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Review

Artificial Intelligence-Based Methods for Drug Repurposing and Development in Cancer

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Abstract: Drug discovery and development remains a complex and time-consuming process, often hindered by high costs and low success rates. In the big data era, artificial intelligence (AI) has emerged as a promising tool to accelerate and optimize these processes, particularly in the field of oncology. This review explores the application of AI-based methods for drug repurposing and natural product-inspired drug design in cancer, focusing on their potential to address the challenges and limitations of traditional drug discovery approaches. We delve into various AI-based approaches (machine learning, deep learning, and others) that are currently being employed for these purposes, and the role of experimental techniques in these approaches. By systematically reviewing the literature, we aim to provide a comprehensive overview of the current state of AI-assisted cancer drug discovery workflows, highlighting AI's contributions to accelerating drug development, reducing costs, and improving therapeutic outcomes. This review also discusses the challenges and opportunities associated with the integration of AI into the drug discovery pipeline, such as data quality, interpretability, and ethical considerations.

Keywords: drug repurposing; artificial intelligence; machine learning; cancer

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1. Introduction

The drug discovery and development pipeline remains a complex and resource-intensive process that requires significant time and financial investment. Typically, the journey from the identification of a lead compound to obtaining market authorization spans a lengthy period of 10 to 15 years. This extensive timeline underscores the considerable technical, regulatory, and economic obstacles that must be navigated throughout the process. Financial investments in this pipeline often exceed USD 1 billion, reflecting the high costs associated with research, development, and regulatory compliance [1]. These

challenges are not only financial, but also involve overcoming numerous scientific and logistical hurdles, which can delay progress and increase costs.

Despite notable advances in technology and methodology, the drug development process continues to face significant impediments, particularly in the form of high clinical trial failure rates. These failures are primarily attributed to ongoing concerns regarding the safety and efficacy of compounds. While efforts to optimize the physicochemical properties of compounds have yielded some benefits, ensuring the safety and efficacy of novel therapeutics remains a critical challenge that the industry must address [2]. This challenge is further exacerbated in the context of complex diseases such as cancer. Cancer is characterized by diverse genetic and molecular heterogeneity, which complicates the development of effective treatments. The variability in genetic profiles and molecular pathways among different cancer types and even among patients with the same type of cancer adds layers of complexity to the drug development process [3].

Consequently, given the severity and high global incidence of cancer, there is an urgent need to prioritize the search for new strategies to optimize drug discovery. This priority is driven by the necessity to develop more effective and targeted therapies that can address the unique challenges posed by cancer's heterogeneity. The integration of innovative technologies and approaches, such as artificial intelligence and machine learning, into the drug discovery process holds promise for overcoming some of these challenges by enabling more precise targeting of therapies and improving the efficiency of the development pipeline.

In this context, artificial intelligence (AI) has emerged as a transformative tool with great potential to significantly impact drug discovery. Through techniques such as machine learning (including convolutional neural networks [CNNs] and recurrent neural networks [RNNs]), deep learning, and evolutionary algorithms, AI makes it possible to analyze extensive biomedical data, predict molecular interactions, and optimize drug development with unparalleled accuracy, leading to significant reductions in time and costs [4]. These technologies also facilitate the identification of potential drug candidates, the prediction of their effects, and the tailoring of treatments to individual patients, enabling personalized medicine [5] (Figure 1).

For example, by using dynamic computational models of the pathophysiological processes derived from drugs, it has been possible to achieve personalized immunotherapy in cancer patients.

AI also plays a fundamental role in the analysis of omics data mining, particularly in the context of integrating genomic information from next-generation sequencing of thousands of individuals with clinical data and predictive computational models. This integration has been demonstrated to represent a significant advancement in the automation of the research and identification of novel therapeutic targets. Omics technologies also facilitate drug repositioning by identifying new therapeutic uses for existing drugs, accelerating the process and reducing attrition rates in development and clinical trials. This is primarily based on analyzing large datasets to identify patterns and relationships between drugs and diseases through computational modeling [6]. Consequently, multi-omics technologies, in conjunction with machine learning (ML) and deep learning (DL), have facilitated substantial progress in data integration. This is attributable to their substantial processing capacity for both linear and non-linear data, thereby establishing a linkage between genomic alterations and specific therapeutic options for patients. However, integration tools have not demonstrated significant performance since they use data generated from multiple databases, which has not allowed for standardized databases, but it is estimated that these challenges can be solved with AI approaches and standardization [7,8]. Furthermore, advances in AI are not only helping to develop more effective targeted therapies but also to predict patient response. For example, AI-based algorithms can identify subgroups of patients

likely to respond to specific immunotherapies or combination treatments [4]. AI also plays an increasingly significant role in optimizing polypharmacology strategies and predicting drug side effects. Machine learning models can predict potential side effects even for new substances by analyzing databases of adverse events and drug–protein interactions [9,10]. AI-driven methods pave the way for designing multi-target medications, maximizing treatment effectiveness and reducing side effects [11]. Both strategies contribute to efficient drug development and reduce late-stage clinical trial failures by integrating diverse datasets (Figure 1).

