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Mini Review

The Artificial Intelligence-driven Revolution in Solid Tumor Drug Development

Yi-Han Li[1] and Jiang-Jiang Qin[1,2,3*]

[1]College of Traditional Chinese Medicine, Shandong Second Medical University, Weifang, Shandong, China; [2]Center for Innovative Drug Research, Hangzhou Institute of Medicine (HIM), Chinese Academy of Sciences, Hangzhou, Zhejiang, China; [3]Key Laboratory for Molecular Medicine and Chinese Medicine Preparations, Hangzhou Institute of Medicine (HIM), Chinese Academy of Sciences, Hangzhou, Zhejiang, China

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Abstract

Artificial intelligence (AI) is profoundly transforming the paradigm of solid tumor drug development. By integrating multi-omics data, spatial transcriptomics, and advanced computational models, AI has significantly accelerated the discovery and validation of new targets, compressing the traditional ten-year research and development cycle to two to three years. Generative AI platforms have optimized small molecule inhibitors, biologics, and messenger RNA vaccines, achieving breakthroughs in overcoming tumor heterogeneity, improving efficacy, and predicting drug resistance. However, clinical translation still faces challenges such as data bias, algorithm transparency, and the validation gap between models and real-world human experience. This review aims to systematically elaborate on the transformative role of AI in solid tumor drug development and to promote interdisciplinary cooperation as well as the construction of ethical frameworks to enable the full realization of precision oncology.

Introduction

Solid tumor (ST) represents a key frontier in oncology, accounting for approximately 90% of cancer-related deaths. However, the path to developing effective therapies remains challenging, as evidenced by a mere 5% drug approval success rate, a stark contrast to the 15% seen in hematologic malignancies.[1,2] This high failure rate highlights the substantial unmet needs and unique complexities inherent in ST treatment. The development of effective ST therapies is notably hindered by two interwoven challenges. First, prominent tumor heterogeneity, both within individual tumors (intra-tumor) and between patients (inter-tumor), leads to varied treatment responses and facilitates the emergence of drug resistance. Second, the complex tumor microenvironment (TME) constitutes a formidable barrier. Stromal components, particularly cancer-associated fibroblasts (CAFs), play a crucial role in drug resistance. CAFs can secrete factors that directly protect tumor cells from chemotherapy or remodel the extracellular matrix to impede drug penetration.[3] Beyond the TME, the persistent challenge of "undruggable" targets further limits therapeutic options, such as the notoriously elusive kirsten rat sarcoma viral oncogene homolog (KRAS) oncoprotein or transcription factors like myelocytomatosis oncogene (MYC) that lack conventional small-molecule inhibitor binding sites.[4]

Artificial intelligence (AI) is emerging as a powerful catalyst poised to revolutionize drug discovery for ST. It significantly shortens the timeline, compressing the traditional decade-long process to just two to three years. Companies such as Insilico Medicine exemplify this progress by leveraging generative AI to rapidly identify and validate a novel ubiquitin specific peptidase 1 (USP1) inhibitor preclinical candidate. AI also reduces costs through sophisticated *in silico* methods such as virtual screening and predictive modeling of absorption, distribution, metabolism, excretion, and toxicity (ADMET) modeling, prioritizing the most promising candidates for expensive wet-lab experiments. Furthermore, AI plays a crucial role in addressing the "undruggability" paradigm. By facilitating the rational design of complex modalities such as proteolysis-targeting chimeras (PROTACs), which hijack the cell's ubiquitin-proteasome system to degrade target proteins rather than inhibit them, AI is opening avenues for targeting previously inaccessible oncogenic proteins like KRAS and MYC. AI algorithms assist in predicting effective warheads, linkers, and E3 ligase binders, optimizing PROTAC design, and overcoming key challenges associated with this promising technology.[5]

Keywords: Artificial intelligence; AI; Anticancer drug development; Solid tumor; Target discovery; Precision therapy.

***Correspondence to:** Jiang-Jiang Qin, Center for Innovative Drug Research, Hangzhou Institute of Medicine (HIM), Chinese Academy of Sciences. Hangzhou, Zhejiang 310018, China. ORCID: https://orcid.org/0000-0002-8559-616X. Tel/Fax: +86-571-88121791, E-mail: jqin@ucas.ac.cn

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This review systematically elaborates on the transformative role of AI across the ST drug development continuum, from target discovery to clinical translation, aiming to foster interdisciplinary collaboration and the construction of ethical frameworks for precision oncology implementation.

AI-driven target discovery

Advances in single-cell and spatial omics

Over the past decade, single-cell sequencing technologies have rapidly advanced in speed and cost-effectiveness. Currently, more than ten distinct commercial platforms are available for high-throughput single-cell data collection.[6] This technological progress has driven a remarkable expansion in single-cell RNA sequencing (scRNA-seq) research, with nearly 2,000 studies published to date.[7] The integration of scRNA-seq with AI has emerged as a cornerstone methodology for deciphering tumor heterogeneity. In pancreatic ductal adenocarcinoma (PDAC) research, spatial transcriptomics combined with single-cell sequencing revealed high expression of TNFRSF10A/TRAILR1 (death receptor) at the tumor-stromal interface, which drives immune escape via activation of pro-survival signaling. Based on this, researchers utilized the SELFormer deep learning (DL) model to perform virtual screening of drugs approved by the U.S. Food and Drug Administration (FDA) and found that the mechanistic target of rapamycin (mTOR) inhibitor temsirolimus enhances TRAILR1-mediated apoptotic pathways by downregulating cellular FLICE (FADD-like IL-1β-converting enzyme)-inhibitory protein, providing a novel targeted therapy strategy for PDAC through targeting death receptors.[8] Similarly, another PDAC study using a patient-derived xenograft model treated with gemcitabine led to the development of the scConGraph model. scRNA-seq analysis revealed upregulation of growth differentiation factor 15 (GDF15) in acquired resistant clones. Functional validation confirmed that inhibition of GDF15 restored tumor sensitivity to chemotherapy, establishing it as a therapeutic target.[9]

