TOXICOGENOMICS IN CONTEMPORARY HEALTHCARE: INTEGRATING MULTI-OMICS FOR PRECISION MEDICINE AND SAFER DRUG DEVELOPMENT

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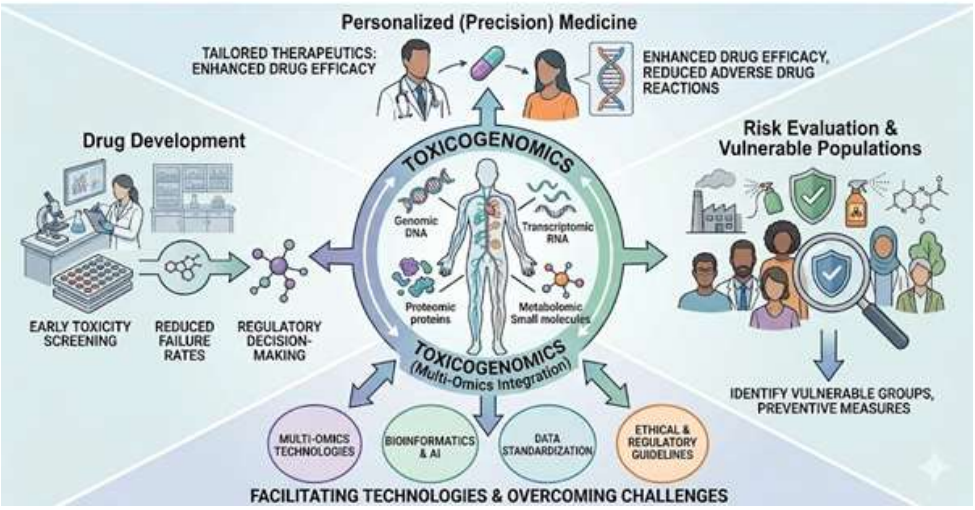
ABSTRACT

Toxicogenomics is a new interdisciplinary field that combines toxicology with the latest technological developments in genomics to learn the effects of genetic variation on personal reactions to environmental toxicants, chemicals, and pharmaceutical substances. Toxicogenomics can be used as a combination of genomic, transcriptomic, proteomic, and metabolomic data to give a global picture of what toxicity mechanisms involve at the molecular scale. This strategy helps to identify biomarkers to detect risk, adverse effects and prevent them at an early stage.Toxicogenomics integrating with personalized (precision) medicine is an important development in the field of contemporary healthcare. It allows personalized therapeutic approaches, which has been tailored to an individual genetic composition, surrounding exposures and lifestyle, which enhances drug efficacy and reduces adverse drug reactions. Applications of toxicogenomics in drug development improve early toxicity screening, improve drug failure rates, and aid regulatory decision-making.Moreover, the field is essential to environmental and occupational health as it helps to identify vulnerable groups and provide preventive measures. Multi-omics technologies, bioinformatics, and artificial intelligence have continued to make strides in their field, despite obstacles like data complexity, standardization, regulatory restrictions, and ethical issues surrounding the field of genomic data, which has only increased its capabilities. In general, toxicogenomics has the potential to revolutionize healthcare, as it will facilitate safer drug development, accurate risk evaluation, and tailor therapeutic regimens.

Keywords: Bioinformatics; Genomics; Personalised; Toxicity; Toxicogenomics



INTRODUCTION

Toxicogenomics is a new interdisciplinary field which involves the convergence of toxicology and high-tech genomic technologies to learn the role of genetic composition in the manner in which such an individual responds to environmental toxins, chemicals and pharmaceutical agents. Toxicogenomics allows defining the molecular pathways and gene expression patterns that are related to toxic exposure by combining the data of genomics, transcriptomics, proteomics, and metabolomics[1]. The method has given a mechanistic perspective of the toxicity on the molecular level which has made it very easy to discover biomarkers of early detection, risk assessment and prevention of adverse effects[2].

Also known as precision medicine, personalized medicine is a

medical revolution that seeks to customize medical care to the individual differences of an individual patient. It considers the genetic variability, environmental exposures and lifestyle factors to enhance the therapeutic effectiveness and reduce the drug reactions[3]. Genomic sequencing and bioinformatics have greatly enhanced the application of personalized medicine and now, clinicians are able to know the tendency of a disease and the response of a drug much better. The integration of toxicogenomics and personalized medicine is one of the major healthcare innovations in the contemporary healthcare domain[4]. Toxicogenomics will offer important information on inter-individual differences in toxic responses that is fundamental in the development of safer and effective therapeutic interventions. It aids in tailoring drug therapies by determining the genetic predispositions and molecular biomarkers of toxicity and aids in preventing detrimental exposures. Such integration is not only beneficial to the safety and efficacy of drugs but also helps to achieve better health outcomes in society due to the possibility to assess the risk more accurately and intervene more specifically[5,6].

