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REVIEW ARTICLE

Artificial Intelligence and Multi-Omics for Anticancer Drug Development and Repurposing

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Abstract: The escalating complexity and financial burden associated with de novo drug development necessitate a transition toward more efficient therapeutic discovery models. Conventional pipelines often span over fifteen years with costs exceeding two billion dollars, yet they remain plagued by a ninety percent failure rate in clinical phases. Drug repurposing offers a viable alternative by identifying novel oncological applications for existing, safety-validated compounds, thereby bypassing early-stage toxicological bottlenecks. The integration of artificial intelligence (AI) has emerged as a transformative force in this domain, enabling the high-throughput analysis of vast chemical libraries and multi-omics biological datasets. Researchers can now predict drug-target interactions, model therapeutic outcomes, and prioritize lead candidates with unprecedented precision by utilizing sophisticated machine learning, deep neural networks, and network-based algorithms. Modern computational strategies leverage genomic, proteomic, and metabolic signatures to map the intricate interactions between pharmacological agents and the neoplastic microenvironment. This review provides the current state of AI-driven repositioning, emphasizing the transition from target-centered to disease-oriented models. Case studies involving antibiotics, cardiovascular agents, and psychotropic drugs show the clinical viability of repurposed therapies in reducing tumor proliferation and overcoming chemoresistance. Overcoming the challenges of data heterogeneity and algorithmic bias is essential for the future implementation of these technologies in precision oncology.

Keywords: Artificial intelligence; Drug repurposing; Oncology; Machine learning; Deep learning.

1. Introduction

The pharmaceutical industry faces a critical juncture characterized by diminishing returns in traditional drug discovery. The standard techniques for bringing a novel molecule to market involves extensive preclinical optimization followed by three phases of clinical trials, a process frequently extending to a 15-year horizon with expenditures often reaching 1.3 to 2.8 billion per approved agent [1]. Despite significant investment, the attrition rate remains high; approximately 90% of candidates fail during clinical development due to lack of efficacy or unforeseen toxicity [1]. To mitigate these risks, computational screening and molecular docking have been utilized for decades; however, their predictive accuracy is often limited by the complexity of biological systems.

The advent of artificial intelligence (AI), specifically machine learning (ML) and deep learning (DL), provides a robust framework for managing the "Big Data" generated by high-throughput screening and clinical registries. AI technologies facilitate the identification of non-linear relationships within macromolecular properties and pharmacological datasets, offering high-accuracy predictions with reduced computational overhead [2]. Applications such as de novo molecular design, retrosynthesis prediction, and virtual screening are now augmented by neural network architectures that evolve from basic ML models to complex transformers and generative adversarial networks (GANs).

Drug repurposing, also termed drug repositioning or redesigning, involves the identification of novel therapeutic indications for previously approved or investigational agents. This strategy significantly accelerates the development timeline by leveraging existing safety profiles and pharmacokinetic data, allowing compounds to proceed directly to Phase II or III clinical trials [1][2]. In the context of oncology, where rare cancers and rapid resistance development pose major hurdles, repurposing provides a mechanism to expand the available armamentarium quickly and cost-effectively.

The role of AI in repositioning is centered on the analysis of digital health records, genomic databases, and biochemical literature to reveal latent links between existing drugs and disease-specific targets. AI models can forecast pharmacological traits and generate

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novel molecular scaffolds by employing feature-based and matrix-based approaches [3]. Reinforcement learning and deep neural networks (DNNs) enable the detection of cardiotoxic or hepatotoxic risks early in the computational phase, refining the selection of candidates for further validation [2].

2. AI-Driven Methods in Target Discovery

The identification of tumor-suppressive targets has been revolutionized by the convergence of multi-omics methods and computational intelligence. The landscape of target discovery is currently defined by five distinct but interconnected domains: genomics, epigenetics, proteomics, metabolomics, and multi-omics integration.

2.1. Genomic and Epigenetic Profiling

Genomics focuses on characterizing every genomic component to establish correlations between genotype and phenotype. AI algorithms assist in identifying biomarkers for patient stratification and mapping transcriptional promoters within genomic regions [4]. Simultaneously, epigenetics investigates alterations in gene regulation such as DNA methylation and histone modification that occur without changing the underlying DNA sequence. AI-driven epigenetic analysis allows for the identification of regulatory targets that may be susceptible to pharmacological intervention, even when primary genetic sequences remain intact [4].