Visium spatial transcriptomics has been instrumental in mapping target interaction niches within TME. In a pan-cancer analysis, multiple machine learning approaches revealed lactate metabolism gradients and lactate dehydrogenase A (LDHA)-mediated immune suppression, where lactate accumulation inhibits T-cell infiltration. Clustered regularly interspaced short palindromic repeats (CRISPR) validation confirmed that LDHA knockout enhances anti-tumor immunity, driving the AI-constructed 84-gene LM.SIG signature for predicting resistance to immunotherapy. This signature has guided combination therapies targeting LDHA and anti- programmed death 1 (PD-1) drugs, currently undergoing preclinical studies.[10] In colorectal cancer, VisiumHD resolved spatially confined selenoprotein P and secreted phosphoprotein 1 macrophage subpopulations that drive immune escape through the NF-κB signaling pathway and extracellular matrix remodeling, respectively, providing new insights for preclinical development of macrophage-targeted immunotherapy.[11]

Co-detection by indexing (CODEX) multiplexed imaging further quantifies co-expression patterns of immune checkpoints at single-cell resolution. Using CODEX to analyze tumors from bladder cancer patients, it was found that $CDH12^+$ epithelial cells expressed programmed cell death ligand 1 (PD-L1) and PD-L2 and co-localized with $CD8^+$ T cells exhibiting an exhausted phenotype. This demonstrates that spatial information obtained through this technology can uncover the cellular basis for improved responses to immune checkpoint blockade.[12] Additionally, AI models trained on intercellular communication networks derived from patient tumor transcriptomes predict patient responses to immune checkpoint inhibitors in ST with over 80% accuracy, guiding ongoing clinical trials.[13] Meanwhile, a research team developed a strategy co-delivering vitamin D receptor ligand and chemokine C-X-C motif chemokine ligand 9 (CXCL9) via a nano-chaperone. Using CODEX to quantify PD-1/lymphocyte activation gene-3 (LAG-3) co-expression within CAF barriers, this approach significantly enhanced $CD8^+$ T cell infiltration and synergistically improved the therapeutic efficacy of anti-PD-1 and gemcitabine by reversing CAF activation status and establishing a CXCL9 gradient.[14]

AI-driven targeting of historically undruggable targets

The intersection of AI with structural biology and computational chemistry is revolutionizing research strategies for historically "undruggable" targets, opening new avenues for targeting key oncogenic proteins such as KRAS (Fig. 1). Mutations in KRAS exist in approximately 25% of human ST, and breakthroughs in targeting KRAS represent significant progress in cancer treatment. Recent advances demonstrate AI's capacity to overcome KRAS's smooth surface and minimal binding pockets through diverse strategies. For allosteric inhibitors, KRAS conformations predicted by AlphaFold2 combined with reinforcement learning (RL) enabled optimization of covalent compounds targeting the G12C mutation. This approach supported the development of drugs such as AMG510 (sotorasib) and MRTX849 (adagrasib). AMG510 became the first clinically approved drug targeting KRAS (G12C), indicated for non-small cell lung cancer (NSCLC).[15] Additionally, novel candidates such as glecirasib have been approved for KRAS G12C mutant NSCLC and pancreatic cancer, demonstrating promising clinical efficacy and manageable safety profiles.[16]

PROTAC molecular design typically involves three components: the warhead, linker, and E3 ligand. The design of the warhead and E3 ligand generally follows small-molecule drug design principles. However, linker design is more complex and challenging, as it critically influences PROTAC conformation and protein degradation efficiency. AI tools model and evaluate the POI-PROTAC-E3 ligase ternary complex structure, assisting or automatically generating the linker portion, greatly improving design efficiency and accuracy.[17] The DL model PROTAC-RL integrates the Transformer network and molecular dynamics to design BRD4 degraders with enhanced pharmacokinetic properties; these are currently in preclinical studies.[18] KT-333, a PROTAC targeting STAT3 via a von Hippel-Lindau tumor suppressor (VHL)-dependent mechanism, is in phase 1a/1b trials for various conditions including R/R B- and T-cell lymphomas, classical Hodgkin lymphoma, ST, and large granular lymphocytic-leukemia/T-cell prolymphocytic leukemia, exhibiting a 31.4% objective response rate with 51 patients enrolled.[19]

For molecular glues, generated surface pocket prediction models have enabled targeting of non-G12C KRAS mutants. One research team proposed a quantum-classical hybrid framework combining a quantum variational generative model and a long short-term memory network. After training, ISM061-018-2 exhibited superior binding potency to the target protein compared to other molecules and showed no significant nonspecific cytotoxicity at high concentrations.[20] MRT-2359, an oral GSPT1 molecular glue degrader designed by Monte Rosa using the QuEEN platform, recruits the CRBN E3 ligase to degrade KRAS. It demonstrates effective GSPT1 degradation and anti-tumor activity *in vitro* and *in vivo*, and is currently undergoing Phase I clinical trials.[21]

