Acta Pharmaceutica Sinica B 2026;16(7):3994−3995

Chinese Pharmaceutical Association
Institute of Materia Medica, Chinese Academy of Medical Sciences

Acta Pharmaceutica Sinica B

www.elsevier.com/locate/apsb
www.sciencedirect.com

EDITORIAL

Editorial of special column on machine learning in drug discovery

The development of new drugs is inherently a lengthy, costly, and high-risk endeavor, with the path from initial discovery to regulatory approval often exceeding a decade. These challenges arise from the complexity of disease biology, stringent safety and efficacy requirements, and the frequently unpredictable pharmacological behavior of candidate compounds in humans. Drug discovery itself requires the screening of vast chemical libraries—often containing millions of compounds—to identify a handful of promising compounds, followed by extensive preclinical and clinical evaluation.

In recent years, artificial intelligence (AI) has emerged as a transformative force across the drug discovery and development continuum. In target identification, AI-driven analysis of multi-omics and biomedical datasets enables the discovery of novel disease-associated targets with greater accuracy and efficiency. During lead discovery and lead optimization, machine learning algorithms can predict target−compound interactions, prioritize promising candidates, and generate *de novo* chemical structures with desirable pharmacological properties. AI also facilitates the simulation of disease pathways and mechanistic modeling of drug responses, providing valuable biological insights and informing decision-making before costly clinical trials are initiated.

Beyond discovery, AI is increasingly influencing clinical development by improving trial design, accelerating patient recruitment, and enhancing the analysis of complex clinical datasets. Advanced algorithms can identify patient subpopulations most likely to benefit from specific therapies, supporting the advancement of precision and personalized medicine. Collectively, these capabilities are reshaping traditional pharmaceutical research and development workflows, improving efficiency, reducing attrition, and accelerating the delivery of innovative therapies to patients. This special column highlights the growing role of computational intelligence in transforming the future of drug discovery and development.

To establish the theoretical and methodological foundation of this paradigm shift, several researchers provide comprehensive reviews of recent AI-driven advances across a broad range of therapeutic modalities. Jiang and Wei's group[1] provides a comprehensive overview of recent progress in generative AI models for biomolecular sciences, demonstrating how architectures such as variational autoencoders, generative adversarial networks, and diffusion models are profoundly transforming *de novo* molecular design and bioinformatics. Li's group[2] discusses the convergence of AI with microfluidic platforms—spanning single-cell to organ-on-a-chip systems—and argues that this integration enables automated data analysis, complex pattern recognition, and intelligent experimental control, dramatically accelerating precision drug discovery. Li and Li's group[3] systematically map the methodological evolution of AI in biologic drug discovery, exploring its applications from decoding biological sequence grammar and enabling *de novo* molecular creation to engineering and optimizing novel biologics for clinical viability. Gao, He, Bo, and Zhou's group[4] examines how machine learning is reshaping nanomedicine research, demonstrating that data-driven models critically guide formulation design, pharmacokinetic prediction, and nanotoxicology assessment, steering the field toward more intelligent and precise development strategies.

Building on these theoretical frameworks, robust computational tools are essential for translating AI concepts into practical discovery workflows. Wang and Wu's group[5] developed TeroACT, a terpenoid bioactivity landscape and discovery platform driven by knowledge graphs and deep neural networks, which maps multi-dimensional biological relationships to facilitate disease prediction and anti-melanoma drug screening and discovery. Gao and Bai's group[6] established PhenoModel, a multimodal phenotypic drug design foundation model that employs a dual-space contrastive learning framework to bridge molecular structures with cellular morphological profiles, demonstrating high effectiveness in identifying novel potential inhibitors across multiple cancer cell lines. Liu and Yao's group[7] introduced FlowDock, a unified flow-based framework for flexible protein−ligand docking and binding affinity prediction that harnesses Bayesian flow

Peer review under the responsibility of Chinese Pharmaceutical Association and Institute of Materia Medica, Chinese Academy of Medical Sciences.

https://doi.org/10.1016/j.apsb.2026.06.018

networks to generate high-fidelity complex structures in latent space, achieving state-of-the-art performance in binding pose generation while substantially reducing computational costs. Furthermore, Heng, Hou, and Kang's group[8] presented ERAM, an accurate and task-agnostic model for enzymatic reaction modeling through multimodal relational learning, capturing both structural features and sequence information to markedly improve enzyme retrieval and substrate prediction capabilities.