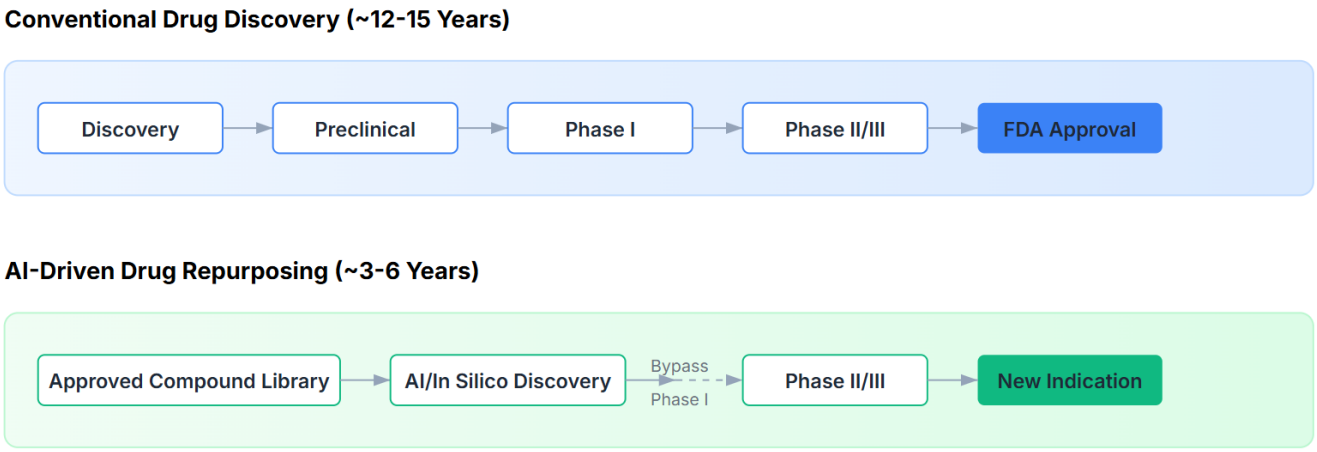

Figure 1: Conventional de novo drug discovery pipeline versus the accelerated AI-driven drug repurposing track. Repurposing utilizes existing toxicological and safety data to bypass early clinical phases.

Table 1. Comparison of Therapeutic Discovery Models

Feature	Conventional Drug Discovery	AI-Driven Drug Repurposing
Average Timeline	12–15 Years	3–6 Years
Estimated Cost	1.3B – 2.8B	< 300M
Success Rate	~10% (Clinical Phase)	Significantly Higher (Validated Safety)
Risk Profile	High (Toxicity & Efficacy)	Lower (Known Safety/Pharmacokinetics)
Early Phases	Required (Phase I Toxicity)	Often Bypassed (Existing Safety Data)
Data Reliance	De Novo Synthesis/Testing	Multi-omics & Real-World Evidence

2.2. Proteomic and Metabolomic Characterization

Proteomics involves the large-scale study of protein-protein interactions (PPIs), protein abundance, and post-translational modifications. AI techniques are essential for organizing PPI networks, which serve as the regulatory framework for most biological processes [5]. In metabolomics, AI is utilized to detect minute fluctuations in metabolic pathways within biological fluids and tissues. Given that cancer cells exhibit distinct metabolic reprogramming, identifying these metabolic signatures through AI provides a direct route to discovering biomarkers and therapeutic vulnerabilities [5].

