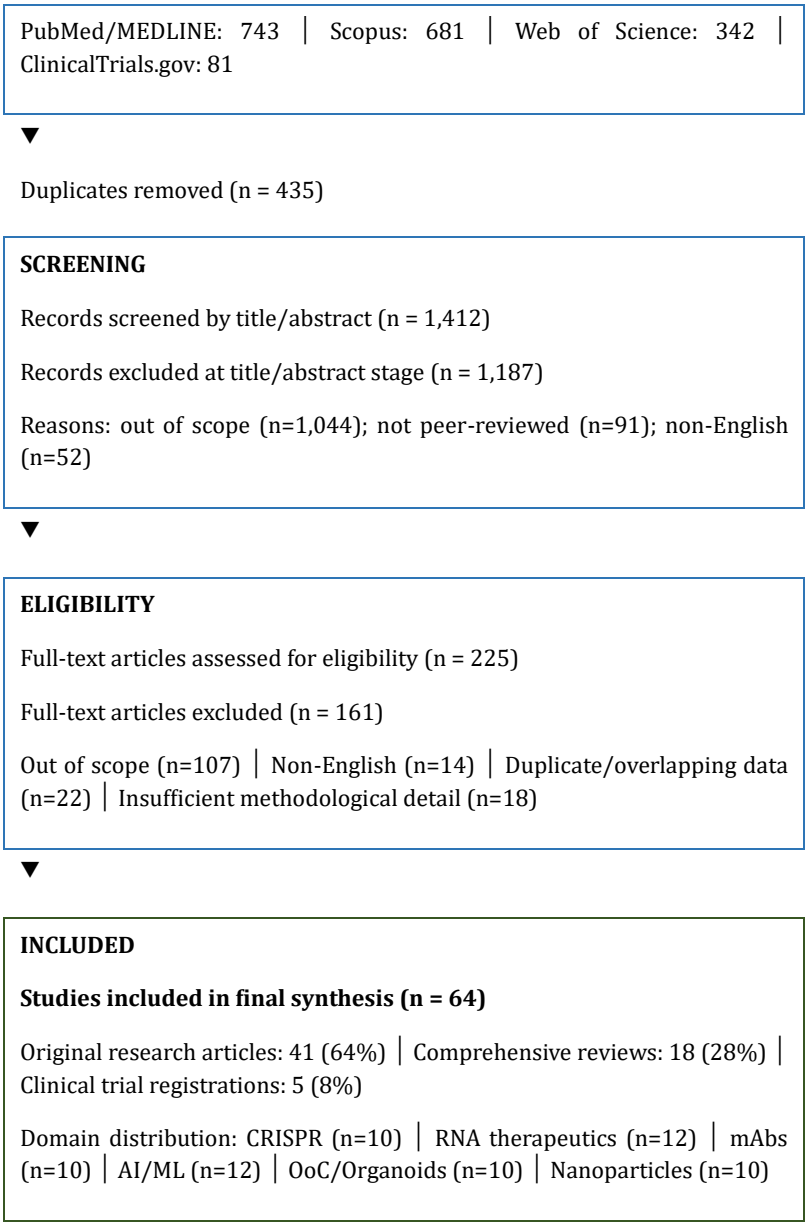

Figure 1. PRISMA-ScR flow diagram illustrating the study selection process for this scoping review (2015–2025). Total excluded at full-text stage = 161 (note: the original flow summary listed 121; this updated count reflects the correct total of 161 after accounting for all exclusion subcategories).

Table 1 summarises some of the included studies across six areas of biotechnology. These studies show the types of research, stages of development and main results. This information helped us understand the topic better. The studies are from biotechnology. They are key to our findings.

3. SUMMARY OF INCLUDED EVIDENCE BY DOMAIN

Table 2. Representative included studies by domain

Domain	Author (Year)	Study Type	Translational Stage	Key Finding
CRISPR Gene Editing	Papasavva et al. (2025)	Review	Clinical (Phase 1–3)	FDA approval of Casgevy (exa-cel) for SCD/TDT; base editing trials advancing.