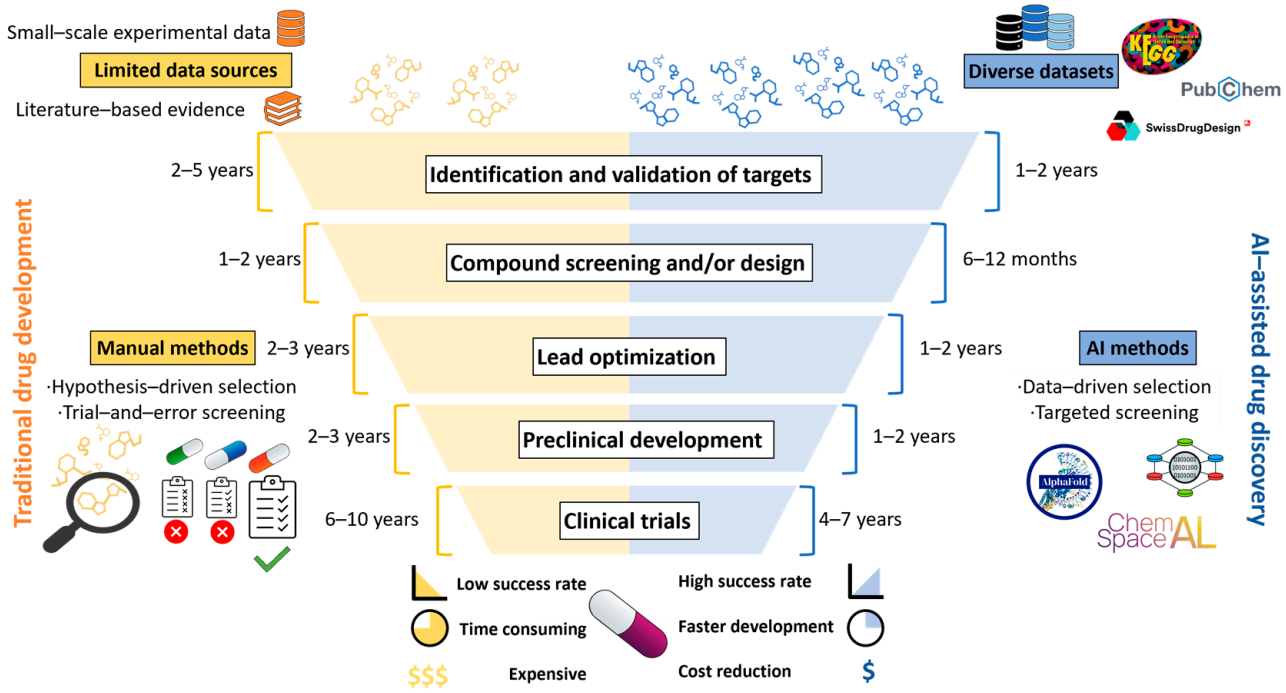

Figure 1. The evolving landscape of AI-assisted drug discovery. The integration of AI-driven approaches can potentially revolutionize each stage of the process, leading to accelerated timelines, reduced costs, and improved success rates. NIAID Visual & Medical Arts. 14/1/2025. Some icons are from NIAID BIOART Source (https://bioart.niaid.nih.gov/).

In the domain of cancer research, AI plays a critical role in identifying biomarkers and therapeutic targets. Deep learning and machine learning models facilitate the analysis of thousands of data points, such as genomic and transcriptomic data, to identify key mutations and molecular alterations driving tumor growth [6]. Integrating these data with clinical information (patient history) can provide insights into the efficacy of different treatments for specific genetic profiles. The field has been revolutionized by tools such as AlphaFold, which can predict protein structures with a high degree of accuracy, thus providing essential information for the design of targeted drugs [12].

The integration of AI with multi-omics technologies signifies a paradigm shift in precision oncology. Integrative multi-omics data methods utilize genomic, transcriptomic, epigenomic, and proteomic information to identify crucial interactions between genes, proteins, and molecular pathways [13]. This integration facilitates the design of combined therapies specific to tumor subtypes and accelerates the identification of optimal drug combinations using neural networks and generative approaches, thereby optimizing therapeutic efficacy and minimizing side effects [13,14]. In addition, advances in deep learning have proven effective in predicting the binding affinity between drugs and proteins, a crucial step in the drug discovery and development process for cancer [15].

Complementing these technologies, reinforcement learning in oncology has made it possible to optimize treatment pathways by dynamically adjusting therapies according to the patient's individual response. This approach holds particular promise in complex treatments such as immunotherapies and target therapies, where the management of multiple clinical variables poses a significant challenge [16].

On the other hand, the increasing interest in the discovery of drugs derived from natural products is also driving the use of computational approaches. AI-based algorithms have improved the identification and optimization of bioactive compounds from natural product databases, enabling the development of innovative strategies in oncology [17].