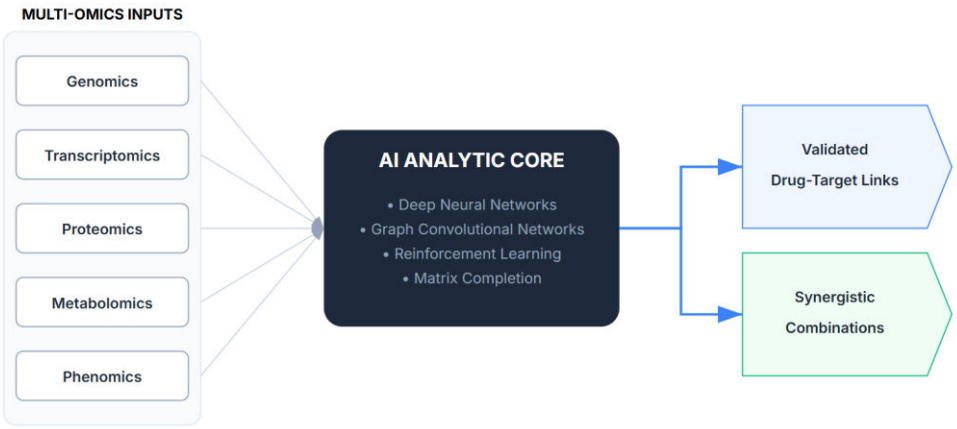

Figure 2. AI Multi-Omics Integration

Table 2. Multi-Omics Data Sources for AI-Driven Target Identification

Data Type	Primary Repositories	Description	Role in AI Modeling
Genomics	TCGA, ICGC	Cancer genome sequences	Identifying driver mutations
Transcriptomics	GEO, GTEx	Gene expression profiles	Mapping disease signatures
Proteomics	CPTAC, PRIDE	Protein abundance & PPIs	Understanding signaling networks
Pharmacological	DrugBank, ChEMBL	Drug-target interactions	Training supervised ML models
Clinical	SEER, EHR	Patient outcomes & histories	Validating therapeutic relevance

2.3. Machine Learning Methodologies for Repurposing

Machine learning frameworks are primarily categorized into supervised and unsupervised paradigms, each offering unique advantages for drug recycling.

2.3.1. Supervised Learning Paradigms

Supervised models are trained on labeled datasets where known interactions between drugs and targets serve as the ground truth. These models identify molecular descriptors that differentiate effective binders from inactive compounds [6]. Once trained, the model can predict the potential interaction between any approved drug and a novel oncological target, ranking candidates based on their predicted binding affinity or therapeutic efficacy [7].

2.3.2. Unsupervised Learning Approaches

Unsupervised learning focuses on detecting inherent structures within unlabeled data, such as chemical composition or patient clinical records. This approach is particularly effective for discovering unanticipated links that traditional methods might overlook [8]. Unsupervised models can suggest novel indications for drugs that appear pharmacologically unrelated to a specific disease pathology by clustering drugs based on side-effect profiles or gene expression changes.

3. Deep Learning Architectures for Pharmacological Prediction

Deep learning (DL) has surpassed traditional machine learning in its ability to handle high-dimensional biological data. These methodologies are typically classified as either target-centered or disease-centered, depending on the primary focus of the predictive task.

3.1. Target-Centered Deep Learning Models

Target-oriented approaches focus on the molecular interaction between a ligand and a receptor. Advanced models capture the localized residual sequences of proteins and process amino acid patterns through neural networks [9].

3.1.1. Neural Integration and Binding Affinity

Frameworks such as the Multi-Input PCM guided Neural Network (MIPNN) use chemical descriptors like Simplified Molecular Line Entry Specification (SMILES) and Extended Connectivity Fingerprints (ECF) to forecast drug-receptor binding (DRB) [10]. Graph-based models such as GraphDRBA have replaced conventional convolutional neural networks (CNNs) to better represent molecular structures as graphs, allowing the model to learn the spatial relationships between atoms more effectively [11].