Toxicogenomics can be used to prevent drug-related morbidity and mortality as it allows the identification of toxicity-related changes in gene expression and signaling pathways before the occurrence of adverse events. It can be useful in the case of personalized medicine to maximize the patient care and assists in estimating the susceptibility of an individual to adverse drug reactions and toxic exposures that will enable clinicians to select drugs and dose them depending on the genetic profile of a patient[7]. This does not only increase the results of the therapeutic process but also reduces the possibility of adverse side effects that is a significant factor in the traditional one size fits all treatment methods. In addition, toxicogenomics can be used to develop safer drugs through enhancement of preclinical and clinical risk assessment. Pharmaceutical industries can use toxicogenomic information to reveal the possible toxicities at an early stage of drug development, which minimizes the downfalls and delays in later stages. Besides, it also helps the regulatory agencies in making more effective decisions on drug approval and safety monitoring[8,9].

It also has a role in health field, particularly in the field of environmental and occupational health, as it aids in the improved evaluation of the environmental and occupational hazards and allows the application of preventive measures to ensure the health of susceptible groups. All in all, its incorporation into the healthcare systems will lead to better accuracy in diagnosis, treatment and prevention, which represents a big leap towards safer, more effective, and personalized medical care[10,11].

MOLECULAR BASIC AND MECHANISM OF TOXICOGENOMICS

Genetic Polymorphisms and Epigenetics

Genetic polymorphisms are some of the most vital factors of inter-individual differences in reaction to xenobiotics and therapeutic agents. Single nucleotide polymorphism (SNPs), deletions, insertions, and copy number variations in genes that encode drug-metabolizing enzymes, transporters, and receptors are variations that contribute greatly to the absorption, distribution, metabolism, and excretion (ADME) of the toxicsubstances[5,12]. As an example, the development of polymorphisms in the cytochrome P450 enzymes (e.g., CYP2D6, CYP2C9, and CYP3A4) may cause changes in the metabolic activity, which may either cause increased toxicity or decreased therapeutic efficacy. Equally, genetic differences in enzymes of detoxification like glutathione S-transferases (GSTs) can alter environmental toxin and carcinogen vulnerability[13].

Also significant in the regulation of gene expression but not the sequence of DNA are the epigenetic mechanisms, which include DNA methylation, histone-modifications and non-coding RNAs (including microRNAs). The exposure to toxicants can result in either reversible or hereditary epigenetic alterations, which can affect the disease susceptibility and toxic responses[14,15]. As an illustration, the chemical-induced carcinogenesis has been attributed to the aberrant patterns of DNA methylation, whereas the oxidative stress and inflammation have been attributed to the altered patterns of microRNA expression. These epigenetic changes can be useful mediators of environmental exposure and gene regulation, which helps in the variation in the outcome of toxicology[14].

Gene-Environment Interactions

Gene-environment interactions are dynamic relationships between the genetic composition of an individual and the external environmental factors in influencing the toxicological responses. The environmental exposures that include pollutants, food ingredients, drugs, and work-related chemicals may alter the expression of genes and cellular processes and produce a variety of biological effects based on the genetic composition of the affected person[16].

Toxicogenomics can be used to identify individual genes and molecular pathways which are variedly expressed when toxic agents are administered. As an example, people who have genetic variations that cause impairment on the pathways to detoxification could be more sensitive to the environmentally harmful substances like heavy metals, pesticides or air pollutants[17]. On the other hand, some genetic types can be resistance or adaptation to toxic exposures. This communication is especially applicable to multifactorial diseases like cancer, neurodegenerative conditions and metabolic syndromes[18], both genetic predisposition and environmental stimuli are important components of the disorder. Knowing about gene-environment interactions is critical to the risk assessment and the creation of special prevention measures. It enables distinguishing between the high-risk groups and facilitates the execution of individualized interventions that would help to minimize exposure and minimize the negative health outcomes[19].

Biomarkers of Toxicity

Biomarkers of toxicity are quantifiable biological markers, which indicate exposure to toxic substances, early biological effects, or vulnerability to adverse effects. Biomarkers in toxicogenomics can be based on gene expression changes, protein concentrations, or metabolite changes, and give information on the pathophysiology of toxicity[20]. The biomarkers can basically be categorized into three, including, biomarkers of exposure, biomarkers of effect, and biomarkers of susceptibility. Biomarker of exposure are used to show the presence of a toxicant, or its metabolites, in the body whereas biomarker of effect are used to show biochemical or physiological changes induced by exposure. Biomarkers of susceptibility, in their turn, refer to the people who are more susceptible to the toxic effects because of genetic or epigenetic factors[21].