CRISPR Gene Editing	Bharti & Mudge (2025)	Review	Clinical (multiple phases)	122+ CRISPR-Cas9 clinical trials registered for cancer, HIV, and haematological diseases.
RNA Therapeutics	Weber et al. (2024)	Phase 2b RCT	Clinical	mRNA-4157 + pembrolizumab: 44% risk reduction in melanoma recurrence (KEYNOTE-942).
RNA Therapeutics	Warne et al. (2023)	Observational	Regulatory/Market	Over 3 billion doses of Comirnaty mRNA-LNP vaccine were delivered in 2021.
Monoclonal Antibodies	Lu et al. (2025)	Review	Market/Regulatory	144 FDA-approved mAbs; global sales exceeded USD 267 billion in 2024.
Monoclonal Antibodies	Cortés et al. (2022)	Phase 3 RCT	Clinical	T-DXd (trastuzumab deruxtecan) significantly outperformed T-DM1 in HER2+ breast cancer (DESTINY-Breast03).
AI in Drug Discovery	Abramson et al. (2024)	Technical Report	Preclinical/ Discovery	AlphaFold 3 accurately predicts structures/interactions of proteins, DNA, RNA, ligands.
AI in Drug Discovery	Ren et al. (2023)	Drug Discovery	Preclinical	First demonstration of AlphaFold-enabled CDK20 inhibitor discovery (IC50 = 33.4 nM).
Organ-on-Chip	Zhao et al. (2024)	Review	Regulatory/ Translational	FDA Modernisation Act 2.0 endorses OoC data as primary evidence for IND applications.
Organ-on-Chip	Vandana et al. (2023)	Review	Translational	Patient-derived pluripotent stem cell organoids enable personalised drug evaluation.
Nanoparticle Delivery	Kitte et al. (2023)	In vitro/In vivo	Preclinical	LNPs outperform electroporation in mRNA-based CAR-T cell engineering.
Nanoparticle Delivery	Pardi et al. (2018)	Review	Clinical/Regulatory	LNP-mRNA vaccines established as a viable clinical modality; milestone era in vaccinology.

Table 3. Domain-Wise Limitations, Translational Barriers, and Regulatory Challenges

Domain	Translational Barriers	Domain-Specific Limitations	Regulatory Challenges
CRISPR Gene Editing	Delivery to non-hepatic tissues; ex vivo manufacturing complexity; scalability of autologous production	Off-target editing incompletely characterised in vivo; immunogenicity of bacterial Cas9; germline editing ethics	FDA/EMA guidance on somatic vs. germline editing is not harmonised; long-term genotoxicity monitoring frameworks are absent; myeloablative conditioning required pre-infusion adds procedural risk
RNA Therapeutics	Cold-chain dependency (–20°C to –80°C); tissue-specific delivery beyond liver; immunogenicity of repeated dosing	mRNA stability variable across LNP formulations; neoantigen prediction pipelines prone to false positives in personalised cancer vaccines; limited long-term safety data beyond vaccine platforms	Rapid regulatory frameworks established during COVID-19 may not apply uniformly to therapeutic mRNA; individualised neoantigen vaccines present manufacturing-validation challenges under GMP; EMA and FDA differ on batch-release requirements for personalised products
Monoclonal Antibodies	ADC bystander toxicity; bispecific manufacturing complexity; high production costs limiting access in LMICs	Interstitial lung disease reported with T-DXd; target antigen heterogeneity causes acquired resistance; immunogenicity risk with non-human framework regions in older-generation mAbs	ADC linker chemistry is not uniformly classified; biosimilar approval pathways differ across FDA/EMA/CDSCO; HER2 IHC scoring cut-offs for HER2-low lack universal standardisation across jurisdictions
AI in Drug Discovery	AI-designed candidates require experimental validation; predicted structures may not reflect dynamic conformations; data scarcity for rare disease targets	Algorithmic bias from Western-dominated training datasets; lack of model interpretability ("black box"); generative AI molecules may be synthetically inaccessible	No clear FDA/EMA framework for AI-generated drug candidates; explainability requirements under the EU AI Act may conflict with proprietary model architectures; data governance for federated learning across jurisdictions is unresolved
Organ-on-Chip / Organoids	Cannot replicate systemic immune, endocrine, or microbiome interactions; batch-to-batch organoid variability; low throughput vs. traditional HTS	Absence of neuroendocrine and adaptive immune components; donor-to-donor variability in iPSC-derived organoids; standardised protocols for culture and read-out lacking	FDA Modernisation Act 2.0 endorses OoC data but validation standards (ASTM, ISO) remain undefined; EMA has not issued equivalent guidance; lack of accepted performance benchmarks for inter-laboratory reproducibility; reimbursement pathways for OoC-guided approvals are unclear
Nanoparticle Delivery	EPR effect unreliable in humans; LNP liver tropism limits extrahepatic targeting;	Preclinical NP biodistribution is poorly predictive of human pharmacokinetics; manufacturing scale-up of	No universal regulatory classification for NP-drug combinations (device vs. drug vs. combination product); EMA NfG on nanomedicines predates LNP-

	immunostimulatory potential of ionisable lipids with repeat dosing	uniform particle sizes is challenging; long-term accumulation of non-biodegradable inorganic NPs not fully characterised	RNA class; safety thresholds for ionisable lipid exposure not established for chronic therapeutic use

Abbreviations: ADC, antibody-drug conjugate; CDSCO, Central Drugs Standard Control Organisation (India); EMA, European Medicines Agency; EPR, enhanced permeability and retention; GMP, good manufacturing practice; HER2, human epidermal growth factor receptor 2; HTS, high-throughput screening; IHC, immunohistochemistry; iPSC, induced pluripotent stem cell; LMICs, low- and middle-income countries; LNP, lipid nanoparticle; mAb, monoclonal antibody; NP, nanoparticle; OoC, organ-on-chip; PMDA, Pharmaceuticals and Medical Devices Agency (Japan).