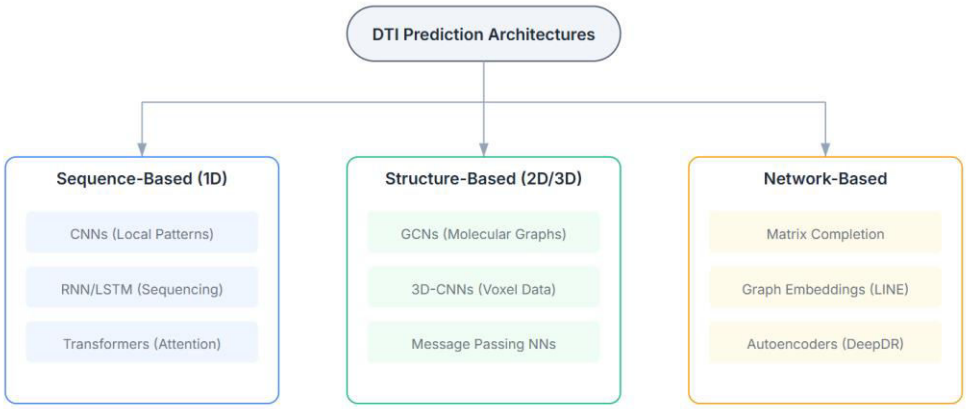

Figure 3. DL Architecture Taxonomy for DTI

Table 3. Deep Learning Architectures for DTI Prediction

Model / Framework	Architecture Type	Primary Input Data	Predictive Task	Reference
DeepConv-DTI	CNN	Protein sequences (local)	Drug-target interaction binary	[9]
GraphDTA	GNN	Molecular graphs (SMILES)	Binding affinity regression	[11]
NeoDTI	Network Integration	Heterogeneous networks	Neighborhood-based DTI	[12]
DeepDRnet	Autoencoder	Multi-network features	Target identification	[13]
SNF-CVAE	Variational Autoencoder	Similarity networks	Drug-disease association	[14]

3.1.2. Network-Driven Discovery

Network integration approaches, such as NeoDTI and deepDRnet, utilize heterogeneous biological networks to identify novel targets [12]. NeoDTI integrates neighborhood information from various systems, while deepDRnet employs deep autoencoders to extract high-quality features from multiple datasets. Notably, deepDRnet has demonstrated superior performance over traditional Support Vector Machines (SVM) and Random Forests, achieving high AUC-ROC metrics in predicting drug-target interactions [13].

3.2. Disease-Oriented Deep Learning Models

Disease-centered models prioritize the therapeutic relationship between a drug and a specific pathology, often utilizing homology-driven or graph-driven categories.

3.2.1. Similarity Network Fusion and Autoencoders

The Similarity Network Fusion-Conditional Variational Autoencoder (SNF-CVAE) integrates drug-disease associations with molecular features to increase the precision of therapeutic predictions [14]. This architecture has been successfully applied to identify treatments for complex conditions like Alzheimer's and rheumatoid arthritis, suggesting its potential for cross-disciplinary oncological applications [15].

3.2.2. Recurrent and Attention-Based Mechanisms

Models incorporating bidirectional Long Short-Term Memory (LSTM) and attention mechanisms allow for the learning of drug-disease path visualizations. These focus-based methods can pinpoint the most relevant mechanisms through which a drug exerts its effect on a specific cancer type by weighting the importance of different biological pathways [16].

4. Therapeutic Case Studies in Oncological Repurposing

The clinical application of repurposed agents spans various pharmacological classes, ranging from antimicrobials to cardiovascular medications.

4.1. Antimicrobials as Potential Anticancer Agents

Antibiotics have shown unexpected utility in oncology due to their ability to target mitochondrial function and inhibit protein synthesis in malignant cells. Doxycycline is tetracycline antibiotic that inhibits the 30S prokaryotic ribosomal subunit. In malignant contexts, it demonstrates pro-inflammatory suppression by inhibiting nitric oxide synthase [17]. Research indicates that doxycycline triggers apoptotic signaling pathways and prevents dissemination in colorectal and melanoma cell lines [18].

Table 4. Clinical Benchmarks for Repurposed Oncological Agents

Agent	Original Indication	Proposed Oncological Mechanism	Target / Pathway	Current Status
Doxycycline	Antibiotic	Mitochondrial dysfunction	30S Ribosomal / Apoptosis	Preclinical/Phase II
Losartan	Hypertension	Stroma normalization	RAAS / Collagen type 1	Phase II (Pancreatic)
Chlorpromazine	Antipsychotic	Autophagy induction	PI3K/AKT/mTOR	Preclinical
Aspirin	Anti-inflammatory	Prevention / HER2 reduction	COX-2 / Proliferation	Clinical Use/Prevention
Metformin	Type 2 Diabetes	AMPK activation	mTOR / Metabolism	Extensive Phase II/III

4.2. Cardiovascular Medications in Oncology

The renin-angiotensin-aldosterone system (RAAS), a primary target for cardiac drugs, is also involved in the tumor microenvironment (TME) regulation. This angiotensin receptor blocker reduces "solid stress" within the TME by inhibiting collagen deposition and increasing vessel density. This normalization of the tumor stroma enhances the delivery and efficacy of co-administered chemotherapy [19]. Phase II clinical trials have demonstrated that losartan can convert previously unresectable pancreatic ductal adenocarcinoma into a localized, operative state [20].