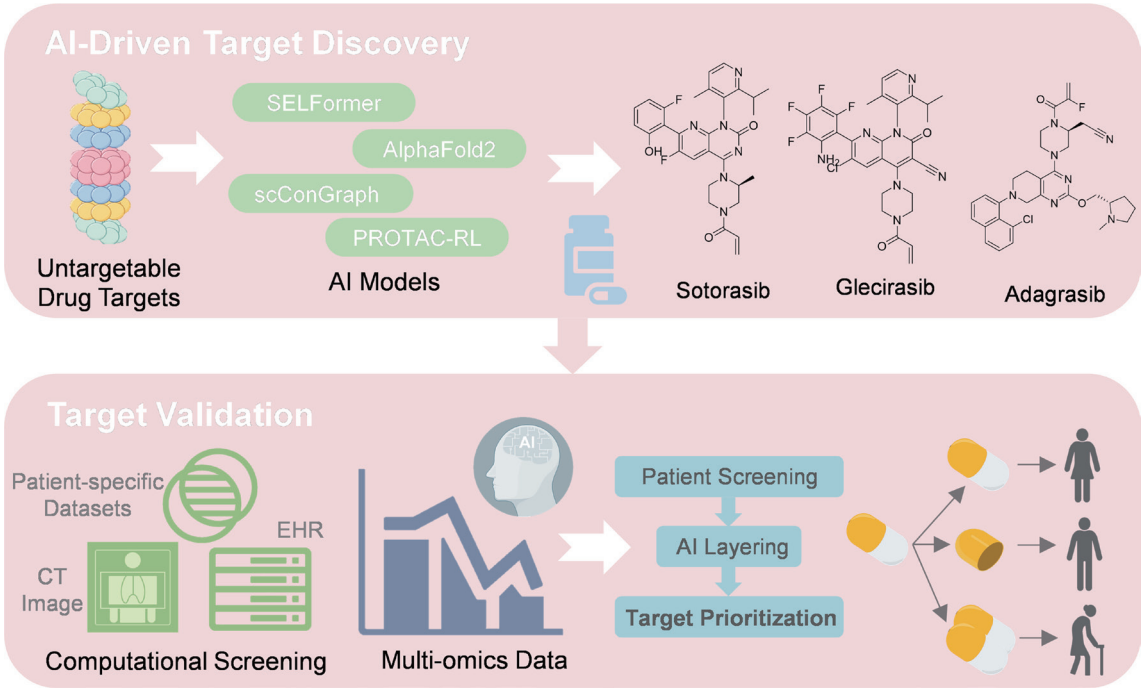

Fig. 1. Schematic of AI-driven target discovery. Integrating computational models (SELFormer, AlphaFold2, scConGraph, PROTAC-RL) with multi-omics data to validate historically undruggable targets (e.g., KRAS via sotorasib/glecirasib/adagrasib), enabling patient-specific screening and prioritization through clinical data (CT/EHR) and computational screening. AI, artificial intelligence; CT, computed tomography; EHR, electronic health record; KRAS, kirsten rat sarcoma viral oncogene homolog; PROTAC-RL, proteolysis-targeting chimeras (PROTAC)-reinforcement learning.

AI-optimized drug design

Small-molecule drugs

The integration of generative chemistry with AI has catalyzed a paradigm shift in drug discovery, enabling unprecedented efficiency in designing novel therapeutics.[22] The AI-driven target discovery platform PandaOmics and the generative AI drug design platform Chemistry42 successfully designed a novel ectonucleotide pyrophosphatase/phosphodiesterase 1 (ENPP1) small-molecule inhibitor, ISM5939, which can more effectively and safely modulate the STING pathway in preclinical models. This study provides evidence supporting ENPP1 as an innate immune checkpoint in STs. Additionally, this drug received clinical trial authorization from the FDA in November 2024 and is being developed as an immunotherapy candidate targeting ENPP1.[23] Similarly, with Chemistry42's assistance, ISM3091, a highly selective orally administered small-molecule inhibitor with "best-in-class" potential, was developed targeting USP1, a novel synthetic lethal target involved in DNA damage and repair pathways. From target identification to FDA approval took only 30 months, with fewer than 80 compounds synthesized, a 70% reduction compared to traditional timelines. ISM3091 is currently being evaluated in a Phase I clinical trial in patients with STs. Through AI prediction, Traf2 and non-catalytic region of tyrosine kinase adaptor protein 1 (NCK)-interacting kinase was successfully identified as a new target.[24] Using an AI-driven approach, INS018_055, a small-molecule Traf2 and NCK-interacting kinase inhibitor, was generated. This inhibitor demonstrates favorable pharmacological properties and anti-fibrotic activity in multiple organs following oral, inhalation, or topical administration and has been validated in Phase I clinical trials. This work spanned approximately 18 months from target discovery to preclinical candidate nomination, showcasing the capabilities of the generative AI-driven drug discovery pipeline.[25] To overcome epidermal growth factor receptor C797S-mediated drug resistance in NSCLC, multiple small-molecule inhibitors were designed and synthesized by integrating the whole quadratic effect model and the Lasso model. Virtual screening using these models identified four candidate compounds with their pharmacokinetic and toxicological properties.[26] Similarly, the Delete framework, based on RL, combines equivariant neural networks and structural modeling to design allosteric inhibitors. The leukocyte tyrosine kinase inhibitor CA-B-1 achieves nanomolar potency *in vivo* through optimization of protein-ligand interactions. This study highlights the transformative potential of structure-based molecular generation techniques, accelerating drug design within one and a half months.[27]

The integration of AI into drug design has dramatically accelerated early-stage discovery, particularly hit identification and toxicity prediction. Traditional hit discovery, which typically took six to twelve months via high-throughput screening, is now compressed to two to four weeks using generative AI platforms. Identifying cytotoxic compounds early is crucial, as cytotoxicity is a major cause of drug development failures, particularly in the preclinical stage. Traditional toxicity prediction methods have an accuracy of approximately 60%, while AI tools integrating multi-omics data and chemical properties can now exceed 85% accuracy. Machine learning-based toxicity prediction tools such as BoneToxPD and Cyto-Safe enhance organ-specific toxicity assessment by analyzing data from multiple databases, enabling early risk mitigation in environmental and clinical settings.[28,29] Meanwhile, the CURATE. AI platform analyzes small patient-specific datasets to dynamically adjust chemotherapy dosages. This method has been success-

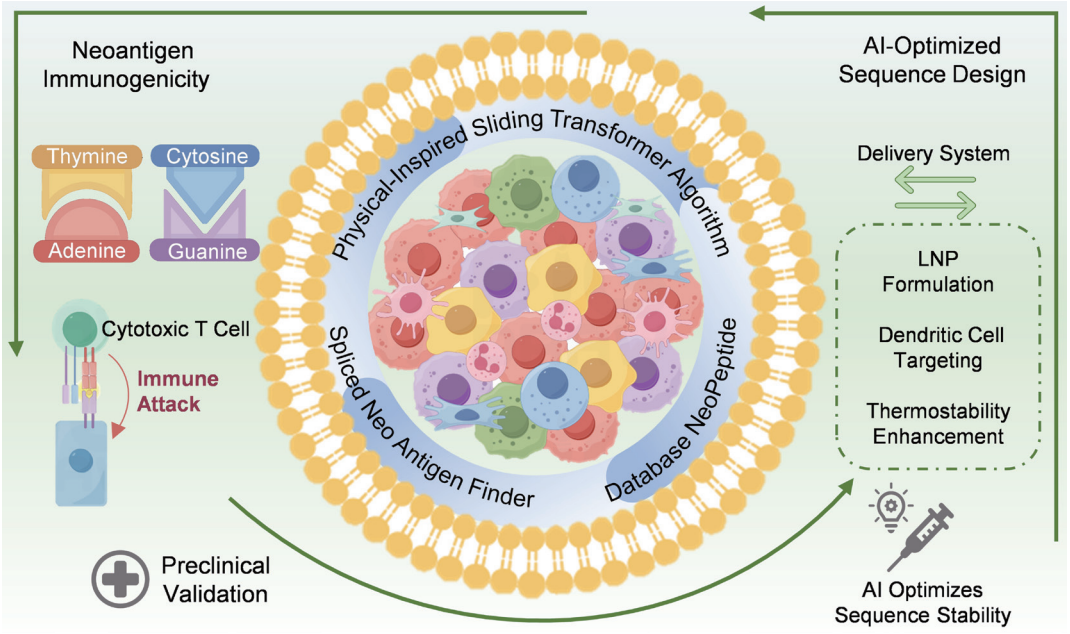

Fig. 2. Workflow for AI-optimized mRNA vaccine design. Predicting neoantigen immunogenicity to activate cytotoxic T cells, followed by AI-enhanced mRNA sequence stabilization and LNP formulation tuning for dendritic cell targeting, thermostability, and preclinical validation. AI, artificial intelligence; LNP, lipid nanoparticle; mRNA, messenger RNA.