The practical impact of these computational advances is ultimately demonstrated through the discovery and development of novel therapeutics. Cheng, Wang, Lu, and Chen's group[9] employed machine learning in combination with molecular hybridization to engineer selective PI3Kγ inhibitors, identifying a promising candidate capable of suppressing tumor cell proliferation while remodeling the immunosuppressive tumor microenvironment. Wang, Zhan, and Tang's group[10] reported the computation-driven discovery of novel chromone derivatives for triple-negative breast cancer, successfully identifying a highly potent mTOR-targeted inhibitor that triggers antitumor immunity and demonstrates robust *in vivo* efficacy. Zhao and Yu's group[11] integrated deep learning with structural biology to discover and optimize a minimalist conopeptide targeting the α7 nicotinic acetylcholine receptor, elucidating its unique binding modes and inhibitory mechanism. Li's group[12] explored the synergy between AI and multi-omics to synergistically prioritize bioactive compounds, support retrosynthesis, and unravel complex biosynthetic and regulatory networks. Lastly, Zhang, Zhu, and Gao's group[13] developed a cross-attention transformer framework (TransDIG) based on deep transfer learning to characterize the bioactive landscape of drug inactive ingredients (DIGs), successfully predicting and experimentally validating their unintended biological activities and offering critical new perspectives on drug formulation safety.

In conclusion, the contributions featured in this special column collectively underscore that machine learning has evolved from a supportive tool into a fundamental driver of innovation in drug discovery. Through the integration of advanced predictive algorithms, deep generative models, and rigorous experimental validation, AI is overcoming longstanding challenges in pharmaceutical research and development. These advances are accelerating the discovery of highly targeted, safe, and personalized therapeutics, ultimately reshaping the future of precision medicine and healthcare.

References

1. Jiang J, Li DX, Wang GL, Hayes N, Shi YZ, Qiu HH, et al. A review of recent advances in generative artificial intelligence models for biomolecular sciences. *Acta Pharm Sin B* 2026;**16**:1201−18.
2. Yin HY, Li ZY, Shen ZN, Wang SY, Du N, Cheng SB, et al. AI-integrated microfluidics for drug screening: from single cell to organ-on-a-chip. *Acta Pharm Sin B* 2026;**16**:1175−200.
3. Tang JX, Gong DH, Li HL, Li SL. Artificial intelligence in biologic drug discovery: a review of methodological evolution and therapeutic applications. *Acta Pharm Sin B* 2026;**16**:3996−4023.
4. Wei Z, Zhuo SJ, Zhang YX, Wu LL, Gao X, He S, et al. Machine learning reshapes the paradigm of nanomedicine research. *Acta Pharm Sin B* 2026;**16**:4024−50.
5. Shen XJ, Yan SJ, Kang X, Xu KW, Jian YX, Zeng T, et al. TeroACT: a terpenoid bioactivity landscape and discovery platform. *Acta Pharm Sin B* 2026;**16**:1233−49.
6. Wang SH, Han QL, Qin WC, Wang L, Yuan JH, Cai FY, et al. PhenoModel: a multimodal phenotypic drug design foundation model for discovering novel potential inhibitors of multiple cancer cells. *Acta Pharm Sin B* 2026;**16**:1219−32.
7. Li J, Lu RQ, Tan Y, Liang PY, Liu B, Gu SK, et al. FlowDock: a unified flow-based framework for flexible protein−ligand docking and binding affinity prediction. *Acta Pharm Sin B* 2026;**16**:4067−82.
8. Huang YS, Li LQ, Qian WJ, Yu JH, Zhao HF, Wang XR, et al. Accurate and task-agnostic modeling of enzymatic reactions through multimodal relational learning. *Acta Pharm Sin B* 2026;**16**:4051−66.
9. Zuo Y, Pu YR, Liu JN, Chen HY, Chen Y, Li XL, et al. Engineering selective PI3Kγ inhibitors with antitumor and immunomodulatory potentials. *Acta Pharm Sin B* 2026;**16**:4083−102.
10. Zhang JQ, Zhang NN, Ran YS, Yu QY, Lu JR, Chen R, et al. Computation-driven discovery of novel chromone derivatives for the treatment of triple-negative breast cancer *via* mTOR-targeted inhibition and triggering antitumor immunity. *Acta Pharm Sin B* 2026;**16**:4166−95.
11. Zhang JH, Yin ZJ, Li Y, Ge C, Zhang ZX, Yuan P, et al. Deep learning-driven discovery and mechanism of action study of a minimalist conopeptide targeting α7 nicotinic acetylcholine receptor. *Acta Pharm Sin B* 2026;**16**:4147−65.
12. Wang BY, Liu QY, Zhao WB, Zhang TY, Zhang DF, Sutcharitchan C, et al. Revolutionizing drug discovery from natural products: the roles of artificial intelligence and multi-omics in accelerating innovation. *Acta Pharm Sin B* 2026;**16**:4103−27.
13. Mou MJ, Zhang JS, Liu XG, Yang H, Fu TT, Zhang HB, et al. Unveiling the bioactive landscape of drug inactive ingredients (DIGs) using deep transfer learning. *Acta Pharm Sin B* 2026;**16**:4128−46.

Guobo Li[a,*], Changguo Zhan[b,*]

[a]*Department of Medicinal Chemistry, West China School of Pharmacy, Sichuan University, Chengdu 610041, China*

[b]*Molecular Modeling and Biopharmaceutical Center and Department of Pharmaceutical Sciences, College of Pharmacy, University of Kentucky, KY 40536, USA*

*Corresponding authors.

E-mail addresses: liguobo@scu.edu.cn (Guobo Li), zhan@uky.edu (Changguo Zhan).