In summary, the confluence of drug development challenges, advances in AI, and the urgent need for effective cancer treatments underscores the importance of integrating advanced technologies in this field. This review examines the current state and potential impact of AI in cancer drug repurposing and design, highlighting the opportunities and challenges of this technology in modern medicine (Figure 2).

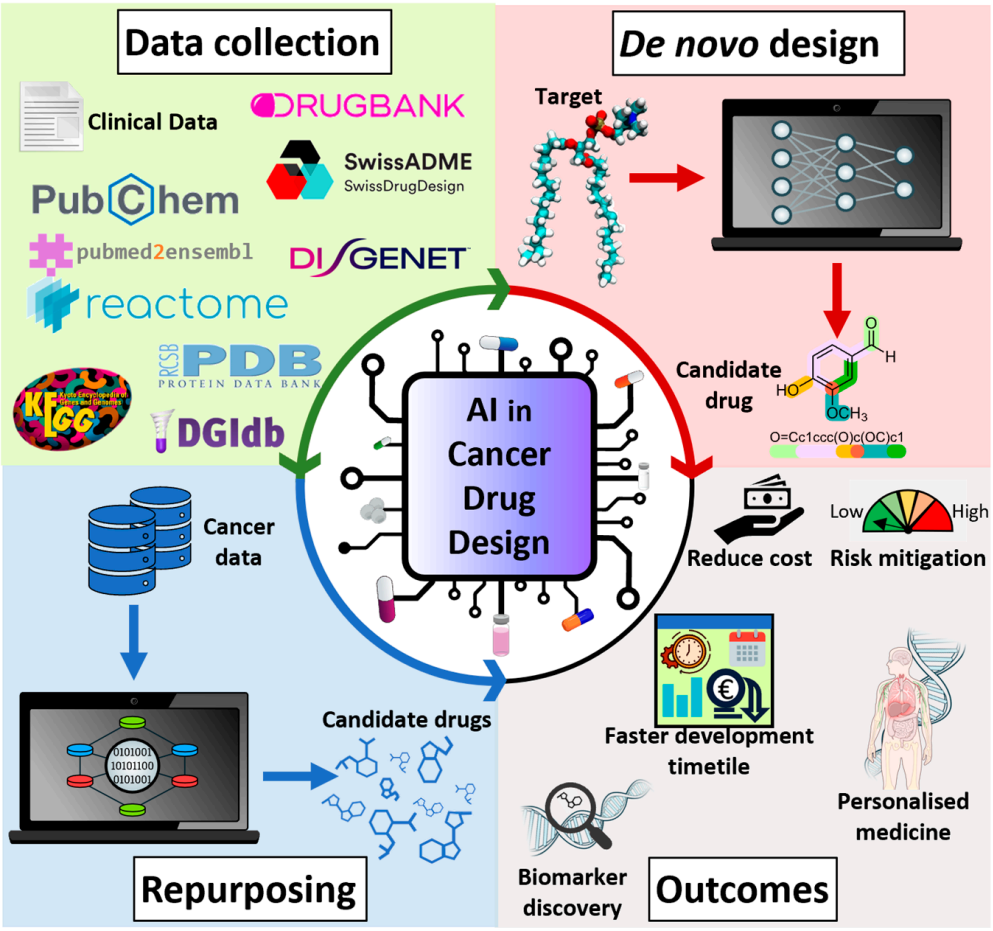

Figure 2. The role of AI in the drug discovery workflow for repurposing and *de novo* designing. Some icons are from NIAID Visual & Medical Arts. 14/1/2025. DNA (124); Pill (#407); Three Quarters Human Anatomy (519). Some icons are from NIAID BIOART Source (https://bioart.niaid.nih.gov/). #. # = number code of icon.

2. AI Techniques for Drug Repurposing and *De Novo* Drug Design

The use of artificial intelligence techniques has recently become a fundamental part of the process of both drug repurposing and *de novo* drug design. These techniques have a wide range of applications in drug development and discovery such as virtual screening, toxicity monitoring of the drug, drug efficacy, or dosage prediction, drug repurposing,

and drug–target interaction predictions [18]. The selection of AI-based tools depends on the specific application and can significantly impact the results. Machine learning, deep learning, and knowledge graph-based tools are commonly used for drug repurposing, while generative models and reinforcement learning are more suitable for de novo drug design. Other machine learning techniques such as quantum computing have also been used for the prediction of ADMET (absorption, distribution, metabolism, excretion, and toxicity) properties [19], but these applications fall out of the scope of this review. In this sense, although different AI approaches have been used in all stages of drug development, some of them are more effective. Neural networks and classical machine learning are effective for target identification due to their ability to analyze drug–target and protein–protein interaction networks, identify novel binding sites, and predict protein structures. Natural language processing (NLP) and large language models can be very useful in mining data in order to develop clinical trials or monitor adverse effects. Furthermore, multimodal AI models improve drug efficacy prediction by integrating diverse data sources, leading to more comprehensive and accurate insights. Some of this information can be chemical structure data, omics data, biomedical texts, histopathology data, medical imaging data, or electronic health records. Recently, Qiu et al. provided a very thorough list of AI-based methods for drug discovery [20].