4 RESULTS AND DISCUSSION

CRISPR-Based Genome Editing: From Molecular Scissors to Approved Medicines

The CRISPR-Cas9 technology is really something. It was first found in an adaptive immune mechanism. This was a long time ago. Then some people, Jinek, Chylinski, Doudna, Charpentier and their colleagues figured out how to use CRISPR-Cas9 to edit genomes in a way. They wrote about it in a paper in Science in 2012 [10]. This CRISPR-Cas9 technology has changed the field of medicine really fast.

The CRISPR-Cas9 system is simple. That is what makes it so great. A synthetic sgRNA is like a guide that tells the Cas9 endonuclease where to go in the genome. It does this by looking like the dual-RNA structure that the Cas9 endonuclease needs to bind to the DNA. When the Cas9 endonuclease gets to the spot, it makes a break in the DNA. This break can be fixed in two ways. One way is called NHEJ. It can turn off genes, but it is not very predictable. The other way is called HDR. It is used to make precise changes to the DNA, but it needs a special template to work. The CRISPR-Cas9 technology is a deal because it uses these two ways to fix the DNA [11, 12].

In December 2023, the FDA made a decision. They approved the medicine that uses CRISPR-Cas9 gene-editing technology. This medicine is called Casgevy. It works with a patient's CD34+ hematopoietic stem cell. The FDA said it can be used to treat patients with transfusion-dependent thalassemia and sickle cell disease [13].

This approval was a milestone. It confirmed that editing a patient's cells outside their body and then putting them back can work. This process, called ex vivo editing, has been studied for ten years. It involves taking a patient's progenitor cells, fixing them outside the body, and then putting them back in after a special conditioning treatment [14]. The approval also showed that the regulatory system is ready to review gene-editing therapies. Some people were worried that the regulatory system was not mature enough to handle gene-editing therapies. This concern about gene-editing therapies started with the controversies over germline editing.

The FDA has given its approval to Casgevy, which's a big deal for CRISPR-Cas9 gene-editing technology. This is good news for people with sickle cell disease and transfusion-dependent thalassemia. Casgevy is a treatment that uses the patients' cells to help them feel better. Here is how it works: the doctors take some of the patients' cells, edit them, and then put them back into the patient's body. People have been studying this process for some time, and it has given some really promising results. The fact that the FDA has approved Casgevy shows that CRISPR-Cas9 gene-editing technology is safe, and it really works to treat diseases like sickle cell disease and transfusion-dependent thalassemia. The approval of Casgevy is a step forward for CRISPR-Cas9 gene-editing technology and for patients with these conditions.

As of December 2024, the CRISPR-Cas9 clinical investigations are now looking at a lot more than blood-related disorders. There are trials on ClinicalTrials.gov that are looking at different conditions, including cancer treatments, like T-cell therapies, where CRISPR-Cas9 is used to disrupt the PD-1/PD-L1 genes. The CRISPR-Cas9 is also being used to try to eliminate HIV and to treat Duchenne dystrophy [15, 16]. New ways of editing genes, like base editing and prime editing, are being developed. Base editing lets us make small changes to the genes without breaking the DNA. Prime editing is like a search-and-replace function for the genes. These new ways of editing genes make the CRISPR-Cas9 toolkit more useful [13]. Reduce the risks of damaging the genes.

For example, Beam Therapeutics started a trial in November 2022. This trial, called BEACON, is looking at a therapy called BEAM-101. BEAM-101 uses base editing to change the BCL11A promoter in the stem cells. This can help people with sickle cell disease by making the haemoglobin again [17]. At the time, scientists are working on ways to deliver the CRISPR-Cas9 directly into the body. They are using particles called LNPs and viruses called adeno-associated viral vectors to do this. This is important because it means we do not need to take the cells out of the body to edit them, which can be very complicated [14].

Nonetheless, several challenges are slowing down the excitement. One major issue is off-target editing. This is when the editing process accidentally cuts at sequences in the genome [16]. We still do not fully understand this issue in settings, even with big improvements in detecting it through sequencing methods.