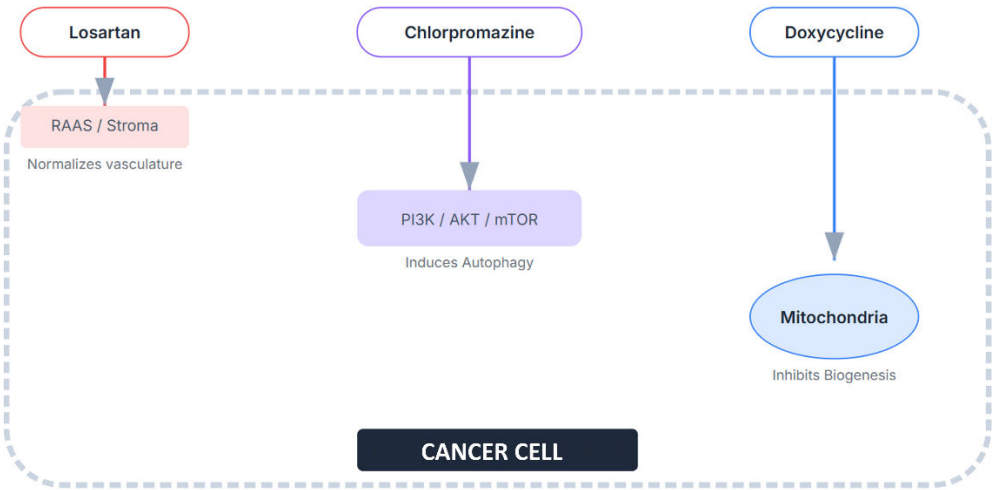

Figure 4. Repurposing Mechanisms in Oncology

4.3. Psychotropic and Antipsychotic Agents

The psychotropic class, particularly phenothiazines, has been investigated for its ability to disrupt cell cycle progression and induce autophagy. Primarily used for psychotic disorders, CPZ suppresses tumor cell proliferation by blocking the PI3K/AKT/mTOR pathway. It induces cell cycle arrest at the G2/M phase and disrupts mitotic kinesin KSP/Eg-5, leading to mitotic arrest and apoptosis in glioma and colorectal cancer models [21].

5. Challenges

Despite the success of AI-driven pipelines, several obstacles persist in the transition from computational prediction to clinical implementation.

5.1. Data Heterogeneity and Accessibility

A primary challenge involves the unorganized and diverse nature of clinical datasets, which include imaging, genomic profiles, and morphological features. The disparity between the volume of generated data and the capacity to integrate and analyze it remains significant [22]. While gene expression profiles are often publicly available, high-quality clinical response data is frequently restricted or proprietary.