2.1. Machine and Deep Learning Techniques

Some of the most common machine learning algorithms used for drug repurposing include k-nearest neighbor (kNN), random forest (RF), or support vector machine (SVM). Furthermore, with the development of deep learning, and thanks to its ability to automatically extract features from raw data, the impact of AI-based approaches in drug repurposing has increased significantly. The use of deep learning algorithms such as artificial neural networks (ANNs), CNNs, and long short-term memory (LSTM) has revolutionized the field. One of the best examples in this field is AlphaFold2, a commonly known, neural network-based model technology that predicts the 3D conformation of proteins, even those without known structures, and therefore offers emerging opportunities for structure-based drug discovery [12].

General machine learning approaches in drug repurposing can be classified according to the type of datasets used. As an example, structural information related to proteins or small molecules has been used for the development of structure-based virtual screening methods, such as molecular docking [21] or, together with binding activity data, ligand-based chemometric modeling methods such as quantitative structure–activity relationship (QSAR) modeling [22]. Other types of data commonly used in machine learning-based drug repurposing approaches include cell phenotype, employed for example through the CellProfiler software (v.4.2.8) [23]. Also, the use of transcriptomic data allows us to uncover novel drug mechanisms. Among this, the use of the L1000 assay data, an improvement over the old Connectivity Map (CMap), stands out, covering information on the variation in gene expression in response to more than 42,000 perturbing agents (including drugs) [24]. Finally, data related to electronic health records, and even social media, are also very helpful to develop deep learning approaches based on natural language processing (NLP) and other algorithms [25].

2.2. Knowledge Graph-Based AI Techniques

The use of graph-based approaches relies on the knowledge of drug–target interactions from databases. The generation and analysis of these networks has been crucial in many recent drug repurposing discoveries [26]. For example, Zeng et al. developed a network-based deep learning model (DeepDR) for the integration of networks, such as drug–disease

and drug–target networks, that enabled them to learn high-level drug features through a random walk approach [27].

Another useful strategy involves the integration of genome wide association studies (GWASs) and multi-omics data within network-based AI approaches [20]. As an example, the network topology-based deep learning framework (NETTAG) uses an interpretable AI model to identify disease-associated genes based on multi-omics data and integrate them within the human protein–protein interaction (PPI) network in order to predict repurposable drugs [28].

2.3. Generative AI Models

Generative artificial intelligence models are progressing rapidly, and their use in novel drug discovery presents advancements faster than anybody can recall. Although these models are performing quite well in small-scale and controlled laboratory settings, doubts remain about their performance in more complex conditions [29]. In this sense, the implementation of large language models (LLMs), such as the commonly known ChatGPT, a generative pre-trained transformer technology developed by OpenAI, has recently made this type of tool more approachable and amenable to biomedical researchers [30]. Several generative AI-based tools, such as ChemSpaceAL (v.2.0.1) [31], GraphGPT (v.0.3.1) [32], PEtrans (v.1.0) [33], or DrugChat (v.5.1.4) [34], have been recently developed for different aspects of *de novo* drug design, such as molecular generation, the selection of contextual molecular features, or the determination of novel targetable sites in proteins.

2.4. Reinforcement Methods

Reinforcement learning methods are AI algorithms used to resolve decision problems with a dynamic approach, combining ANNs with deep reinforcement learning architectures. These methods are based on the analysis and estimation of the statistical relationship between all the possible actions and their outcomes. Afterwards, the algorithm tries to determine the most desirable outcome. The implementation of these approaches has been used for the optimization of the design of chemical libraries for screening and *de novo* drug design with the ReLEASE software (v.1.0) (Reinforcement Learning for Structural Evolution) [35]. In general, in reinforcement methods, a multilayer ANN serves as the generative model, using inputs like SMILES (structural codification of molecules) or molecular graphs. The model is then trained with data from known bioactive molecules by means of iterative learning and decision-making steps, and finally constructs new outputs and tests their response for optimization. In this sense, they act as a virtual agent that modifies molecules to optimize their properties under the guidance of the neural network [36]. An example of this approach is the development of reinforcement method models for the generation of analogues to a query structure or the generation of compounds predicted to be active against a biological target [37].

3. AI-Guided Applications in Cancer Drug Discovery

This section presents recent projects that use AI-guided approaches for cancer drug development and design. Table 1 summarizes the key aspects of these studies, including the computational methodology, AI model/algorithm, cancer type, and main findings. The studies are categorized based on the AI techniques described in Section 2.

Table 1. AI-guided studies in cancer drug discovery.