The next-generation sequencing and microarrays have enabled the identification of new genomic biomarkers due to the advancements in high-throughput technologies. As an illustration, hepatotoxicity, nephrotoxicity, and carcinogenicity of different compounds have been predicted using specific signs of gene expression[10]. Moreover, the emerging indicators of toxicity and disease progression are circulating microRNAs and epigenetic marks which are non-invasive and sensitive. The clinical application of biomarkers data helps to improve the diagnosis in the early stages of the disease, better the risk assessment, and the creation of the personal therapeutic plan. Nonetheless, issues like validation, standardization and clinical translation are to be overcome in order to realize their potential in healthcare as depicted in Table 1[22].

S. No.	Component	Key Features	Examples / Significance	References
1.	Genetic Polymorphisms	Variations in DNA sequence that affect how genes work	SNPs, insertions and deletions that influence how drugs work	[22]
2.	Drug-Metabolizing Enzymes	Enzymes that help our body to process medicines and other substances	CYP2D6, CYP2C9 and CYP3A4 enzymes that affect how our body breaks down medicines	[23]
3.	Detoxification Enzymes	Enzymes that help get rid of stuff in our body	Glutathione S-transferases (GSTs) that help clean up toxins	[24]
4.	Epigenetic Mechanisms	Gene expression affecting DNA function	DNA methylation and histone modification that affect gene expression	[25]
5.	Non-coding RNAs	RNAs controlling genes work	microRNAs that are linked to stress and inflammation	[26]
6.	Gene–Environment Interaction	Interaction between genes and environmental exposures	Pollutants, drugs, dietary factors influencing gene expression	[27]

Table 1:Molecular Basis and Mechanisms of Toxicogenomics

TOXICOGENOMIC TECHNOLOGIES AND TOOLS

The data provided above indicates that the study includes omics technology or genomics (genomics, proteomics, metabolomics). The development of high-throughput technologies in the area of omics has greatly increased the toxicogenomics process through the ability to analyze a large-scale perspective of changes induced on the molecules by toxicants. Genomics is interested in the analysis of genetic variations and gene expression, next-generation sequencing (NGS) and RNA sequencing (RNA-seq) are some of the technologies used to identify polymorphisms and differentially expressed genes in response to toxics[28]. As an example, transcriptomic profiling has extensively been applied in the detection of early gene expression alterations associated with hepatotoxicity by drugs like acetaminophen, and has been used to predict liver damage early[29]. The large-scale study of proteins and their interactions, that is, proteomics, employs mass spectrometry (MS), two-dimensional gel electrophoresis (2D-GE), and protein microarrays, to identify biomarkers of toxicity and detect protein changes as a result of chemical-induced toxicity; proteomics studies have identified proteins of stress-response and inflammatory mediators of toxicity. These methods are further complemented by metabolomics which is the study of small-moleculemetabolites that are indicative of cell physiological conditions with such techniques as nuclear magnetic resonance (NMR) and liquid chromatography-mass spectrometry (LC-MS) usually being used to detect alterations in the metabolism of cells due to toxic exposure[30]. Combining these methods is referred to as multi-omics, which offers a systems-level view of the action of toxicity, and data sharing and biomarker discovery can be further facilitated by public databases and tools such as Comparative Toxicogenomics Database (CTD), Gene Expression Omnibus (GEO), and the Cancer Genome Atlas (TCGA), to complement the application of personalized medicine[31,32].

Bioinformatics and Data Analysis

Bioinformatics is relevant in the analysis and interpretation of large-scales of omics data. It entails pre-processing of data, normalization and statistical analysis to find significant changes in the molecules. Patterns and toxic responses are identified by computational means clustering, principal component analysis (PCA), hierarchical analysis, and machine learning algorithms) to classify the responses of the toxicants[33]. Gene annotation, molecular interaction network analysis and visualization are commonly performed with the help of tools such as BLAST, Cytoscape, and STRING. Kyoto Encyclopedia of Genes and Genomes (KEGG) and Gene Ontology (GO) are examples of platforms that aid in the identification of affected biological pathways as well as the molecular functions. The tools allow the researcher to correlate the changes in gene expression with a particular toxicity pathway, including oxidative stress, apoptosis, and inflammation as shown in Fig 1[34].