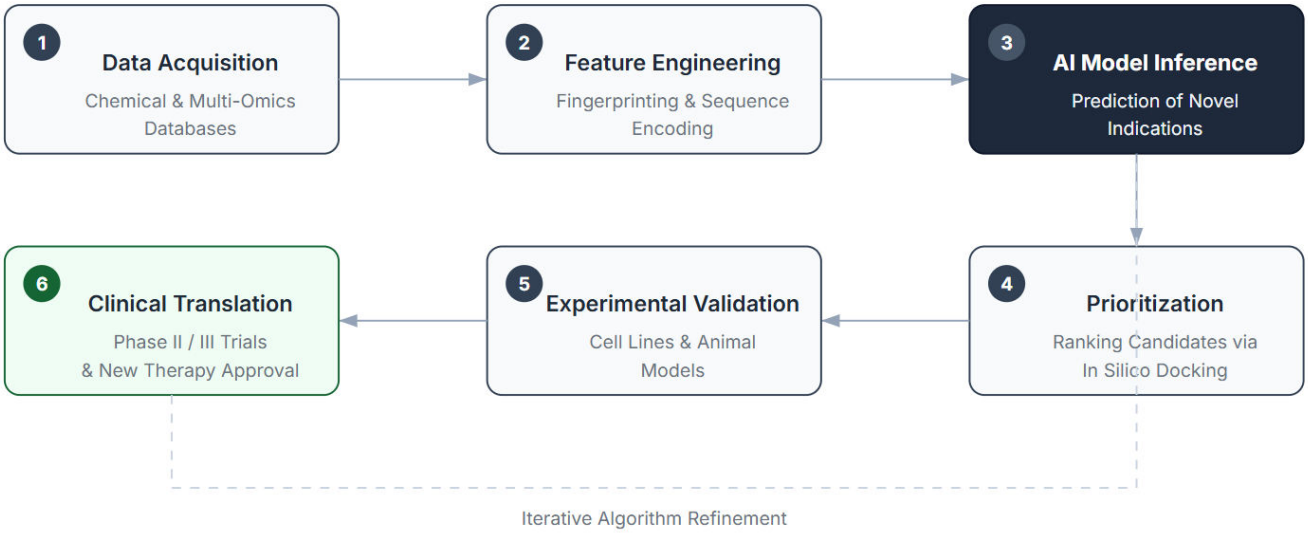

Figure 5. Process for AI-Powered Drug Repositioning

5.2. Algorithmic Bias and Knowledge Gaps

AI models tend to favor well-researched compounds, creating a bias toward "popular" drugs while leaving molecules with sparse data understudied. The requirement for extensive manual curation of chemical and biological information increases the complexity and potential for human error in the training phase [23].

Table 5. Strategic Challenges in AI-Based Repositioning

Challenge Category	Specific Bottleneck	Impact on Discovery	Mitigation Strategy
Data Quality	Heterogeneity	High noise in multi-omics	Data normalization & GANs
Algorithmic	Popularity Bias	Neglect of understudied drugs	Few-shot learning models
Regulatory	IP Constraints	Complexity in repurposing patents	Value-based pricing models
Clinical	Validation	*In silico* vs. *In vivo* disparity	High-throughput organoid screening

5.3. Evolution of Algorithmic Power

The future of drug repurposing lies in the evolution of AI algorithms and the growth of computational power. Advances in generative models and the integration of AI tools into standard laboratory workflows will likely drive more efficient therapeutic discoveries. Addressing ethical considerations and ensuring the quality of training data are paramount for the long-term success of these technologies [24].

6. Conclusion

Artificial intelligence-based drug repositioning offers a revolutionary path for oncological drug discovery, significantly reducing developmental timelines and financial risks. Researchers can now identify therapeutic opportunities within the existing pharmacopeia that were previously invisible by leveraging multi-omics integration and sophisticated deep learning architectures. The transition from target-centric binding models to holistic, disease-oriented evaluations allows for a more comprehensive strategy in treating complex malignancies. The integration of AI in drug repurposing will likely become the cornerstone of precision oncology as computational models become increasingly refined and data accessibility improves providing rapid and effective treatment options for patients worldwide.

References

[1] Pushpakom S, Iorio F, Eyers PA, Escott KJ, Hopper S, Wells A, et al. Drug repurposing: progress, challenges and recommendations. Nature Reviews Drug Discovery. 2019;18(1):41-58.

[2] Dara S, Dhamercherla S, Jadav SS, Babu CM, Ahsan MJ. Machine learning in drug discovery: a review. Artificial Intelligence Review. 2022;55(3):1947-99.

[3] Vamathevan J, Clark D, Czodrowski P, Dunham I, Ferran E, Lee G, et al. Applications of machine learning in drug discovery and development. Nature Reviews Drug Discovery. 2019;18(6):463-77.

[4] You Y, Lai X, Pan Y, Zheng H, Vera J, Liu S, et al. Artificial intelligence in cancer target identification and drug discovery. Signal Transduction and Targeted Therapy. 2022;7(1):156.

[5] Manzoni C, Kia DA, Vandrovcova J, Hardy J, Wood NW, Lewis PA, et al. Genome, transcriptome and proteome: the triad of omics data-integration for multi-omics. Briefings in Bioinformatics. 2018;19(2):286-302.