	Case Study	Computational Approach	Model/ Algorithm	Relevant Results
AI drug repurposing	Chondrosarcoma (CS) [38]	Knowledge + network-based methods 1. Genetic data of disease: pubmed2ensembl. 2. Drug–gene interaction: Drug Gene Interaction Database (DGIdb). 3. Drug–target information: DeepPurpose.	Deep learning-based algorithm	A total of 25 candidate drugs were identified. Among the listed drugs, there are drugs that have been approved for various solid tumors and have been applied to patients with CS: everolimus, paclitaxel, sirolimus, 2-methoxyestradiol, and sunitinib.
	Familiar Melanoma [39]	Knowledge + network-based methods 1. Genetic data of disease: databases + disease knowledge. 2. Disease Mechanistic Map: HiPathia + Genotype-Tissue Expression Project. 3. Drug–target information: Drexml.	Explainable machine learning model	A total of 78 candidate drugs correspond to currently approved chemotherapeutic agents used to treat various types of cancer. Paclitaxel, docetaxel, moxetumomab, and ruxolitinib are drugs that target specific melanogenesis circuits.
	Liver and lung cancers [40]	Similarity-based, artificial intelligence-based, signature-based, and network-based methods 1. Integrating heterogeneous data (drugs, targets, diseases, side effects and pathways) from databases and the literature. 2. Drug–target information: DrugRepoBank.	Artificial intelligence model	AI-predicted a CYP3A4 target for sildenafil repositioning in the treatment of liver cancer. The drug candidate verteporfin may influence lung cancer by modulating the Hippo signaling pathway and insulin secretion.
	Breast cancer [41]	Network-based method 1. Genetic data of disease: breast cancer gene expression profiles from GEO database. 2. Drug–disease interaction: DRviaSPCN.	Random walk with restart algorithm	Four of ten candidate drugs have been demonstrated to be associated with breast cancer: azacitidine, valproic acid, doxorubicin, and exemestane.
	Breast and lung cancers [42]	Network-based method 1. Genetic data of disease: breast cancer and lung cancer gene expression profiles from GEO database. 2. Drug–disease interaction: DrugSim2DR.	Random walk with restart algorithm	Five potential anti-breast cancer drugs were identified: fluoxymesterone, gestrinone, pyrazole, fomepizole, and medroxyprogesterone acetate. Fluoxymesterone has received approval for breast cancer treatment. Of nine candidate drugs, methotrexate and pemetrexed have been approved for the treatment of lung cancer.

Table 1. *Cont.*

	Case Study	Computational Approach	Model/ Algorithm	Relevant Results
AI *de novo* drug design	Hepatocellular carcinoma [43]	Structure-based drug design of novel targets 1. Target selection: PandaOmics. 2. Determination of putative binding sites: Chemistry42. 3. Generation of novel hits targeting CDK20 inhibitor: AlphaFold.	Deep learning-based algorithm	A novel therapeutic target was identified from a pool of dark targets (without experimental structure) that were predicted using AlphaFold (v.2.3.0). ISM042-2-048 generated a compound that showed good CDK20 inhibitory activity.
	Carcinoma and neuroblastoma [44]	Reinforcement learning approach 1.Genetic data of disease: carcinoma and neuroblastoma gene expression profiles. 2. Generation of anticancer hit molecules: PaccMann^{RL}.	Deep learning-based algorithm	The generated compounds exhibited similar physicochemical properties to real cancer drugs.
	Breast and lung cancers [45]	Counter-propagation artificial neural networks (CPANNs) 1. Two peptide datasets targeting breast and lung cancer cells were assembled and curated manually from CancerPPD. 2. Training CPANN model to classify peptides according to their activity. 3. Library class generation with 1000 presumed alpha-helical peptides sequences with the amino acid distribution of alpha-helical anticancer peptides (ACPs): modlAMP. 4. Evaluation and ranking of the activity of de novo designed peptides from the library: CPANNs. 5. Selection of candidate peptides with anticancer activity to *in vitro* assays.	Deep learning-based algorithm	From a total of 1000 *de novo* designs, 6 peptides showed anticancer activity *in vitro*, including 5 against both MCF7 and A549 cell lines.

AI in computational biology has significantly advanced cancer therapies by providing innovative tools to address the challenges of traditional drug development. Researchers have developed bioinformatics tools using various AI algorithms, such as DeepPurpose, to tackle drug repositioning in chondrosarcoma [38,40,42]. Most of these approaches require the use of huge amounts of diverse data (specifically, information about disease pathway, proteomic metabolism, drug–disease interaction, gene expression, etc.). The case study of familial melanoma conducted by Esteban-Medina et al. [39] exemplifies the importance of integrating diverse data sources and methodologies. The implementation

of a machine learning model allowed for the contextualization of protein drug targets in terms of the functional landscape of the disease and for the identification of candidate drugs for the treatment of melanoma. Similarly, pathway-level analysis and disease-specific modeling further enhance AI-driven drug discovery efforts [41,42]. DRviaSPCN introduces a novel approach by analyzing subpathway (SP) crosstalk networks, capturing the intricate interactions between tumor pathways critical for cancer progression and therapy resistance. Validated through breast cancer datasets, DRviaSPCN demonstrated very good predictive performance, identifying FDA-approved drugs and novel candidates [41].