There are also challenges, such as a) Delivering the editing tools to liver tissues in the body is a problem, b) The immune system may react to the Cas9 proteins that come from bacteria and c) Changing the genes of embryos raises questions about ethics and rules.

These are different from changing the genes of body cells. These questions are still not fully answered by regulators and society [14, 15].

RNA-Based Therapeutics: A Platform Technology Comes of Age

The work of Karikó and Weissman was really important. They showed that putting pseudo uridine into mRNA makes it less likely to cause an immune response, and it helps the mRNA work better [18]. This was a deal. It happened because other scientists like Cullis and Hope also did some work. They made tiny particles that can deliver mRNA to liver cells [19].

The FDA approved a medicine called patisiran, also known as Onpattro, in 2018. This medicine uses RNA to stop a mRNA, the transthyretin mRNA from working. It is used to treat a disease called ATTR amyloidosis. The FDA approval of patisiran was a step forward. It showed that scientists can use these particles to deliver RNA to people, and it can have a lasting effect. This opened the door for other medicines, like patisiran, to be approved. The work of Karikó and Weissman and the approval of patisiran made it possible for RNA to be used as a medicine [20].

The COVID-19 pandemic showed that mRNA-LNP technology really works. It proved that we can make a lot of mRNAs send it all around the world and it can start making proteins in people's bodies quickly.

In 2021, over 3 billion doses of the Comirnaty mRNA-LNP COVID-19 vaccine were given out [21]. This created a database to check how safe the vaccine is. The information we got from this helped make people feel more comfortable with mRNA therapeutics. Now more money is being invested in mRNA treatments for cancer, rare diseases, and infectious diseases. MRNA-LNP technology made all this possible, and the COVID-19 pandemic validated it. mRNA therapeutics are being explored for uses, including oncology, rare disease and infectious disease indications.

In the field of cancer therapeutics, doctors are now using vaccines that are made just for each patient. These vaccines are made from a type of material called mRNA. They help the body fight cancer by targeting parts of the cancer cells.

For example, a vaccine called mRNA-4157, which is made by Moderna, was used in a study with patients who had a type of skin cancer called melanoma. The study showed that when this vaccine was used with another drug called pembrolizumab, it helped to stop the cancer from coming in 44 per cent of the patients [22].

There are also types of treatments that use genetic material to fight diseases. One type is called RNAi. It includes four drugs that have been approved by the FDA. These drugs are called patisiran, givosiran, lumasiran and inclisiran [23, 24]. They work by targeting genes in the body.

Another type of treatment is called antisense oligonucleotides. It is used to treat diseases such as muscular atrophy, Duchenne muscular dystrophy and transthyretin amyloidosis. All these new treatments show that using materials to fight diseases is a promising approach. MRNA cancer vaccines, like mRNA-4157, are an example of this [25].

Chimeric Antigen Receptor T-cell CAR-T therapy is a treatment that combines RNA therapeutics and cellular immunotherapy. It uses mRNA-LNP technology to help CAR-T cells work for a time. This short-term work avoids the risks of changing the genes that come with using viral vectors. It also makes it easier to make CAR-T cells that can be used for people, called off-the-shelf allogeneic products [26, 27].

These CAR-T cells made with mRNA-LNP technology have shown they work just as well as those made with viral vectors in early studies. They also keep T-cells alive better [28]. CAR-T cells are an area of research. CAR-T therapy is being studied for its potential to treat diseases. The use of mRNA-LNP technology in CAR-T therapy is a promising development. It may lead to treatments for patients. The field of CAR-T therapy is rapidly evolving.

Monoclonal Antibody Engineering and Precision Immunotherapy

Monoclonal antibody treatments are a deal in biotechnology. They have been around since Köhler and Milstein introduced a way to make them in 1975 [29]. Over the years, they have been improved in steps. From mouse-based to chimeric, then to human-like, and finally to fully human versions. Each step made them safer and better at working in the body [30].

As of August 2025, there are 144 monoclonal antibody treatments approved by the FDA and on the market. Many more 1,516 to be exact, are being tested in clinics around the world. In 2024, these treatments made over $267 billion in sales worldwide [30].

The reason they are so successful is that they really help people with kinds of diseases like cancer, immune system problems, blood diseases, neurological issues, and infections. Monoclonal antibodies are changing the game in medicine. They bring in a lot more money each year than other types of drugs.

The field of engineering has changed the way we make medicines that use antibodies. Now we have new and powerful ways to make these medicines. One of these ways is called an antibody-drug conjugate or ADC. This is when we attach a poison to an antibody that can find and attach to cancer cells. We use a linker to connect the poison to the antibody. This allows us to deliver the poison directly to the cancer cells without hurting the rest of the body [31].