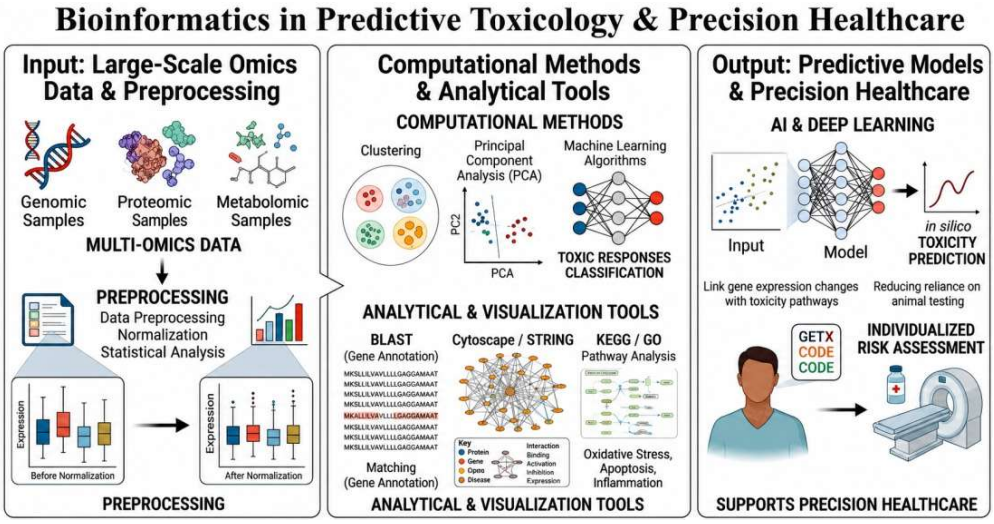


Fig.1 Bioinformatics in Predictive Toxicology and Precision Healthcare

Also, the predictive toxicology is actively implemented using artificial intelligence (AI) and deep learning models. These methods permit the in-silico models to be developed in order to predict toxicity, which decreases the use of animal tests and enhances the efficiency of drug discovery. The multi-omics data integration by bioinformatics will improve personalized risk and precision healthcare as shown in **Table 2.**

S. No.	Category	Technology/Tool	Key Features	Applications in Toxicogenomics	References
1.	Genomics Genomics	NGS, RNA-seq	High-throughput sequencing of DNA/RNA	[22Identification of genetic polymorphisms and gene expression changes]	[35]
		Transcriptomic Profiling	Analysis of differentially expressed genes	Early detection of hepatotoxicity (e.g., acetaminophen-induced)	[36]
3.	Proteomics	Mass Spectrometry (MS)	Protein identification and quantification	Detection of toxicity-related protein biomarkers	[37]
		2D-GE, Protein Microarrays	Protein separation and interaction analysis	Study of stress-response proteins and signaling pathways	[38]
5.	Metabolomics	NMR Spectroscopy	Non-destructive metabolite analysis	Detection of metabolic changes due to toxic exposure	[39]
7.	Multi-omics	Integrated Omics Approaches	Combines genomics, proteomics, metabolomics	Systems-level understanding of toxicity mechanisms	[40]

Table 2. Various Tools Used in Toxicogenomics

DRUG DEVELOPMENT AND PERSONALIZED MEDICINE

The predicted drug safety and adverse drug reactions rely on the predictive behavior of the drug data. Toxicogenomics is now a crucial instrument in improving the safety of the drug since it allows early identification of the molecular pathways of toxicity. In the process of drug development, the toxicity-related signatures in reaction to candidate compounds are identified by gene expression profiling and pathway analysis10. The indicators are molecular, which means that the adverse drug reactions (ADRs) can be predicted prior to clinical manifestation which minimizes the risk of drug failure in later stages41. The toxicogenomic biomarkers also have the ability to track the organ-specific toxicities, including hepatotoxicity, nephrotoxicity, and cardiotoxicity. This enables the pharmaceutical investigators to make changes or remove possibly hazardous substances at the early stages of the development process. Combining the toxicogenomic information with the standard toxicological testing enhances the quality of safety testing and aids in regulatory decision-making[42,43].

Tailored Therapy and Precision Medicine

Toxicogenomics enjoys the center stage in the development of personalized medicine through promoting personalized therapy. The differences in genetic makeup of enzymes that process drugs, drug transporters, and receptors play a significant role in the response and toxicity of different people to drugs[44]. Toxicogenomics can be used in analyzing these variations to predict the response of a patient on a particular drug[45]. The information will allow clinicians to select drugs, dose, and treatment regimens based on the genetic profile of the patient, which will enhance therapeutic efficacy and reduce drug side effects. Indicatively, the patients with a decreased metabolic rate might need lower doses of the drug because they will not be toxic, and others might need an increased amount of the drug to achieve maximum effectiveness. These individual strategies are especially helpful in the process of the treatment of complicated diseases like cancer when the variability of drug response is large[46,47].