AI-driven insights into molecular mechanisms reveal new potential therapeutic targets. Different AI approaches are used throughout drug development, but some are more effective than others. For example, neural networks and classical machine learning are effective for target identification due to their ability to analyze drug–target and protein–protein interaction networks, identify novel binding sites, and predict protein structures. In the field of neuroscience, these methods are used to identify new therapeutic targets for neurodegenerative diseases such as Alzheimer's and Parkinson's. For example, machine learning models can analyze large gene expression and neuroimaging datasets to identify genes and pathways involved in these diseases. Many of these targets lack known ligands or structural data. Advances in deep generative modeling and machine learning in *de novo* oncology drug design are providing solutions to this challenge [44,45]. For instance, in a recent paper by Ren et al., they designed and synthesized molecules based on AlphaFold-predicted structures for cyclin-dependent kinase 20 (CDK20). This enzyme had previously been identified *in silico* as a novel target against hepatocellular carcinoma (HCC). This workflow resulted in a potent molecule with selective anti-proliferative activity against HCC cell lines overexpressing CDK20. Surprisingly, the development process of the *de novo* compound required only 30 days and involved the synthesis of only seven compounds [43]. These results highlight the efficiency and precision of AI-powered platforms in accelerating early-stage drug discovery, particularly for targets lacking experimental structural data.

4. Integration of AI with Experimental Techniques

AI has become an indispensable tool in the field of drug discovery, offering advanced methods to enhance experimental workflows by increasing efficiency, precision, and data integration.

4.1. AI-Guided High-Throughput Screening (HTS)

Traditionally, HTS involves testing thousands of compounds to identify potential therapeutic candidates, a resource-intensive endeavor. AI-powered models, such as CNNs, optimize this process by analyzing chemical libraries and predicting compound activity, thereby prioritizing candidates with the highest therapeutic potential. For example, the already mentioned AlphaFold algorithm has significantly advanced protein structure prediction, allowing researchers to identify molecular interactions that were previously elusive [12]. This has enabled the development of more targeted and cost-effective screening strategies, revolutionizing the early stages of drug development.

4.2. AI-Assisted Drug Synthesis and Optimization

In addition to screening, AI also plays a critical role in drug synthesis and optimization. Traditional methods of synthesizing complex molecules often rely on iterative and time-consuming experimental approaches. AI-driven retrosynthesis tools, such as Chemprop and MoleculeNet, leverage reaction databases to predict chemical pathways and propose efficient synthesis routes [46,47]. These tools not only streamline the development of new compounds but also minimize costs and reduce the time needed to bring potential drugs to

preclinical testing. By automating the prediction of reaction outcomes and toxicity, these models ensure a higher success rate for synthesized molecules, accelerating the transition from lab to clinic.

4.3. AI-Driven In Vitro and In Vivo Testing

AI's contributions extend to *in vitro* and *in vivo* testing, where predictive models guide experimental designs and reduce reliance on labor-intensive methods. Generative adversarial networks (GANs), for instance, simulate cellular responses to novel compounds, offering preliminary insights into efficacy and safety before traditional testing begins [48]. Furthermore, multi-omics AI models integrate genomic, transcriptomic, and proteomic data to predict how specific drug candidates might interact with patient-specific biological pathways. These integrative approaches not only enhance the precision of experimental assays but also facilitate the development of personalized treatment strategies.

4.4. AI for Data Integration in Preclinical Studies

Lastly, AI has proven invaluable for integrating diverse datasets into preclinical studies. By analyzing imaging data, omics datasets, and physiological measurements simultaneously, AI models can identify biomarkers and therapeutic targets that might otherwise remain undetected. For example, deep learning algorithms have been employed to analyze histological images in conjunction with gene expression profiles, uncovering novel insights into tumor microenvironments and drug interactions [49]. This holistic approach enhances the translational potential of preclinical research, paving the way for more effective clinical applications.

5. Challenges and Opportunities

While the integration of artificial intelligence (AI) in drug discovery offers transformative potential, realizing its full benefits requires addressing several key challenges (Figure 3).