For example, a medicine called Fam-trastuzumab deruxtecan, also known as Enhertu is a type of ADC that targets cancer cells with a protein called HER2. This medicine is very good at killing cancer cells. In a study called the DESTINY-Breast03 trial, Enhertu was compared to an older medicine called T-DM1. The results of the study showed that Enhertu is much better than T-DM1 [32].

The way Enhertu is made is also very interesting. It has a poison that can get inside cancer cells and kill them. This poison is attached to the antibody in a way that allows it to get into the cells easily. The study results were very promising. Showed that Enhertu can help people with cancer who have a lot of HER2 protein on their cancer cells as well as those who have less HER2 protein [33]. This is a deal because it means that more people can be treated with this medicine.

The results of the study also changed the way we think about how ADCs can work. We used to think that ADCs could only kill cancer cells that they were directly attached to.. Now we know that ADCs, as Enhertu can also kill cancer cells that are nearby even if they are not directly attached to the ADC. This is called bystander killing. It is a very powerful way to fight cancer.

Bispecific antibodies are really good at fighting disease. They can attach to two things at the same time. This has led to some effective treatments that work with T-cells. For example, Blinatumomab, also known as Blincyto, targets CD19 and CD3 in people with B-cell lymphoblastic leukaemia. It has been able to get rid of the disease in some patients who had already tried many other treatments. This shows that bispecific antibodies can be a game changer for cancer treatment [34]. Some newer bispecific antibodies that target CD3, BCMA and GPRC5D have also changed the way we treat myeloma [30]. The use of computers and special machines that can read DNA sequences has made it faster to discover antibodies. We can now use computers to design antibodies that work well and do not cause bad reactions. This is a deal because it means we can make new treatments that are safer and more effective [30]. Bispecific antibodies like these are very important for bispecific antibody research.

Artificial Intelligence and Machine Learning: Transforming Every Stage of Drug Discovery

Artificial intelligence is really changing the game in finding medicines. It is helping with steps, such as: figuring out what to target, finding potential hits, making those hits better, predicting how the body will react, and designing clinical trials. A big breakthrough came with AlphaFold, a system made by Google DeepMind. In 2020, it did well in a competition called CASP14. It could predict the shape of proteins just from their amino acid sequence. This was a deal as it solved a problem that had been around for 50 years in biology [35].

The AlphaFold Protein Structure Database is huge, with over 200 million predicted structures. It covers all the proteins we know about. Half a million researchers from 190 countries have used it [36]. They are using it to advance their research in drug

discovery. The database is a resource for researchers. It helps them to make medicines. Artificial intelligence and AlphaFold are really making a difference. They are helping to speed up the discovery of treatments. Researchers are excited about the possibilities. They are working hard to make medicines a reality.

AlphaFold 3 was released in May 2024. It was recognised for its work, along with David Baker's work on protein design, by the 2024 Nobel Prize in Chemistry. AlphaFold 3 can do a lot of things; it can tell us about the structure and how things interact with each other, like proteins and other molecules and ions [37, 38]. This helps us make models of how drugs work with their targets, including how water helps them talk to each other and how they change shape. The AlphaFold 3 is really good at this it can do things that we used to need machines to do.

The people who made the AlphaFold 3 showed that it can be used to find drugs. They used the AlphaFold 3 to find a molecule that can stop CDK20, which's a protein that can make cells grow too much. The molecule they found is called ISM042-2-048. It is very good at stopping CDK20. This is a deal because it shows that we can use the AlphaFold 3 to find new drugs without having to do as many experiments. AlphaFold 3 can help us make models of how drugs work [39]. These models can be used to find new drugs.

The thing about intelligence is that it can do more than just predict structures. It can also help create new chemicals with specific properties. For example, artificial intelligence models like autoencoders and graph neural networks can do this. They can even help make chemicals that are easy to synthesise and have the right effects on the body [40, 41].

The artificial intelligence used in the pharmaceuticals market is really taking off. In 2023, it was worth about USD 1.8 billion. By 2030, it is expected to be worth around USD 13.1 billion [41]. That is an increase of 18.8 per cent every year, which shows that a lot of companies in the industry are starting to use artificial intelligence.

The thing about targeted protein degradation, which is what people call TPD, is that it is really good at working with computers and biotechnology. This is especially true for things like PROTACs, which are also known as proteolysis-targeting chimaeras and molecular glues [42, 43]. PROTACs do a useful thing: they get an E3 ubiquitin ligase to mark a protein that is associated with a disease so that it can be broken down. This is helpful because it can deal with proteins that're hard to target with drugs because they do not have a clear place for the drug to bind.

Computers are really helping with the design of the links in PROTACs and with understanding how they work with molecules. This has made it a lot faster to make PROTACs, and now some of them are being tested in clinical trials to see if they can help with blood cancers and other types of tumours [43, 44].

