



AI and Omics-Based Approaches in Predictive Toxicology: Shaping the Future of Drug Safety Assessment

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ABSTRACT

The latest rapid advancement of artificial intelligence (AI) and omics technologies has brought radical innovations into predictive toxicology. These techniques have the potential to strengthen the detection of toxicological risks at an early stage, reduce reliance on animal models, and make the drug discovery process more efficient and accurate. Artificial intelligence (AI), especially machine learning (ML), makes it possible to examine high-dimensional, sophisticated data produced by omics technologies such as genomics, transcriptomics, proteomics, and metabolomics. When combined, these technologies offer a more mechanistic and precise view of toxicity and assist in data-informed decision-making in pharmacology, environmental science, and regulatory toxicology. The integration of AI-omics systems into existing frameworks poses challenges for data quality, interpretability, ethics, and regulatory acceptance. This review critically discusses the promise and limitations of AI and omics in toxicology, with an emphasis on recent developments, challenges in implementation, and the future. Furthermore, it highlights the importance of interdisciplinary collaboration and standardized validation frameworks to ensure ethical, transparent, and reliable application of these technologies in real-world toxicological contexts.

Keywords: Artificial Intelligence, Omics, Predictive Toxicology, Machine Learning, Environmental Toxicology

INTRODUCTION

Toxicology has long been subjected to an empirical procedure such as animal experimentation and in vitro assays to determine the harmlessness and potential hazard of chemical substances and medicine. Despite being effective in the majority of cases, the methods are often time-consuming, ethically questionable, and restrained only to the recording of human-specific reactions. Toxicology has become better mechanistically understood with the introduction of omics technologies which allows the study of large-scale biological knowledge.

According to Lin and Chou, (2022), it is stated that, artificial intelligence, with machine learning and deep learning algorithms, has played a priceless role in dealing with the large amount of data produced by the omics platforms. AI and omics, together, have achieved a paradigmatic shift to mechanistic, personalized and predictive toxicology. According to Son et al. (2024), the methods could also help to increase significantly the quality of safety testing and reduce non-scientific testing of animals and may lead to a more in-depth understanding of biologic activities induced by chemicals.

Although it seems to be a good trend, these tools will not be absorbed easily due to a variety of obstacles. Limitations of uptake are due to data heterogeneity, non-standardization, ethical issues and resistance to the regulatory system. The following review attempts to critically consider the applications of AI and omics in toxicology, as they are used in practice in drug and environmental safety, and overall implications to regulatory science.

Literature Review

Role of Artificial Intelligence in Toxicology

Xu, et al., (2021), researched that AI in the form of machine learning and deep learning provide scientists with the ability to scan through the great bulk of data and identify trends that are not readily perceivable through the traditional methods of statistics. This is significant in toxicology due to extremely high dimensionality of bio response to toxicants. Wang et al. (2024) indicate how AI has enabled automated recognition of automated endpoint classification of toxicity by high-throughput zebrafish screens. The



models analyse movement patterns, morphological features, behavioural change using convolutional neural networks (CNNs) in an objectively faster and more efficient manner than the manual rating method. AI is more than phenotypic assessment. Thereby, Singh et al. (2024) demonstrated that AI could predict chemical carcinogenicity based on the assessment of chemically-caused genomic instability.

According to Zhang, et al., (2025), working with genomics information, they achieved very high rates of being able to distinguish between carcinogenic and non-carcinogenic molecules evidently that AI would be valuable at an early stage of hazard identification. Dose-response modelling, bioavailability prediction and modelling of exposure as appropriate to the long-term have also been carried out using AI.

These benefits notwithstanding, there are problems. Among its most important issues is the aspect of some deep learning models being a black box where a decision is not readily understood. They are not transparent and so it is difficult to confirm AI prediction particularly when concerns regulatory setting. In addition, AI models are very sensitive to the quality of input data. If the training data sets are biased, incomplete, or low-quality annotated, model predictions can be faulty. Accordingly, explainability, interpretability, and data harmonization are still key research and development areas of the future.