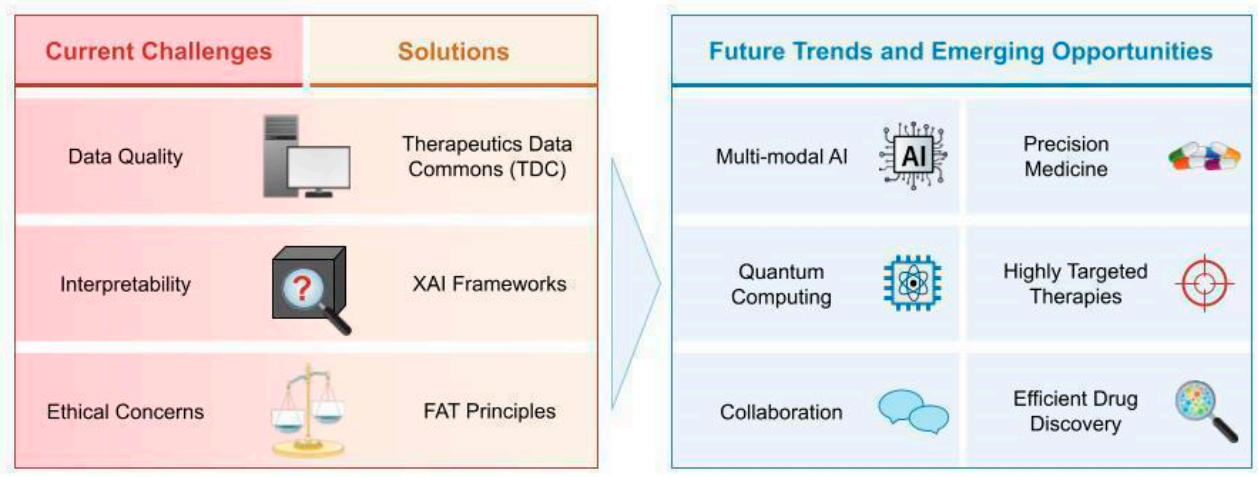

Figure 3. Challenges, solutions, and future trends of AI-driven drug repurposing. Some icons are from Bioicons (https://bioicons.com/); some icons are from SERVIER MEDICAL ART (https://smart.servier.com/).

5.1. Data Quality and Quantity

A primary concern is the quality and quantity of available data for training AI models. Biomedical datasets often suffer from inconsistencies, noise, and biases, which can compromise predictive accuracy. The proprietary nature of much pharmaceutical data

further restricts access for researchers, hindering data sharing and standardization. To overcome these issues, solutions include enhanced data curation, the establishment of standardized dataset preparation protocols, and the use of synthetic data to augment real-world datasets. Initiatives like the Therapeutics Data Commons (TDC) are pivotal in establishing benchmarks for data quality and accessibility, effectively bridging the gap between research institutions and industry [50]. By improving data quality, researchers can enhance the reliability of AI models, leading to more accurate predictions and better therapeutic outcomes [50].

5.2. Interpretability of AI Models

The "black box" nature of many machine learning and deep learning models poses another significant hurdle. The lack of transparency in how these models arrive at their predictions creates challenges in regulatory and clinical settings where trust is paramount. In order to ensure that the predictions of AI models are clinically reliable and understandable to clinicians, explainable AI (XAI) frameworks, such as SHAP (SHapley Additive exPlanations) and LIME (Local Interpretable Model-Agnostic Explanations), are being developed [51,52]. These tools provide insights into the features driving model predictions, thereby building confidence among stakeholders and facilitating regulatory approval. By enhancing model interpretability, researchers can ensure that AI-driven decisions are more transparent and justifiable, which is crucial for gaining acceptance in clinical practice. However, these XAI methods also have their own limitations, including uncertainty in the calculation and distribution of the score estimates, which may lead to generalization of results. Also, LIME struggles with nonlinear dependencies, while SHAP has problems with feature dependencies, as permutation values assume independence. A quantitative comparison between AI models and traditional methodologies in terms of diagnostic and therapeutic efficacy is an active research area, as highlighted in recent studies [53].

Finally, neither method is capable of inferring causality, which limits their applications. All of these limitations need to be overcome in the near future to improve the interpretability of AI models [54].

5.3. Ethical Considerations

The use of AI in drug discovery raises ethical considerations regarding data privacy, algorithmic biases, and equitable access to AI-driven therapies. Biases in training datasets can lead to inequitable treatment predictions, disproportionately affecting under-represented populations. For instance, in drug repurposing, sex-specific differences in genetics, hormones, and metabolism often result in male- or female-biased drug responses and adverse events. Computational approaches are being developed to identify sex-inclusive drug candidates, improving therapeutic options and reducing adverse effects for all patients [55]. Addressing these concerns, an emerging number of members of the scientific community are applying the FAIR (Findable, Accessible, Interoperable, and Reusable) principles. This approach reduces bias in biomedicine by promoting ethical, transparent, and interoperable data management. Biomedical researchers can access diverse, FAIRified datasets, minimizing bias from localized data [56,57]. In 2021, the FDA received 132 regulatory submissions for drugs that included the use of AI in their discovery and development, resulting in a 10-fold increase over the previous year. This federal agency recognizes the transformative potential of AI in drug development and emphasizes rigorous evaluation through well-controlled clinical studies to ensure that the benefits outweigh the risks. Regulatory oversight requires deep technical expertise to review AI-assisted applications, such as target selection or intervention strategies. Maintaining a workforce with technical expertise is vital to provide timely and effective guidance and support innovation in this evolving

field [58]. The European Medicines Agency (EMA) has developed an artificial intelligence (AI) workplan for the European medicines regulatory network to guide the use of AI in medicine regulation in Europe up to 2028 [59]. Regulatory frameworks must evolve to include guidelines for AI in healthcare, ensuring that ethical standards are maintained [60]. By prioritizing ethical considerations, the industry can foster trust and ensure that AI technologies benefit all patients equitably.