fully adapted to the complex conditions of patients with advanced STs, achieving high treatment adherence and personalized therapeutic outcomes.[30]

Biologics

Antibody-drug conjugates (ADCs), which precisely deliver cytotoxic payloads to tumor cells, have emerged as "biological missiles" in cancer therapy.[31] However, ADC development faces multifaceted challenges, including target selection, molecular stability, and controlled toxin release.[32] Recently, AI technologies have markedly enhanced the design efficiency and precision of ADCs by optimizing three core elements: target selection, antibody engineering, and linker design. AI models predict antigen internalization efficiency by analyzing spatial transcriptomics and membrane protein dynamics, enabling prioritization of targets with optimal internalization rates while avoiding markers prone to drug resistance. Compared to traditional methods, this approach shortens target validation time by over 50%. This study accurately predicted the efficacy of next-generation ADC SHR-A1811 in neoadjuvant therapy for human epidermal growth factor receptor 2 (HER2)-positive breast cancer, potentially redefining treatment paradigms.[33] DL frameworks reduce immunogenicity by simulating humanized antibody sequences and paratope-epitope interactions. Lantern Pharma identified multiple potential payload molecules through its proprietary AI platform Response Algorithm for Drug positioning and Rescue (RADR®) and validated their antitumor activity in preclinical studies. The platform's ability to predict mutation-specific responses may enable more precise patient stratification in clinical trials, potentially improving success rates and reducing costs.[34] As a new generation of ADCs, Enhertu increases the drug-antibody ratio from 2–4 in traditional ADCs to 8 through unique structural design and AI-assisted optimization, significantly enhancing antitumor activity. It has achieved a breakthrough in clinical trials by improving the objective response rate by over 40% and has expanded its application to HER2 low/ultra-low expression populations, demonstrating significant potential for pan-cancer indications.[35]

Messenger RNA (mRNA) vaccines

Neoantigens, which are immunogenic peptides derived from tumor-specific mutations, serve as critical targets for activating T cell-mediated antitumor responses.[36] These neoantigens can function as effective targets for cancer vaccines to facilitate tumor rejection.[37] AI, through DL and machine learning models, has significantly enhanced neoantigen screening efficiency and vaccine design precision. Müller developed a machine learning-based approach integrating data from 120 cancer patients across the National Cancer Institute and Tumor Neoantigen Selection Alliance, achieving a 30% improvement in prediction accuracy of immunogenic neoantigens.[38] Feng *et al*.[39] introduced the Physical-Inspired Sliding Transformer algorithm, enabling precise prediction of TCR-antigen-HLA binding and neoantigen prioritization with over 90% accuracy. This method was validated in a prostate cancer clinical study, where physics-inspired sliding transformer (PISTE)-predicted neoantigens induced immune responses in 75% of patients.[39] Li *et al*. created the Spliced Neo Antigen Finder, a computational tool identifying shared spliced neoantigens in over 90% of melanoma patients, offering novel therapeutic targets.[40]

mRNA vaccines have emerged as a rapid, flexible, and scalable strategy in cancer immunology, eliciting robust and targeted immune responses. In mRNA vaccine design, AI further optimizes sequence encoding and delivery systems (Fig. 2). The LinearDesign algorithm leverages computational linguistics concepts to optimize mRNA stability and codon optimality concurrently, designing optimal mRNA sequences in as little as 11 m. This provides a rapid solution for developing mRNA-based vaccines and other therapeutics encoding proteins such as monoclonal antibodies and anticancer agents.[41] XGBoost, optimized through hyperparameter

tuning, can precisely quantify critical formulation characteristics including mRNA thermodynamic stability, lipid nanoparticle (LNP) encapsulation efficiency, and cellular delivery performance, enabling rational design of next-generation RNA therapeutics.[42] Recent applications demonstrate that integrating these technologies enhances critical mRNA-LNP performance metrics, including improved vaccine thermostability and tailored lipid formulations for efficient intracellular delivery to antigen-presenting cells such as dendritic cells.[43] Additionally, deep neural networks can optimize formulations to enhance cancer antigen presentation to immune cells within the TME, significantly improving mRNA-based cancer vaccine efficacy.[44] By integrating complex structural, chemical, and biological datasets, graph convolutional networks (GCN) provides a comprehensive computational framework to address challenges in mRNA-LNP vaccine development. These advances accelerate the creation of vaccines with precise cellular delivery mechanisms and enhanced immunogenicity, driving innovation in cancer immunotherapy and infectious disease prevention.[45]

Challenges in clinical translation

Three major validation gaps

The clinical translation of AI-driven oncology drugs faces three critical validation gaps, each demanding innovative computational solutions. The *in vitro–in vivo* gap remains a major bottleneck, as traditional cell lines do not adequately mimic the human TME. To address this, an organ-on-a-chip platform combined with federated learning has emerged. The InSMAR-chip technology enables high-throughput drug testing on patient-derived organoids from lung cancer patients, preserving tumor-stroma interactions and shortening the testing period to one week. This cutting-edge technology, combining chips with organoids, promises breakthroughs in predicting clinical drug responses for tumor organoids.[46] The GLI-SMARchip model combines lung cancer patient-derived organoids with peripheral immune cells to simulate systemic tumor-immune interactions. By evaluating the response index after immunotherapy, this platform found that the response index was highly correlated with actual clinical outcomes. This study is the first to reconstruct *in vitro* the systemic tumor immune components of lung cancer patients and simulate corresponding tumor immune response processes, overcoming limitations of traditional models in assessing systemic immunity.[47]