Omics Technologies in Toxicology

Bahl, et al., (2024), mentioned that the Omics technologies yield profound insights into the biological reactions of organisms to chemical stressors. Each omics field makes distinct contributions as genomics discloses DNA mutations; transcriptomics identifies gene expression changes; proteomics determines alterations in protein synthesis and signalling and metabolomics quantitates changes in metabolic pathways. These layers enable researchers to reveal the molecular basis of toxicity long before symptoms can be observed.

From Son et al. (2024), the incorporation of omics into toxicology has increased the detection of early biomarkers of toxicity. For instance, transcriptomic signatures can identify liver toxicity through sub-toxic doses, which opens the door to early intervention. Proteomic and metabolomic profiling has also unveiled interruption of cellular pathways, including oxidative stress and inflammation, following chemical exposure.

Efferth and Greten (2012) took these findings to the field of phytotherapeutically toxicology, proposing that omics can be used to assess the complex mixtures in classical herbal medicine. These treatments, frequently administered without standardized dosages or toxicity assessments, have risks that the traditional toxicology cannot adequately estimate.

Capone, et al., (2024), mentioned that Omics technologies, by revealing active and potentially toxic constituents at the molecular level, can bridge this void and facilitate the safe utilization of natural products. But the omics data are also of high dimensionality, and this also presents difficulties. Expertise and computational power are needed to preprocess, normalize, and interpret data. Biological noise, experimental variability, and interindividual variability may make it difficult to integrate data and decrease reproducibility. Furthermore, omics research also tends to have low sample numbers, which can undermine statistical power and generalizability.

AI-Omics Convergence: A Synergistic Framework

The AI and omics combination can potentially fill in the cracks between personal strategies. In the study of nanomaterials, Ahmad et al. (2021) present a very compelling argument based on how transcriptomic data have been applied in ML models to be able to predict probable toxicity. This synergy allowed identifying such toxicological signatures, which would have proved difficult to detect through conventional means. AI can help derive practical conclusions based on the multi-omics data by decreasing the dimensions of the data and discovering the relevant biological pathways.

According to Kumar and Metta, (2024), this synergy is particularly strong in discovery of adverse outcome pathways (AOPs), which present the passage of biological events with chemical exposure to its adverse effects. Automated construction and validation of AOPs with omics data may be supported by AI to support the development of mechanism-based toxicity models. Further, integrated models permit a prediction at the population level taking into account the diversity of the genome and, thereby, allow the field to prepare towards personalised toxicology.

Fullen, et al., (2025), mentioned that despite these progresses, however, the integration of multi-omics remains a novelty. Focusing on individual omics layers, the majority of the studies are not able to capture system-level interactions. Standardized pipelines and validation frameworks are also required which can provide guarantees for reproducibility as well as comparability across studies.



Efforts must be on constructing interpretable and transparent models that can be applied reliably in decision-making scenarios as the field matures.

AI and Omics in Environmental Toxicology

The use of AI and omics is not limited to drug development into environmental health. Wang et al. (2024) describe how environmental toxicology is ever more frequently using AI-powered models to evaluate how pollutants affect aquatic and terrestrial life. Zebrafish models, for example, enable the high-throughput screening of several hundred compounds, detecting behaviour, development, and metabolism abnormalities caused by environmental pollutants.

According to Maitre, et al., (2023), Omics data from environmental research have identified exposure and susceptibility biomarkers for pollutants such as heavy metals, pesticides, and endocrine-disrupting chemicals. AI models can categorize these pollutants according to toxicogenomic responses, allowing regulatory bodies to focus monitoring and remediation efforts.

However, the form of environmental data is more likely to be complex mixtures and a dynamic exposure scenario, making standardization difficult. The addition of confounding variable, e.g. temperature and pH contribute toward complexity in toxicity interpretation. In that regard, AI models will have to be trained and tested sensitively to take into account the ecological variation. Also, AI-omics platforms must be integrated with environmental monitoring systems, stakeholder involvement approaches, and risk communication systems to enable an approach to risk assessment as a whole.