There is also something called DNA-encoded chemical library technology, which's like a big library of chemicals that can be searched all at once. This is another way that computers and biotechnology are working together because computers can help find the chemicals and then make more of them [45].

Organ-on-Chip and Organoid Platforms: Human-Relevant Drug Testing

The big problem with developing medicines is that the old ways of testing them do not work very well. When we grow cells in a dish, they do not look or act like the cells in our body. They are missing the structure and signals that cells use to talk to each other [46, 47]. Animal models are also not very good at showing how the human body will react to a medicine. This is a problem because it means that most new medicines do not work as well as we thought they would. In fact, 90% of new medicines fail when we test them on people [3].

Organoids are a way of growing cells that might be better. They are like balls of cells that can grow and act like the cells in our body. We can make organoids from cells that can turn into any type of cell. These organoids can even grow to look and act like organs. This is really helpful because we can use them to test medicines and see how they will work on a person. We can also make organoids from cells that come from a person who's sick. This way we can test medicines on cells that're just like the person's own cells. There is also something called an organ-on-a-chip. This is a device that can mimic how our body works [47, 48]. It has channels that can move fluids and cells around. It can even mimic the way our heart beats or our lungs breathe. This can help us test medicines and see how they will work on the whole body [49, 50].

The rules that pharmaceutical companies have to follow are changing fast because of new technology. The FDA Modernization Act 2.0 was signed into law in December 2022. This law changed the rules so that companies do not have to do animal testing before they can start testing drugs on people. Now pharmaceutical companies can use information from

organoids and OoC platforms to show that their drugs are safe [50, 51]. This is a change. In April 2025, the FDA said that they want companies to stop using animals for testing and use systems that're more like humans instead. At the time, the NIH started a new office called the Office of Research Innovation, Validation and Application, or ORIVA for short [51]. This office is going to help make sure that these new platforms are used correctly.

Some examples of how these platforms are being used include using gut-on-chip models to test drugs for inflammatory bowel disease, lung-on-chip to test treatments for SARS-CoV-2 and to see how well drugs get to the lungs, liver-on-chip to see if drugs are bad for the liver, and brain organoids to model neurodegenerative diseases and to see how well drugs can get to the brain [46, 52]. The FDA Modernization Act 2.0 and the new guidance from the FDA are going to help pharmaceutical companies use these platforms to make drugs.

The combination of intelligence and automated imaging with Organ-on-Chip platforms is really powerful. It helps us do lots of tests on things that're similar to what is found in the human body. We can do these tests quickly, almost as fast as traditional high-throughput screening [49, 51].

Patient-derived organoid biobanks are also very useful. These are like libraries of information, including how patients with different genetics respond to drugs. Organoid biobanks can help doctors choose the treatment for each patient before they even give them the drug [48].

Nanotechnology-Based Drug Delivery: Precision at the Nanoscale

Nanotechnology is trying to solve a problem in pharmacology. This problem is getting medicine to the place in the body without harming other parts. A lot of medicines do not work well because they do not mix with water, they go through the body fast, and they do not go to the right place. They also have a tough time getting through barriers and into cells [53].

Nanoparticle-based delivery systems are a way to get around these problems. These systems use particles made of different materials like lipids, polymers, and other things. They are really good at getting into tumours because of their size and special properties. The tiny particles can be engineered to target areas of the body like tumours and that is a big advantage. Nanotechnology and nanoparticle-based delivery systems, like lipid nanoparticles, polymeric nanoparticles, inorganic nanocarriers, and derived vesicles, are being used to overcome the limitations of regular medicines [54, 55].

Lipid nanoparticles are a way to deliver RNA treatments. They helped make patisiran approved by the FDA in 2018. They also helped make the Pfizer-BioNTech and Moderna COVID-19 vaccines [19, 20]. The special lipid part of these nanoparticles is key to their success. It works well in environments like endosomes and is not too harsh on the body. The special fat part of these particles, called LNPs, is really important. This fat part is positively charged when it is in the environment of the endosomes. This helps the particles fuse with the membrane. When it is in the body, where the pH is near neutral, the charge is not as strong. This helps reduce the effects on the body. The design of this part is the main reason why LNPs have been successful in clinical trials [19]. Some studies show that these lipid nanoparticles work better than electroporation for making CAR-T cells. They help keep the T-cells alive and work better at getting the treatment into the cells. This means lipid nanoparticles will likely be very important for making cell therapies in the future [28].