Clinical and Environmental Applications

Toxicogenomics is gradually finding application in clinical practice to diagnose, prognose and monitor therapy of diseases. Molecular biomarkers discovered as a result of the toxicogenomic studies give information on the disease pathogenesis and aid in the early detection of the toxic effects48. Genomic and expression profiling of patients in oncology can be used to direct personalized therapies to enhance treatment effect and decrease unwarranted toxicity. Besides clinical, toxicogenomics is also used in the field of environmental and occupational health. It assists in knowing the biological effects of being exposed to the pollutants, chemicals and other environmental toxins[49,50]. Toxicogenomics helps in risk assessment and the formulation of preventive measures by determining the interaction between genes and the environment and the vulnerable populations. Moreover, it also assists in making decisions regarding the health of the population and this is because it helps in giving scientific support to set safety rules and limits of exposure. All in all, safety, efficacy, and precision of therapeutic and environmental environments are improved with the introduction of toxicogenomics into drug development and healthcare systemas shown in Fig 2[51].

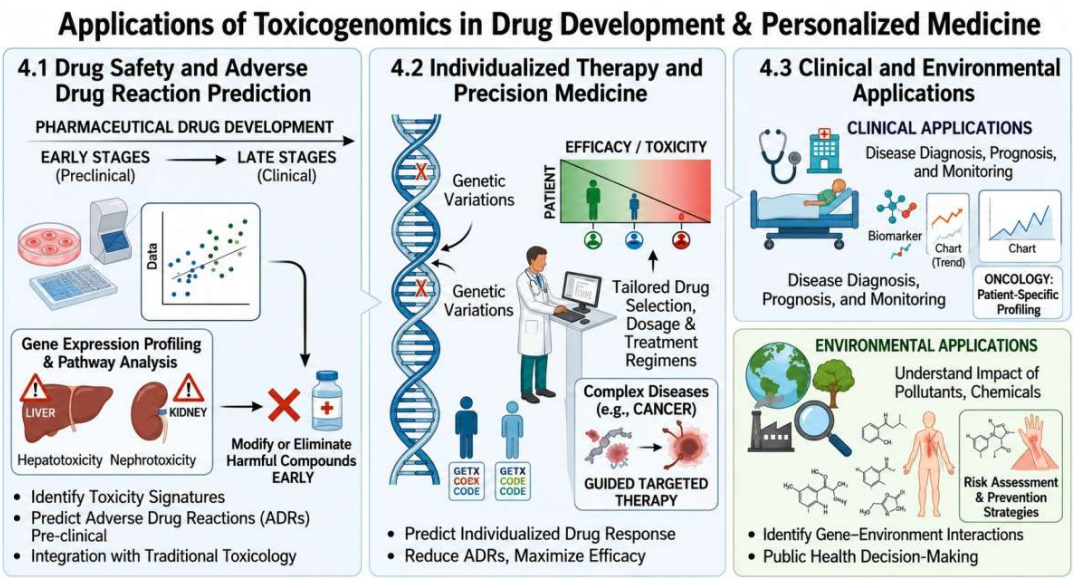


Fig 2: Applications of Toxicogenomics in Drug Development and Personalised Medicine

Technical and Regulatory Challenges

The use of toxicogenomics is also associated with certain technical and regulatory challenges despite the great progress in this field. To make omics data of large scale, the methods of sample collection, processing and analysis need to be standardized so as to achieve reproducibility and reliability52. The inconsistency in the studies may be caused by variability in the experimental platforms and methods of data interpretation. Regulatively, it is still complicated to use toxicogenomic information in the process of approving drugs. The regulatory authorities need strong validation of biomarkers and clear indication of the development of molecular changes to clinical outcomes[53]. Absence of globally agreed-upon principles on how to interpolate and implement toxicogenomic data may curtail its normal usage in decision-making. Nevertheless, there are continuous attempts to introduce these methods into the safety assessment systems[54].

Ethical and Data Privacy

Genomic data is an area of toxicogenomics that has brought a significant ethical issue especially in terms of privacy, confidentiality and informed consent. Genetic information is a very sensitive one and its abuse or unauthorized access can result in discrimination during the employment, insurance or even social spheres[55]. To safeguard the personal privacy of the individuals it is important to have safe storage and management of the genomic information. There should be clear policies on informed consent, which will enable the research participants and clinical practice subjects to know what they will do with their information. Alongside, ethical issues regarding the data sharing should also be considered in

order to achieve transparency but protect the rights of patients[56].