Racial sensitivity differences in drug efficacy require AI solutions tailored to specific populations. Adversarial debiasing algorithms have been used to address underrepresentation in genomic datasets. Traditional AI models are mostly trained on data from European and American populations, leading to significant prediction biases for groups such as those in Asia and Africa. Research has found that medical AI models may amplify racial disparities if they do not adjust for social determinants of health (e.g., insurance status, healthcare resource accessibility associated with postal codes).[48] Another study indicates that AI models can help tailor medications specifically for the African population by utilizing population-specific data, enabling safer, more effective treatments and reducing healthcare costs across the continent.[49]

In drug resistance prediction, static models fail to capture the evolutionary dynamics of tumors. Computational models simulating clonal dynamics under therapeutic pressure have shown promise. A novel disentangled synthesis network, DiSyn, effectively generalizes knowledge extracted from tumor cell line models to patient data, achieving state-of-the-art performance in drug response prediction.[50] The research team also constructed a dual-view DL model, JointSyn, to predict synergistic effects of drug combinations. Data showed this model outperformed existing state-of-the-art methods in predictive accuracy and robustness across benchmarks. Furthermore, the fine-tuned JointSyn improved generalization ability to predict new drug combinations and cancer samples with limited experimental data, demonstrating strong generalization performance.[51]

Data and algorithmic biases

AI-driven clinical translation of oncology drugs faces significant barriers as data and algorithmic biases undermine the generalizability of models across diverse populations and technical environments. Fundamental challenges include systematic underrepresentation of minority populations in training cohorts, which propagates through clinical predictions as degraded performance in ethnic subgroups and resource-limited settings, and unmitigated domain shifts when models trained in tertiary hospitals are deployed in community clinics.[52] Technical bias arises from artifacts in scRNA-seq, where tissue dissociation protocols can alter the characterization of cell states. This issue can be addressed through cross-validation with spatial transcriptomics, a method that maps gene expression within intact tissue architecture to confirm cell-cell interaction networks missed in dissociated cells.[11] Temporal bias occurs when training data excludes recent therapeutic targets (e.g., KRAS G12C inhibitors), causing models to overlook emerging resistance mechanisms. Dynamic incremental learning frameworks such as CODE-AE reduce prediction errors by up to 40% for novel targets like PROTAC degraders, through self-supervised adaptation that continuously integrates new clinical trial data.[53]

These issues are compounded by miscalibrated probability outputs that disproportionately misestimate risks for marginalized groups in high-stakes decisions such as survival prediction and treatment allocation. Effective mitigation requires embedding adversarial debiasing during model training to disentangle protected attributes and adopting federated domain adaptation techniques to align feature distributions across heterogeneous healthcare environments without centralizing sensitive data. Such multilayered interventions must be prioritized to prevent perpetuation of healthcare disparities through automated systems.[54]

Future perspective

Short-term breakthrough (two to three years)

The integration of multimodal foundation models with quantum computing holds great promise for overcoming key barriers in ST drug development. IBM's MoLFormer, a multimodal foundation model that integrates spatial transcriptomics, circulating tumor DNA dynamics, and histopathology, has demonstrated superior performance in predicting resistance to immunotherapy compared to single-modal models.[55] Simultaneously, quantum-accelerated PROTAC design is revolutionizing treatments for historically "undruggable" targets. The quantum-optimized B-cell lymphoma-extra-large degrader exemplifies this approach, showing a five-fold increase in degradation efficiency while reducing the risk of thrombocytopenia, thereby showcasing quantum computing's potential in generating experimentally validated drug candidates.[20]

Longitudinal transformation (five to ten years)

Looking ahead, AI is expected to enable a 72h precision oncol-

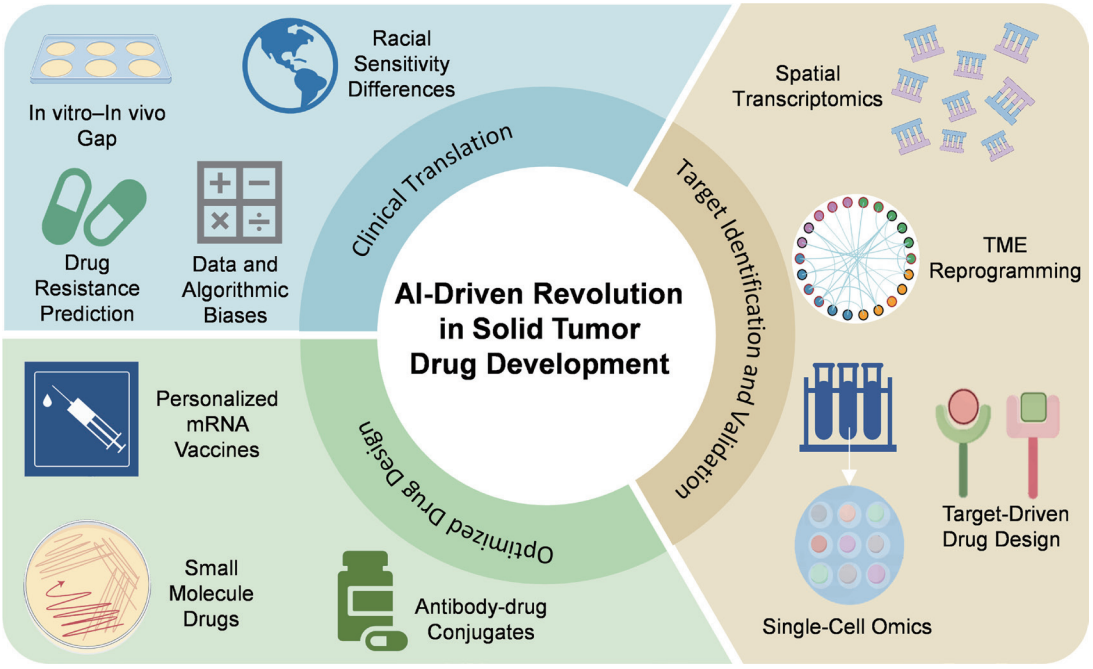

Fig. 3. Integrated AI-driven framework for solid tumor drug development. From target discovery (spatial transcriptomics/single-cell omics) and AI-optimized therapeutics (mRNA vaccines, ADCs, small molecules) to clinical translation—addressing drug resistance, data biases, and social sensitivity differences through TME reprogramming and personalized strategies, ultimately enabling precision oncology. ADCs, antibody-drug conjugates; AI, artificial intelligence; TME, tumor microenvironment.