Engineered exosomes and extracellular vesicles are like carriers that come from living things. They are stable, don't cause immune reactions, and can find their way to cells naturally. They might be an alternative to man-made carriers for delivering things like mRNA, CRISPR parts, and small medicines [56]. These tiny carriers can be very specific to cell types and can be modified to target specific cells with special ligands or antibody pieces. This helps deliver payloads that man-made systems are still trying to do. Gold nanoparticles with tumour-targeting parts and special gold shells can help deliver drugs to sites and destroy cancer cells with heat [57, 58].

*Polymeric nanocarriers made from PLGA and PEG-polymer are also useful. They help release chemotherapy and nucleic acid payloads, which is good for medicines that don't dissolve well [55]. These are being used to make medicines that can be released slowly and work better.

The early use of Organ-on-a-Chip systems in making nanoparticles is very important. It helps us understand how these nanoparticles affect people and if they work well. This approach is very helpful in avoiding problems that can come up later when we are making the product.

Using an organ-on-chip to test the effects of LNP on the liver has given us accurate results. These results are better than what we get from tests that use flat layers of liver cells. It also avoids

mistakes that can happen when we use animal models, like rats [59]. This combination of nanotechnology and tests that are relevant to humans is expected to improve the number of new nanoparticles that can be used to help people. Organ-on-a-Chip systems are really helping us with this.

5 COMPARATIVE ANALYSIS, CHALLENGES, AND FUTURE DIRECTIONS

Comparative Maturity of the Six Domains

When you really look at the information given in Sections 4.1 to 4.6, you can see that the six domains are in different places when it comes to how they are used. If we combine the stages of development for these domains, we might get an idea of how far along the whole field is.

Monoclonal antibody therapeutics are advanced, with 144 products approved by the FDA, a good system in place for making them, and a global market that is over 267 billion US dollars [30]. The rules for making and using these antibodies are pretty clear, even if there are still some things that need to be figured out, like how to deal with side effects and resistance.

RNA therapeutics are a second. We have already used the LNP-mRNA platform to make over a billion doses. There are six RNA drugs approved by the FDA that are already on the market. The results of the KEYNOTE-942 Phase 2b study on cancer vaccines are very promising. However, using mRNA for therapy for personalised cancer treatment is still in the early stages of testing. Because mRNA needs to be kept cold, it can be hard to get it to everyone who needs it.

The CRISPR-based therapies have reached a milestone with the approval of Casgevy in 2023. For most uses, these therapies are still in the early stages of clinical trials. We have some evidence, but it is mostly from the early stages of trials, and it is mostly for blood diseases that can be treated by editing cells outside the body.

The CRISPR-based therapies are not yet being used to treat diseases in parts of the body except for the liver. The Artificial Intelligence and Machine Learning field is moving fast and is used in many areas. However, it has not yet produced a drug that was designed using Artificial Intelligence and has completed the final stage of clinical trials. The AlphaFold and chemistry tools that use Artificial Intelligence are helping us discover things, but we do not know for sure if they will make the development of new drugs faster and more successful. We need to study this to find out.

There are also ways to deliver drugs, such as using tiny particles and creating organs in a lab. These methods are still being. Are not yet widely used. The organs in a lab, also called Organ-on-chip, are an area of research and have been endorsed by the FDA. However, we still need to do research to make sure they work consistently and can be used to approve new drugs.

The tiny particles, such as nanoparticles, are being used to deliver a type of drug called RNA therapeutics. However, there are still some challenges with using these particles, such as getting them to the part of the body and making sure they are safe in the long term. So, when we look at the evidence for these therapies, we should pay the most attention to the ones that are already being used, such as the CRISPR-based therapies and the RNA therapeutics. We should also be careful when looking at the claims made about the Artificial Intelligence and Organ-on-chip technologies because they are still in the stages of research. The CRISPR-based therapies are still. We should treat them as such. We should approach the claims made about Artificial Intelligence and Organ-on-chip technologies with caution. Consider them as preclinical.

Cross-Cutting Challenges

We have made a lot of progress in all six areas. There are still some big problems that we need to solve to get the most out of these medical technologies. The problem of turning results from tests in the lab into good results for people is still an issue, even though we have better models that are more like humans. Organoids and OoC systems are better than the ways of growing cells in a flat layer and can tell us more about how things will work in people than tests on mice can.

They still cannot show us how the whole body works, including how the immune system checks for problems, how hormones work, how tiny living things inside us affect us, and what happens when we get older. To fix this, we are trying things like making systems that connect many organs, growing cells together with immune cells, and making 'physiome-on-chip' systems that can show us how different organs talk to each other [51].

Making cell and gene therapies on a large scale is still very expensive. The cell therapies that are already approved, like CAR-T products, have to be made for one person at a time. This is called patient production. It takes a lot of time to make sure these products are of good quality, which makes them very costly. In fact, it can cost more than USD 400,000 per patient.