[6] Lavecchia A. Machine-learning approaches in drug discovery: methods and applications. Drug Discovery Today. 2015;20(3):318-31.

[7] Lo YC, Racker SE, Bujotzek A, Tokarski JT, Caflisch A. Machine learning in drug discovery: what is the hope and where is the hype? Drug Discovery Today. 2018;23(8):1538-46.

[8] Libbrecht NW, Noble WS. Machine learning applications in genetics and genomics. Nature Reviews Genetics. 2015;16(6):321-32.

[9] Lee I, Keum J, Nam H. DeepConv-DTI: Prediction of drug-target interactions via deep learning with convolution on protein sequences. PLOS Computational Biology. 2019;15(6):e1007129.

[10] Lee M, Kim H, Joe H, Kim HG. Multi-channel PINN: investigating scalable and transferable neural networks for drug discovery. Journal of Cheminformatics. 2019;11(1):46.

[11] Nguyen T, Le H, Quinn TP, Nguyen T, Le TD, Venkatesh S. GraphDTA: predicting drug–target binding affinity with graph neural networks. Bioinformatics. 2021;37(8):1140-47.

[12] Luo Y, Zhao X, Zhou J, Yang J, Zhang Y, Kuang W, et al. A network integration approach for drug-target interaction prediction and computational drug repositioning from heterogeneous information. Nature Communications. 2017;8(1):571.

[13] Zeng X, Zhu S, Lu W, Liu Z, Huang J, Zhou Y, et al. Target identification among known drugs by deep learning from heterogeneous networks. Chemical Science. 2020;11(7):1775-97.

[14] Jarada TN, Rokne JG, Alhajj R. SNF–CVAE: Computational method to predict drug–disease interactions using similarity network fusion and collective variational autoencoder. Knowledge-Based Systems. 2021;212:106585.

[15] Cheng F, Desai RJ, Handy DE, Yan R, Wang R, Ituarte-Vazquez ME, et al. Network-based approach to data-driven drug repositioning of approved drugs for Alzheimer's disease. Nature Communications. 2021;12(1):4615.

[16] Xuan P, Ye Y, Zhang T, Zhao L, Sun C. Convolutional neural network and bidirectional long short-term memory-based method for predicting drug-disease associations. Cells. 2019;8(7):705.

[17] Pulvino M, Chen L, Olearczyk J, Brunelle J, Roos V, Eberle D, et al. Inhibition of proliferation and survival of diffuse large B-cell lymphoma cells by a small-molecule inhibitor of the p90 ribosomal S6 kinase. Blood. 2011;117(8):2405-13.

[18] Ghasemi K, Ghasemi K. A brief look at antitumor effects of doxycycline in the treatment of colorectal cancer and combination therapies. European Journal of Pharmacology. 2022;916:174593.

[19] Chauhan VP, Martin JD, Liu H, Lacorre DA, Jain SR, Kozin SV, et al. Angiotensin inhibition enhances drug delivery and potentiates chemotherapy by decompressing tumour blood vessels. Nature Communications. 2013;4(1):2516.

[20] Murphy JE, Wo JY, Ryan DP, Clark JW, Jiang W, Yeap BY, et al. Total neoadjuvant therapy with FOLFIRINOX in combination with losartan followed by chemoradiotherapy for locally advanced pancreatic cancer: a phase 2 clinical trial. JAMA Oncology. 2019;5(7):1020-27.

[21] Fu L, Jin W, Zhang J, Zhu L, Lu J, Zhen Y, et al. Repurposing non-oncology small-molecule drugs to improve cancer therapy: Current situation and future directions. Acta Pharmaceutica Sinica B. 2022;12(2):532-57.

[22] Bongiovani F. Drug repositioning and artificial intelligence: is it a promising approach to be used for neglected diseases? Journal of the Brazilian Chemical Society. 2024;35.

[23] Bender A, Cortés-Ciriano I. Artificial intelligence in drug discovery: what is realistic, what are the illusions? Part 1: Ways to make data driven predictions, and areas of application. Drug Discovery Today. 2021;26(2):511-24.

[24] Lee H. Role of artificial intelligence in drug discovery and development. International Journal of Drug Development and Research. 2024;16(2):1-5.