New Trends and Future Scope

The future of toxicogenomics is highly related to the development of the emerging technologies and interdisciplinary methods. The capability to analyze and predict toxicity through the integration of artificial intelligence (AI) and machine learning is becoming increasingly accurate with the integration of these two technologies. The multi-omics methods and systems biology are offering a more in-depth knowledge of the biological reaction to toxicants. In the future, the field of toxicogenomics in healthcare is likely to grow due to the production of more personalized risk assessment models and the creation of targeted drugs that are currently under the development of precision medicine. Moreover, the prediction of human-specific toxic responses is becoming better with the help of innovations like organ-on-chip models or platforms of high-throughput screening. With the further development of these technologies, toxicogenomics will probably become one of the key factors to enhance drug safety, optimise the pharmacologic interventions, and promote the well-being of the population, as it will help to apply more specific and personalised methods of disease prevention and treatment.

CONCLUSION

Toxicogenomics has become a revolution in which the application of toxicology is combined with the latest technology in the field of genomics to get a deeper insight into the molecular pathogenesis of toxicity and personal differences in reactivity to xenobiotics. It can be used to analyze the changes in gene, proteins and metabolites caused by toxic exposures in a comprehensive manner by integrating high-throughput omics technologies with bioinformatics tools. Toxicogenomics has been used in the drug development process to increase the predictive ability of the adverse drug reactions and also to augment the safety profile of the therapeutic agent.

Simultaneously, the introduction into the field of personalized medicine has helped to create personalized treatment plans, which maximize the effectiveness of the therapeutic process and reduce the adverse effects. Moreover, its impact on clinical and environmental health has led to improved disease pathophysiology, exposure hazards and susceptibility of the population. Nevertheless, in spite of the current issues associated with the complexity of the data, regulatory approval, and ethical issues, the current development of the multi-omics integration, artificial intelligence and novel experimental models still broaden the area of toxicogenomics. With the development of these technologies, toxicogenomics is likely to be at the center of precision healthcare, which will allow developing safer drugs, better patient outcomes, and more effective strategies to promote the overall health of the population. To sum it up, toxicogenomics is an essential step towards the unification of the molecular science with personalized medicine and has a lot of potential to transform the current healthcare to be more precise, predictive, and preventive.

REFERENCES

[1] A. V. Singh et al., "Integrative toxicogenomics: Advancing precision medicine and toxicology through artificial intelligence and OMICs technology," (in eng), Biomed Pharmacother, vol. 163, p. 114784, Jul 2023, doi: 10.1016/j.biopha.2023.114784.

[2] A. Urbaniak et al., "Experimental pharmacology in precision medicine," (in eng), Pharmacol Res Perspect, vol. 11, no. 6, p. e01147, Dec 2023, doi: 10.1002/prp2.1147.

[3] G. R. Trevor, Y. J. Lim, and B. L. Urquhart, "Pharmacometabolomics in Drug Disposition, Toxicity, and Precision Medicine," (in eng), Drug Metab Dispos, vol. 52, no. 11, pp. 1187-1195, Oct 16 2024, doi: 10.1124/dmd.123.001074.

[4] I. W. Chen, L. C. Chang, and K. C. Hung, "Non-pharmacological interventions improve sleep quality after cardiac surgery: Subgroup analysis based on care settings," (in eng), J Clin Nurs, vol. 33, no. 9, pp. 3790-3791, Aug 2024, doi: 10.1111/jocn.17153.

[5] M. J. Meier et al., "Progress in toxicogenomics to protect human health," (in eng), Nat Rev Genet, vol. 26, no. 2, pp. 105-122, Feb 2025, doi: 10.1038/s41576-024-00767-1.

[6] T. M. Polasek, "Pharmacogenomics - a minor rather than major force in clinical medicine," (in eng), Expert Rev Clin Pharmacol, vol. 17, no. 3, pp. 203-212, Mar 2024, doi: 10.1080/17512433.2024.2314726.

[7] P. W. Underwood and T. M. Pawlik, "Precision Medicine for Metastatic Colorectal Cancer: Where Do We Stand?," (in eng), Cancers (Basel), vol. 16, no. 22, Nov 19 2024, doi: 10.3390/cancers16223870.

[8] Z. He, X. Fu, Z. Xu, O. Alshargi, R. Rodríguez-Labrada,

and X. B. Zhong, "Editorial: Pharmacogenomics for improving drug safety and efficacy in cancer," (in eng), Front Pharmacol, vol. 16, p. 1649258, 2025, doi: 10.3389/fphar.2025.1649258.