ogy closed-loop system that integrates robotic biopsy, nanopore sequencing, federated learning-driven variant detection, and on-demand good manufacturing practice production of tumor-specific LNPs. This workflow has already proven feasible in patient-specific KRAS G12D inhibitor trials using pancreatic cancer organoids, completing the process from biopsy to infusion in just three days, thereby significantly enhancing treatment efficiency.[33] In parallel, AI-guided chimeric antigen receptor macrophages (CAR-M) are transforming immunotherapy. An mRNA-LNP delivery system has been developed for intraperitoneal programming of customized CAR-M *in vivo*, facilitating reprogramming of the TME. These advancements are deepening our understanding of CAR-M regulation and feedback mechanisms in ST treatment.[56]

Conclusions

AI has fundamentally reshaped the paradigm of cancer research and clinical oncology, demonstrating transformative potential across the entire continuum of cancer management, from early detection and target discovery to drug development and personalized treatment (as shown in Fig. 3). However, significant challenges remain in translating these advancements into clinical practice. Key issues include data and algorithmic bias, lack of model transparency, the validation gap between preclinical models and human physiology, and inequitable application across diverse populations. Addressing these challenges will require interdisciplinary collaboration, robust ethical frameworks, standardized evaluation protocols, and adaptive learning systems. Emerging technologies, such as quantum computing and multimodal foundation models, may further strengthen AI's role in oncology. Ultimately, the continued development of AI is indispensable to achieving truly personalized, effective, and equitable cancer treatment, translating scientific breakthroughs into tangible improvements in patient survival and quality of life.

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Conflict of interest

The manuscript was submitted during Dr. Jiang-Jiang Qin's term as an Associate Editor of *Oncology Advances*. The authors declare that they have no conflicts of interest regarding the publication of this research.

Author contributions

Study design, manuscript writing (YHL), critical revision, critical funding, and administration (JJQ). Both authors have made significant contributions to this study and have approved the final manuscript.