Regulatory Science and Implementation Challenges

D'Adamo, et al., (2021), stated that the pace of translation of omics and AI technologies into regulation has been low despite the hope of science. The regulatory bodies such as the U.S. FDA, EPA and EMA continue to stress the use of traditional animal models and past control information.

Anklam et al. (2022) argue that such normative inertia, more than limited standards for omics data interpretation, is a primary hindrance to innovation.

In the case of machine learning models, insufficiency of the transparency and reproducibility limits the acceptance of such models with respect to regulation. Confidence in safety evaluations is of regulatory high demand but the model of AI tends to be sensor algorithms that are opaque. To overcome this, efforts in "explainable AI" (XAI) are picking up pace to generate interpretable outputs and traceable decision paths. Regulatory agencies are also investigating the application of hybrid models that integrate mechanistic knowledge with data-driven mechanisms to boost credibility across.

With omics, the hurdles are the absence of standard data formats, inadequate reference databases, and ambiguity regarding the clinical significance of any biomarkers found. Frameworks for validation, e.g., OECD's adverse outcome pathway (AOP) guidelines, provide a possible connection point, but more extensive international harmonization is needed. Notably, regulatory science itself must evolve to incorporate computational literacy, interdisciplinarity, and adaptive validation criteria in order to keep pace with rapidly changing tools.

Genotoxicity, Carcinogenicity, and AI-Based Risk Assessment

One of the particularly valuable areas of application is genotoxicity and carcinogenicity prediction. Alnasser (2025) comments on the limitations of conventional genotoxicity tests, such as high false-positive rates and poor mechanistic insights. Omics technologies, on the other hand, deliver rich information on DNA damage, repair pathways, and chromosomal changes, while AI tools are able to combine these signals to forecast long-term consequences.

Singh et al. (2024) propose a model in which genomic instability information are input to ML models to classify carcinogenic and non-carcinogenic chemicals. According to their findings, AI models that are trained using omics data can have higher specificity and sensitivity than standard assays. The approach shows promise to improve the current process of drug screening at an early stage and reduce wasteful testing.

Lin, et al., (2025), mentioned that the field must address basic questions concerning biological plausibility, cross species extrapolation, and threshold effect. To be relevant and reliable, AI models should not misalign with the toxicological principles and should be supported by empirical evidence to become valid. It must use independent datasets and real-world exposures to validate and have credible models.



Ethical and Social References

Jordan, (2024), stated that Omics and AI technologies intersections are also of essential importance to society and ethics. Omics data, in particular genomics, are strongly personalized and raise issues in terms of privacy, consent and the right to the data itself. Informed consent and safe data storage is crucial in carrying out researches. The open use of data and humanly open-ended algorithms are the basis of trust in AI models by the population.

According to Akter, et al., (2022), stated that the issues with the algorithmic bias also exist. The models developed using data reflective of smaller groups demonstrate improper learning on a population that is not wholly represented, which can further enhance health disparities. Moreover, there might be low degrees of human monitoring and moral reasoning in decisions as a result of automation of risk evaluation.

To curb these problems, guidelines of ethical considerations as well as the technological development in this regard are required. These must be data anonymization processes, all-inclusive data collection models and audit systems to identify bias and fairness in AI models. The core of the development of the responsible AI-omics research will be stakeholder consultations and interdisciplinary ethics boards.

Future Perspectives and Recommendations

Shaki, et al., (2024), mentioned that AI and omics technologies are definitely setting the future of toxicology. However, in order to achieve potential, several steps should be made. To start with, research should be done about measurements involving the integration of multi-omics (e.g. aligning genomics to metabolomics) to create models of toxicity. Second, there should be attempts to improve explainability and visibility of AI algorithms in order to be used in practice and the regulatory domain.