5.4. Collaboration Across Sectors, Future Trends, and Emerging Opportunities

In addition to the aforementioned challenges, collaboration between academia, industry, and regulatory bodies represents a significant opportunity for advancing AI-driven drug discovery. Cross-sector partnerships can facilitate the sharing of data, tools, and expertise, fostering innovation and reducing barriers to implementation. By working together, stakeholders can address challenges collaboratively and leverage AI's capabilities to achieve unprecedented levels of efficiency, accuracy, and impact in drug discovery. This collaborative approach not only accelerates the pace of discovery but also ensures that the resulting therapies are safe, effective, and accessible to patients worldwide.

Cross-sector collaboration is a key driver for advancing AI-driven drug discovery. Numerous initiatives exemplify the power of partnerships between academia, industry, and regulatory agencies. For example, major pharmaceutical companies such as Pfizer, Novartis, and AstraZeneca have formed strategic alliances with AI technology companies, leading to the development of innovative tools and platforms for drug discovery. These collaborations have significantly accelerated target identification, drug design, and clinical trial optimization. Additionally, renowned research centers such as the Broad Institute and the National Cancer Institute have established AI research centers dedicated to drug discovery. These centers foster interdisciplinary collaboration, bringing together experts in biology, chemistry, and computer science to develop new AI methodologies and applications. Additionally, public–private initiatives such as the Alliance for Drug Discovery Innovation (ADDI) facilitate collaboration between academia, industry, and regulatory agencies, providing funding, resources, and expertise to drive the development of AI technologies.

Despite these challenges, the opportunities presented by artificial intelligence (AI) in drug discovery are vast and transformative. Emerging technologies, such as multimodal AI, are at the forefront of this revolution, integrating diverse data types—from clinical records to genomic data—into cohesive analytical frameworks. This integration is crucial as it allows for a more comprehensive understanding of the biological systems involved in drug interactions and disease mechanisms. These advancements are driving significant progress in precision medicine, enabling the development of highly targeted therapies that are tailored to the unique genetic and molecular profiles of individual patients. This personalized approach not only enhances treatment efficacy but also minimizes adverse effects, thereby improving overall patient outcomes.

As AI-driven drug discovery advances, ensuring the reliability and clinical applicability of AI models remains a key priority. Experimental validation plays a crucial role in this process, incorporating preclinical testing, real patient data comparisons, and ongoing monitoring to assess model performance. Preclinical studies allow researchers to evaluate AI-generated predictions in controlled settings before transitioning to real-world clinical applications [61]. Furthermore, comparisons with patient data help confirm that AI models provide meaningful and actionable insights [62]. To maintain long-term effectiveness, continuous monitoring systems are being explored to oversee AI performance post-deployment, ensuring adaptability to evolving clinical practices and patient demo-

graphics [61–63]. These validation strategies are essential for bridging the gap between theoretical AI models and practical, clinically relevant applications in drug discovery.

Furthermore, quantum computing, although still in its infancy, holds immense potential in addressing complex molecular problems that traditional computational methods struggle to solve [64]. By accelerating simulations and optimizing chemical structures, quantum computing could revolutionize de novo drug design, allowing researchers to explore vast chemical spaces and identify promising drug candidates more efficiently. This capability could significantly shorten the drug development timeline and reduce costs, making it a game-changer in the pharmaceutical industry.

Collaboration between academia, industry, and regulatory bodies represents another significant opportunity for advancing AI-driven drug discovery. High-performance computing and cloud computing play a critical role in AI frameworks for drug discovery. These technologies facilitate the processing of large genomic, proteomic, and chemical datasets, as well as the execution of complex computational simulations. For example, cloud computing enables researchers to access scalable and affordable computational resources, which accelerates the development and deployment of AI models. Cross-sector partnerships can facilitate the sharing of data, tools, and expertise, fostering innovation and reducing the barriers to implementation. Such collaborations can lead to the establishment of standardized protocols and best practices that enhance the reliability and reproducibility of AI applications in drug discovery. By addressing challenges collaboratively and leveraging AI's capabilities, the field of drug discovery can achieve unprecedented levels of efficiency, accuracy, and impact. This collaborative approach not only accelerates the pace of discovery but also ensures that the resulting therapies are safe, effective, and accessible to patients worldwide.

In summary, the integration of AI into drug discovery processes, coupled with advancements in quantum computing and collaborative efforts across sectors, allows the pharmaceutical industry to overcome existing challenges and unlock new therapeutic possibilities. As these technologies continue to evolve, they promise to reshape the landscape of drug development, ultimately leading to more effective treatments and improved health outcomes for patients globally.

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