References

[1] Sinha S, Vegesna R, Mukherjee S, Kammula AV, Dhruba SR, Wu W,

et al. PERCEPTION predicts patient response and resistance to treatment using single-cell transcriptomics of their tumors. Nat Cancer 2024;5(6):938–952. doi:10.1038/s43018-024-00756-7, PMID:38637658.
[2] Zhao S, Wang D, Zhao H, Gong J, Zhang J, Fang W, *et al*. Time to raise the bar: Transition rate of phase 1 programs on anticancer drugs. Cancer Cell 2022;40(3):233–235. doi:10.1016/j.ccell.2022.01.007, PMID:35290782.
[3] Niu N, Shen X, Wang Z, Chen Y, Weng Y, Yu F, *et al*. Tumor cell-intrinsic epigenetic dysregulation shapes cancer-associated fibroblasts heterogeneity to metabolically support pancreatic cancer. Cancer Cell 2024;42(5):869–884.e9. doi:10.1016/j.ccell.2024.03.005, PMID:38579725.
[4] Casacuberta-Serra S, González-Larreategui Í, Capitán-Leo D, Soucek L. MYC and KRAS cooperation: from historical challenges to therapeutic opportunities in cancer. Signal Transduct Target Ther 2024;9(1):205. doi:10.1038/s41392-024-01907-z, PMID:39164274.
[5] Nagra NS, van der Veken L, Stanzl E, Champagne D, Devereson A, Macak M. The company landscape for artificial intelligence in large-molecule drug discovery. Nat Rev Drug Discov 2023;22(12):949–950. doi:10.1038/d41573-023-00139-0, PMID:37644185.
[6] Mereu E, Lafzi A, Moutinho C, Ziegenhain C, McCarthy DJ, Álvarez-Varela A, *et al*. Benchmarking single-cell RNA-sequencing protocols for cell atlas projects. Nat Biotechnol 2020;38(6):747–755. doi:10.1038/s41587-020-0469-4, PMID:32518403.
[7] Svensson V, da Veiga Beltrame E, Pachter L. A curated database reveals trends in single-cell transcriptomics. Database (Oxford) 2020;2020:baaa073. doi:10.1093/database/baaa073, PMID:33247933.
[8] Sharma S, Singh R, Kant S, Mishra MK. Integrating AI/ML and multi-omics approaches to investigate the role of TNFRSF10A/TRAILR1 and its potential targets in pancreatic cancer. Comput Biol Med 2025;193:110432. doi:10.1016/j.compbiomed.2025.110432, PMID:40424767.
[9] Li X, Liu Y, Zhou F, Guo W, Chen G, Tao J, *et al*. Decipher the single-cell level responses to chemotherapy in pancreatic ductal adenocarcinoma by a cross-time context graph model. Cancer Lett 2025;626:217751. doi:10.1016/j.canlet.2025.217751, PMID:40294840.
[10] Chen D, Liu P, Lu X, Li J, Qi D, Zang L, *et al*. Pan-cancer analysis implicates novel insights of lactate metabolism into immunotherapy response prediction and survival prognostication. J Exp Clin Cancer Res 2024;43(1):125. doi:10.1186/s13046-024-03042-7, PMID:38664705.
[11] Oliveira MF, Romero JP, Chung M, Williams SR, Gottscho AD, Gupta A, *et al*. High-definition spatial transcriptomic profiling of immune cell populations in colorectal cancer. Nat Genet 2025;57(6):1512–1523. doi:10.1038/s41588-025-02193-3, PMID:40473992.
[12] Kuswanto W, Nolan G, Lu G. Highly multiplexed spatial profiling with CODEX: bioinformatic analysis and application in human disease. Semin Immunopathol 2023;45(1):145–157. doi:10.1007/s00281-022-00974-0, PMID:36414691.
[13] Lee J, Kim D, Kong J, Ha D, Kim I, Park M, *et al*. Cell-cell communication network-based interpretable machine learning predicts cancer patient response to immune checkpoint inhibitors. Sci Adv 2024;10(5):eadj0785. doi:10.1126/sciadv.adj0785, PMID:38295179.
[14] Chen J, Ma F, Chen Y, Xu M, Zhang Y, Wang S, *et al*. Synergistic therapy for pancreatic cancer by deactivating cancer-associated fibroblasts and driving T-cell migration into tumor microenvironment using nanochaperone delivery system. Bioact Mater 2025;52:287–299. doi:10.1016/j.bioactmat.2025.06.010, PMID:40575327.
[15] Huang L, Guo Z, Wang F, Fu L. KRAS mutation: from undruggable to druggable in cancer. Signal Transduct Target Ther 2021;6(1):386. doi:10.1038/s41392-021-00780-4, PMID:34776511.
[16] Shi Y, Fang J, Xing L, Yao Y, Zhang J, Liu L, *et al*. Glecirasib in KRAS(G12C)-mutated nonsmall-cell lung cancer: a phase 2b trial. Nat Med 2025;31(3):894–900. doi:10.1038/s41591-024-03401-z, PMID:39762419.
[17] Ge J, Hsieh CY, Fang M, Sun H, Hou T. Development of PROTACs using computational approaches. Trends Pharmacol Sci 2024;45(12):1162–1174. doi:10.1016/j.tips.2024.10.006, PMID:39567313.
[18] Zheng S, Tan Y, Wang Z, Li C, Zhang Z, Sang X, *et al*. Accelerated rational PROTAC design via deep learning and molecular simulations. Nat Mach Intell 2022;4(9):739–748. doi:10.1038/s42256-022-00527-y.
[19] Feldman T, Marchi E, Smith SD, Olszewski AJ, Huen AO, Epstein-Peterson ZD, *et al*. Safety, Pharmacokinetics, Pharmacodynamics and Clinical Activity of KT-333, a Targeted Protein Degrader of STAT3, in Patients with Relapsed or Refractory Lymphomas, Leukemia, and Solid Tumors. Blood 2024;144(Suppl 1):4433. doi:10.1182/blood-2024-210301.
[20] Ghazi Vakili M, Gorgulla C, Snider J, Nigam A, Bezrukov D, Varoli D, *et al*. Quantum-computing-enhanced algorithm unveils potential KRAS inhibitors. Nat Biotechnol 2025. doi:10.1038/s41587-024-02526-3, PMID:39843581.
[21] Tiedt R, Schillo1 M, Osmont A, Bonenfant D, Narayan R, Wallace O, *et al*. Abstract 3294: The GSPT1 molecular glue degrader MRT-2359 is active against prostate cancer. Cancer Res 2024;84(6_Suppl):3294. doi:10.1158/1538-7445.AM2024-3294.
[22] Ocana A, Pandiella A, Privat C, Bravo I, Luengo-Oroz M, Amir E, *et al*. Integrating artificial intelligence in drug discovery and early drug development: a transformative approach. Biomark Res 2025;13(1):45. doi:10.1186/s40364-025-00758-2, PMID:40087789.
[23] Pu C, Cui H, Yu H, Cheng X, Zhang M, Qin L, *et al*. Oral ENPP1 inhibitor designed using generative AI as next generation STING modulator for solid tumors. Nat Commun 2025;16(1):4793. doi:10.1038/s41467-025-59874-0, PMID:40410143.
[24] Li Y, Wu J, Liu J, Qin L, Cai X, Qiao J, *et al*. Abstract 502: ISM3091, a novel selective USP1 inhibitor as a targeted anticancer therapy. Cancer Res 2023;83(7_Suppl):502. doi:10.1158/1538-7445.AM2023-502.
[25] Ren F, Aliper A, Chen J, Zhao H, Rao S, Kuppe C, *et al*. A small-molecule TNIK inhibitor targets fibrosis in preclinical and clinical models. Nat Biotechnol 2025;43(1):63–75. doi:10.1038/s41587-024-02143-0, PMID:38459338.
[26] Chang H, Zhang Z, Tian J, Bai T, Xiao Z, Wang D, *et al*. Machine Learning-Based Virtual Screening and Identification of the Fourth-Generation EGFR Inhibitors. ACS Omega 2024;9(2):2314–2324. doi:10.1021/acsomega.3c06225, PMID:38250375.
[27] Chen S, Zhang O, Jiang C, Zhao H, Zhang X, Chen M, *et al*. Deep lead optimization enveloped in protein pocket and its application in designing potent and selective ligands targeting LTK protein. Nat Mach Intell 2025;7(3):448–458. doi:10.1038/s42256-025-00997-w.
[28] Cui H, He Y, Wang Z, Liu K, Li W, Han W. Unveiling drug-induced osteotoxicity: A machine learning approach and webserver. J Hazard Mater 2025;492:138044. doi:10.1016/j.jhazmat.2025.138044, PMID:40158503.
[29] Feitosa FL, F Cabral V, Sanches IH, Silva-Mendonca S, Borba JVVB, Braga RC, *et al*. Cyto-Safe: A Machine Learning Tool for Early Identification of Cytotoxic Compounds in Drug Discovery. J Chem Inf Model 2024;64(24):9056–9062. doi:10.1021/acs.jcim.4c01811, PMID:39661446.
[30] Blasiak A, Truong ATL, Foo N, Tan LWJ, Kumar KS, Tan SB, *et al*. Personalized dose selection platform for patients with solid tumors in the PRECISE CURATE.AI feasibility trial. NPJ Precis Oncol 2025;9(1):49. doi:10.1038/s41698-025-00835-7, PMID:39984618.
[31] Fu Z, Li S, Han S, Shi C, Zhang Y. Antibody drug conjugate: the "biological missile" for targeted cancer therapy. Signal Transduct Target Ther 2022;7(1):93. doi:10.1038/s41392-022-00947-7, PMID:35318309.
[32] Dumontet C, Reichert JM, Senter PD, Lambert JM, Beck A. Antibody-drug conjugates come of age in oncology. Nat Rev Drug Discov 2023;22(8):641–661. doi:10.1038/s41573-023-00709-2, PMID:37308581.
[33] Ma D, Dai LJ, Wu XR, Liu CL, Zhao S, Zhang H, *et al*. Spatial determinants of antibody-drug conjugate SHR-A1811 efficacy in neoadjuvant treatment for HER2-positive breast cancer. Cancer Cell 2025;43(6):1061–1075.e7. doi:10.1016/j.ccell.2025.03.017, PMID:40215979.
[34] Kathad U, Biyani N, Peru Y Colón De Portugal RL, Zhou J, Kochat H, Bhatia K. Expanding the repertoire of Antibody Drug Conjugate (ADC) targets with improved tumor selectivity and range of potent payloads through in-silico analysis. PLoS One 2024;19(8):e0308604. doi:10.1371/journal.pone.0308604, PMID:39186767.
[35] Bartsch R, Pérez-García JM, Furtner J, Berghoff AS, Marhold M, Starzer AM, *et al*. Results of a patient-level pooled analysis of three studies of trastuzumab deruxtecan in HER2-positive breast cancer with active brain metastasis. ESMO Open 2025;10(1):104092.