[9] J. Faouzi et al., "Assessment of impacts of industrial effluents on physico-chemical and microbiological qualities of irrigation water of the Fez Rriver, Morocco," (in eng), Environ Geochem Health, vol. 45, no. 6, pp. 3933-3946, Jun 2023, doi: 10.1007/s10653-022-01449-9.

[10] A. R. Pandiri, S. S. Auerbach, J. L. Stevens, and E. A. G. Blomme, "Toxicogenomics Approaches to Address Toxicity and Carcinogenicity in the Liver," (in eng), Toxicol Pathol, vol. 51, no. 7-8, pp. 470-481, Oct 2023, doi: 10.1177/01926233241227942.

[11] Z. Dehghani, S. Ranjbar, F. Shahabinezhad, P. Sabouri, and A. Mohammadi Bardbori, "A toxicogenomics-based identification of potential mechanisms and signaling pathways involved in PFCs-induced cancer in human," (in eng), Toxicol Res (Camb), vol. 13, no. 5, p. tfae151, Oct 2024, doi: 10.1093/toxres/tfae151.

[12] Y. Zheng, M. Tang, Z. Deng, and P. Cai, "Genetic polymorphisms and platinum-induced hematological toxicity: a systematic review," (in eng), Front Pharmacol, vol. 15, p. 1445328, 2024, doi: 10.3389/fphar.2024.1445328.

[13] K. E. Caudle et al., "Standardizing CYP2D6 Genotype to Phenotype Translation: Consensus Recommendations from the Clinical Pharmacogenetics Implementation Consortium and Dutch Pharmacogenetics Working Group," (in eng), Clin Transl Sci, vol. 13, no. 1, pp. 116-124, Jan 2020, doi: 10.1111/cts.12692.

[14] E. R. Elkin, C. Higgins, M. T. Aung, and K. M. Bakulski, "Metals Exposures and DNA Methylation: Current Evidence and Future Directions," (in eng), Curr Environ Health Rep, vol. 9, no. 4, pp. 673-696, Dec 2022, doi: 10.1007/s40572-022-00382-4.

[15] A. Romanò, C. Pagiatakis, R. Gornati, G. Bernardini, and R. Papait, "Epigenetics: A link between toxicants and diseases," (in eng), iScience, vol. 28, no. 6, p. 112613, Jun 20 2025, doi: 10.1016/j.isci.2025.112613.

[16] M. Mititelu et al., "Assessing Heavy Metal Contamination in Food: Implications for Human Health and Environmental Safety," (in eng), Toxics, vol. 13, no. 5, Apr 23 2025, doi: 10.3390/toxics13050333.

[17] R. Gautam, E. Priyadarshini, A. K. Patel, and T. Arora, "Assessing the impact and mechanisms of environmental pollutants (heavy metals and pesticides) on the male reproductive system: a comprehensive review," (in eng), J Environ Sci Health C Toxicol Carcinog, vol. 42, no. 2, pp. 126-153, 2024, doi: 10.1080/26896583.2024.2302738.

[18] M. Nabi and N. Tabassum, "Role of Environmental Toxicants on Neurodegenerative Disorders," (in eng), Front Toxicol, vol. 4, p. 837579, 2022, doi: 10.3389/ftox.2022.837579.

[19] D. Sarigiannis et al., "Advancing translational exposomics: bridging genome, exposome and personalized medicine," (in eng), Hum Genomics, vol. 19, no. 1, p. 48, Apr 30 2025, doi: 10.1186/s40246-025-00761-6.

[20] B. Peng, Q. Dong, F. Li, T. Wang, X. Qiu, and T. Zhu, "A Systematic Review of Polycyclic Aromatic Hydrocarbon Derivatives: Occurrences, Levels, Biotransformation, Exposure Biomarkers, and Toxicity," (in eng), Environ Sci Technol, vol. 57, no. 41, pp. 15314-15335, Oct 17 2023, doi: 10.1021/acs.est.3c03170.

[21] M. K. Skinner, "Epigenetic biomarkers for disease susceptibility and preventative medicine," (in eng), Cell Metab, vol. 36, no. 2, pp. 263-277, Feb 6 2024, doi: 10.1016/j.cmet.2023.11.015.

[22] T. Wasilewski, W. Kamysz, and J. G?bicki, "AI-Assisted Detection of Biomarkers by Sensors and Biosensors for Early Diagnosis and Monitoring," (in eng), Biosensors (Basel), vol. 14, no. 7, Jul 22 2024, doi: 10.3390/bios14070356.