Third, international collaboration is needed to achieve compatibility of the data formats, validation controls and reporting standards. Fourth, the investment to build an infrastructure as well as train a group of individuals into developing and analysing AI-omics models needs to be done. Lastly, an ethical code is necessary to defend personal rights and guarantee a responsible innovation.

Discussions

Merging of artificial intelligence (AI) and omics sciences will usher a new revolutionary era in predictive toxicology to promote drug safety, eliminate animal testing, and provide mechanistic insights into the pathways of toxicity. Nevertheless, despite the fact that the studies throughout this area are all full of potential, the critical review finds loopholes in the methodology, implementation hurdles, and ethics subtleties that must be addressed in order to fully exploit these innovations.

As shown by Ahmad et al. (2021), machine learning may effectively integrate transcriptomics data to be used in the nanomaterial toxicity prediction. The technique performs better than conventional assays in terms of predictive capabilities by a significant margin. However, the article focuses more on a certain kind of nanomaterials, and it does not provide the external validation results, which is why the generalizability of their models remains questionable. Besides, their results are highly dependent on feature selection techniques, which, being quite potent, would result in bias in case the original dataset is not representative. The work is superior in proving feasibility but is not enough to provide a scalable framework that applies to all chemical types.

Son et al. (2024) provide a broader overview of omics and computational models, emphasizing how these tools advance preclinical screening. Their adding proteomics and metabolomics as biomarkers of subtle biological changes enhances early safety evaluations. The paper, however, views AI as an auxiliary, not an integrative, technology. The paper fails to take advantage of the possibility to critically examine how AI models may strengthen interpretability and fuse multi-omics layers. A more in-depth examination of standardization, cross-platform harmonization, or reproducibility issues would have made it more practically relevant.

Singh et al. (2024) make a convincing argument in favour of the use of AI to predict carcinogenicity from genomic instability signatures. Their application of supervised learning to high-throughput genomic data is a model that regulatory toxicology would do well to follow. The authors are remiss, though, in not discussing the performance of their model across populations of varying genetic backgrounds, arguably reducing its global utility. Also missing from their discussion is the necessity for transparency and explainability, strong impediments to regulatory uptake.

Alnasser (2025) returns to the theme of genotoxicity testing and presents a persuasive case for the substitution of conventional DNA damage assays with omics-guided AI strategies. Conceptually strong as the review is, its practical regulatory implementation roadmap is fuzzy. The paper does not provide an explanation as to how cross-jurisdictional validation may be possible, or how these



strategies harmonize with current OECD test guidelines. Nevertheless, the challenge to prevailing genotoxicity testing paradigms is persuasive and timely.

Wang et al. (2024) suggest AI-based zebrafish model screening for environmental toxicology, highlighting the potential to minimize observational bias and speed up testing using AI. The technique is novel, but the study sidesteps possible ecological heterogeneity and impact of confounders such as water temperature or pH to a great extent. Such variables may affect zebrafish reactions, which could bias AI predictions. The absence of multi-species testing also restricts the environmental generalizability of the study.

Anklam et al. (2022) write about the challenge of new technologies to regulatory science. Their review is futuristic and thorough but does not have a critical eye toward the institutional reluctance to adopt data-driven approaches. Some ethical issues, like data privacy in omics research, are not examined in depth.

Conclusion

Artificial intelligence and omics-based strategies are a paradigm-changing transition in toxicology. Combined, they hold the promise of quicker, more precise, and mechanistically informed risk assessments. They find application in pharmaceutical development, environmental health, and regulatory science, and they facilitate the objectives of personalized medicine, sustainable development, and ethical research. Yet, substantial challenges remain. Quality of data, transparency in models, ethical issues, and regulatory uptake need to be resolved by cooperative, multidisciplinary approaches. With proper safeguards and infrastructure, AI and omics technologies can lead the way toward a safer, more responsive, data-driven toxicology science.

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