doi:10.1016/j.esmoop.2024.104092, PMID:39754978.
[36] Xie N, Shen G, Gao W, Huang Z, Huang C, Fu L. Neoantigens: promising targets for cancer therapy. Signal Transduct Target Ther 2023;8(1):9. doi:10.1038/s41392-022-01270-x, PMID:36604431.
[37] Hu Z, Ott PA, Wu CJ. Towards personalized, tumour-specific, therapeutic vaccines for cancer. Nat Rev Immunol 2018;18(3):168–182. doi:10.1038/nri.2017.131, PMID:29226910.
[38] Müller M, Huber F, Arnaud M, Kraemer AI, Altimiras ER, Michaux J, *et al*. Machine learning methods and harmonized datasets improve immunogenic neoantigen prediction. Immunity 2023;56(11):2650–2663.e6. doi:10.1016/j.immuni.2023.09.002, PMID:37816353.
[39] Feng ZY, Chen JY, Hai YL, Pang XL, Zheng K, Xie CL, *et al*. Sliding-attention transformer neural architecture for predicting T cell receptor-antigen-human leucocyte antigen binding. Nat Mach Intell 2024;6(10):1216–1230. doi:10.1038/s42256-024-00901-y.
[40] Li G, Mahajan S, Ma S, Jeffery ED, Zhang X, Bhattacharjee A, *et al*. Splicing neoantigen discovery with SNAF reveals shared targets for cancer immunotherapy. Sci Transl Med 2024;16(730):eade2886. doi:10.1126/scitranslmed.ade2886, PMID:38232136.
[41] Zhang H, Zhang L, Lin A, Xu C, Li Z, Liu K, *et al*. Algorithm for optimized mRNA design improves stability and immunogenicity. Nature 2023;621(7978):396–403. doi:10.1038/s41586-023-06127-z, PMID:37130545.
[42] Maharjan R, Kim KH, Lee K, Han HK, Jeong SH. Machine learning-driven optimization of mRNA-lipid nanoparticle vaccine quality with XGBoost/Bayesian method and ensemble model approaches. J Pharm Anal 2024;14(11):100996. doi:10.1016/j.jpha.2024.100996, PMID:39759971.
[43] Castillo-Hair SM, Seelig G. Machine Learning for Designing Next-Generation mRNA Therapeutics. Acc Chem Res 2022;55(1):24–34. doi:10.1021/acs.accounts.1c00621, PMID:34905691.
[44] Raza A, Chohan TA, Buabeid M, Arafa EA, Chohan TA, Fatima B, *et al*. Deep learning in drug discovery: a futuristic modality to materialize the large datasets for cheminformatics. J Biomol Struct Dyn 2023;41(18):9177–9192. doi:10.1080/07391102.2022.2136244, PMID:36305195.
[45] Wang Z, Ding H, Pan L, Li J, Gong Z, Yu PS. From Cluster Assumption to Graph Convolution: Graph-Based Semi-Supervised Learning Revisited. IEEE Trans Neural Netw Learn Syst 2025;36(7):12952–12963. doi:10.1109/TNNLS.2024.3454710, PMID:39374279.
[46] Hu Y, Sui X, Song F, Li Y, Li K, Chen Z, *et al*. Lung cancer organoids analyzed on microwell arrays predict drug responses of patients within a week. Nat Commun 2021;12(1):2581. doi:10.1038/s41467-021-22676-1, PMID:33972544.
[47] Li K, Liu C, Sui X, Li C, Zhang T, Zhao T, *et al*. An organoid co-culture model for probing systemic anti-tumor immunity in lung cancer. Cell Stem Cell 2025;32(8):1218–1234.e7. doi:10.1016/j.stem.2025.05.011.
[48] Kidwai-Khan F, Wang R, Skanderson M, Brandt CA, Fodeh S, Womack JA. A roadmap to artificial intelligence (AI): Methods for designing and building AI ready data to promote fairness. J Biomed Inform 2024;154:104654. doi:10.1016/j.jbi.2024.104654, PMID:38740316.
[49] Turon G, Njoroge M, Mulubwa M, Duran-Frigola M, Chibale K. AI can help to tailor drugs for Africa - but Africans should lead the way. Nature 2024;628(8007):265–267. doi:10.1038/d41586-024-01001-y, PMID:38594395.
[50] Li K, Shen B, Feng F, Li X, Wang Y, Feng N, *et al*. A disentangled generative model for improved drug response prediction in patients via sample synthesis. J Pharm Anal 2025;15(6):101128. doi:10.1016/j.jpha.2024.101128, PMID:40678484.
[51] Li X, Shen B, Feng F, Li K, Tang Z, Ma L, *et al*. Dual-view jointly learning improves personalized drug synergy prediction. Bioinformatics 2024;40(10):btae604. doi:10.1093/bioinformatics/btae604, PMID:39423102.
[52] Ferryman K, Mackintosh M, Ghassemi M. Considering Biased Data as Informative Artifacts in AI-Assisted Health Care. N Engl J Med 2023;389(9):833–838. doi:10.1056/NEJMra2214964, PMID:37646680.
[53] He D, Liu Q, Wu Y, Xie L. A context-aware deconfounding autoencoder for robust prediction of personalized clinical drug response from cell-line compound screening. Nat Mach Intell 2022;4(10):879–892. doi:10.1038/s42256-022-00541-0, PMID:38895093.
[54] Swanson K, Wu E, Zhang A, Alizadeh AA, Zou J. From patterns to patients: Advances in clinical machine learning for cancer diagnosis, prognosis, and treatment. Cell 2023;186(8):1772–1791. doi:10.1016/j.cell.2023.01.035, PMID:36905928.
[55] Ross J, Belgodere B, Chenthamarakshan V, Padhi I, Mroueh Y, Das P. Large-scale chemical language representations capture molecular structure and properties. Nat Mach Intell 2022;4(12):1256–1264. doi:10.1038/s42256-022-00580-7.
[56] Klichinsky M, Ruella M, Shestova O, Lu XM, Best A, Zeeman M, *et al*. Human chimeric antigen receptor macrophages for cancer immunotherapy. Nat Biotechnol 2020;38(8):947–953. doi:10.1038/s41587-020-0462-y, PMID:32361713.