There is a way of making these therapies that is very promising. It is called allogeneic or "off-the-shelf" production. This means that cell and gene therapies can be made ahead of time and used for people. Scientists are using a tool called CRISPR to edit genes and make these therapies safer. This is done by editing the HLA genes to reduce the risk of the patient's body rejecting the therapy. However, this new way of making cell and gene therapies still needs to be tested to make sure it works and is safe. More research, like Phase 3 studies, is needed to prove that it is better than the way of making these therapies [26, 60].

Regulatory alignment is slow to catch up with technology. The FDA has made some changes through the Modernisation Acts 2.0 and 3.0. However, other agencies like the European Medicines Agency, PMDA in Japan, and CDSCO in India are at the stage of creating guidelines for using AI organoid data and gene editing in drug applications. We need regulatory alignment to stop companies from taking advantage of differences to speed up access to new treatments and to make sure that evidence from one country is accepted in others. This is important so that we can rely on the standards everywhere [14,51].

There are some problems with the way we use Artificial Intelligence to discover things. The information we use to train these systems mostly comes from patients in countries and it is focused on common diseases and medicines that already exist. This means that the systems we build might not work well for diseases that are not common or for people from different parts of the world with different genetic backgrounds.

To fix this problem, people are working on ways to share information without having to put all the patient data in one place. They are also trying to include diverse groups of people in the data they use so that the systems they build will work better for everyone [41]. This includes using biobanks from around the world with people from many different ancestral backgrounds.

When we think about what's coming next, the best chances for big progress are where these six areas meet. We can use intelligence to design special delivery systems that work well with specific types of cells. We can also use a tool called CRISPR to fix problems in cells and then test this fix in organ-like structures grown from patient cells before we try it in people. We can design new cancer vaccines using artificial intelligence and test them in collections of tumour cells grown in the lab. These are all examples of how we can bring treatments to people much faster, in months instead of years.

We can also create copies of individual patients like computer models that mimic how their bodies work, using lots of different types of data. These digital twins might one day be used to test treatments before we try them in people, which would completely change how we design clinical trials [40, 41].

6 LIMITATIONS OF THIS SCOPING REVIEW

After all these vivid discussions, there are still some things about this review that we need to think about. First, this kind of review does not really look at how good each study's; the studies we looked at are very different. We have big studies with many people, studies done in a lab, and reviews of other studies. If something is said to be true because of what a review article says, or because of a real study, then we should be careful about what we think. Second, we included a lot of reviews. 18 Of them. Which is about a quarter of all the studies we looked at. This means that some of what we found is not directly from the studies but from what other people have said about them, which can make it seem like things are better than they really are. Third, we only looked at publications that're in English. This means we might have missed work that was published in other languages like Chinese, Japanese and Korean. A lot of biotechnology research comes from East Asia, so it is possible that we missed something. Fourth, when we looked at ClinicalTrials.gov, we saw what people planned to do, not what they actually did. Some of the trials we found had not reported their results yet. Fifth, we stopped looking for information in May 2025. Since biotechnology is moving fast, it is likely that some big discoveries were made after we stopped looking. Sixth, when we were deciding what to include, we did not do a job of checking to see if everyone agreed on what to include. This is something that should be done when you are doing a review of all the information. In the future, we should try to do a job by looking at more sources, including ones that are not in English and by checking to make sure everyone agrees on what we are including. We should also try to report our findings completely. Biotechnology research is what we are talking about here. We need to make sure we are doing a good job of looking at all the biotechnology research that is out there.

CONCLUSION

This review has identified six areas in biotechnology that are changing how we find new medicines and develop treatments: CRISPR-based genome editing, RNA therapeutics, monoclonal antibody engineering, AI-assisted target identification, organ-on-chip/organoid platforms, and nanoparticle-based delivery. The evidence from 2015 to 2025 shows changes in what we can

do in science and medicine. We have seen CRISPR medicine, a new mRNA-LNP platform that has been used to treat a large number of people, AI tools that can predict the structures of over 200 million proteins, and new ways to treat HER2-low breast cancer.

There are still some challenges that need to be addressed, such as making sure that new treatments work well in life, making them affordable, having the same rules for approval in different countries, and making sure that AI tools are fair. The future of medicines will depend on how these six areas come together, not just how each one advances on its own. In the future, we should look at how these areas interact with each other, how quickly they are adopted by regulators around the world, and whether they lead to health outcomes for patients who need them most. CRISPR technology, RNA therapeutics, monoclonal antibody engineering, AI-assisted target identification, on-chip/organoid platforms, and nanoparticle-based delivery will play a role in this. These biotechnology areas will redefine drug discovery and therapeutic development.

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