[23] B. Hossam Abdelmonem et al., "Decoding the Role of CYP450 Enzymes in Metabolism and Disease: A Comprehensive Review," (in eng), Biomedicines, vol. 12, no. 7, Jul 2 2024, doi: 10.3390/ biomedicines 12071467.

[24] L. Manthalkar, Ajazuddin, and S. Bhattacharya, "Evidence-based capacity of natural cytochrome enzyme inhibitors to increase the effectivity of antineoplastic drugs," (in eng), Discov Oncol, vol. 13, no. 1, p. 142, Dec 26 2022, doi: 10.1007/s12672-022-00605-y.

[25] L. M. De Plano, A. Saitta, S. Oddo, and A. Caccamo,

"Epigenetic Changes in Alzheimer's Disease: DNA Methylation and Histone Modification," (in eng), Cells, vol. 13, no. 8, Apr 21 2024, doi: 10.3390/cells13080719.

[26] K. Pierouli et al., "Long non?coding RNAs and microRNAs as regulators of stress in cancer (Review)," (in eng), Mol Med Rep, vol. 26, no. 6, Dec 2022, doi: 10.3892/mmr.2022.12878.

[27] S. J. Virolainen, A. VonHandorf, K. Viel, M. T. Weirauch, and L. C. Kottyan, "Gene-environment interactions and their impact on human health," (in eng), Genes Immun, vol. 24, no. 1, pp. 1-11, Feb 2023, doi: 10.1038/s41435-022-00192-6.

[28] R. Budhwar, A. Tripathi, and B. Mondal, "Modern Approaches in Genetic Toxicology Research: Insights from Next-Generation-Based RNA Sequencing," (in eng), Methods Mol Biol, vol. 2986, pp. 511-545, 2026, doi: 10.1007/978-1-0716-4976-3_24.

[29] Y. Wang et al., "miR-375 protects against acetaminophen-induced acute liver failure by orchestrating pharmacogene expression," (in eng), Mol Ther, vol. 33, no. 10, pp. 4874-4888, Oct 1 2025, doi: 10.1016/j.ymthe.2025.06.038.

[30] P. Dowling, D. Swandulla, and K. Ohlendieck, "Mass Spectrometry-Based Proteomic Technology and Its Application to Study Skeletal Muscle Cell Biology," (in eng), Cells, vol. 12, no. 21, Nov 1 2023, doi: 10.3390/cells12212560.

[31] D. S. Wishart et al., "NMR and Metabolomics-A Roadmap for the Future," (in eng), Metabolites, vol. 12, no. 8, Jul 23 2022, doi: 10.3390/metabo12080678.

[32] S. Vadapalli, H. Abdelhalim, S. Zeeshan, and Z. Ahmed, "Artificial intelligence and machine learning approaches using gene expression and variant data for personalized medicine," (in eng), Brief Bioinform, vol. 23, no. 5, Sep 20 2022, doi: 10.1093/bib/bbac191.

[33] G. Anandhi and M. Iyapparaja, "Systematic approaches to machine learning models for predicting pesticide toxicity," (in eng), Heliyon, vol. 10, no. 7, p. e28752, Apr 15 2024, doi: 10.1016/j.heliyon.2024.e28752.

[34] V. Y. Muley, "Functional Insights Through Gene Ontology, Disease Ontology, and KEGG Pathway Enrichment," (in eng), Methods Mol Biol, vol. 2927, pp. 75-98, 2025, doi: 10.1007/978-1-0716-4546-8_4.

[35] V. Vashisht, A. Vashisht, A. K. Mondal, J. Woodall, and R. Kolhe, "From Genomic Exploration to Personalized Treatment: Next-Generation Sequencing in Oncology," (in eng), Curr Issues Mol Biol, vol. 46, no. 11, pp. 12527-12549, Nov 6 2024, doi: 10.3390/cimb46110744.

[36] D. S. Umbaugh and H. Jaeschke, "Biomarker discovery in acetaminophen hepatotoxicity: leveraging single-cell transcriptomics and mechanistic insight," (in eng), Expert Rev Clin Pharmacol, vol. 17, no. 2, pp. 143-155, Jan-Jun 2024, doi: 10.1080/17512433.2024.2306219.

[37] J. Y. Lee, "The Principles and Applications of High-Throughput Sequencing Technologies," (in eng), Dev Reprod, vol. 27, no. 1, pp. 9-24, Apr 2023, doi: 10.12717/dr.2023.27.1.9.

[38] M. Santi and R. Madonna, "Unbiased serum proteomics in heart failure and associated pulmonary hypertension: From biomarkers discovery to precision medicine," (in eng), Eur J Clin Invest, vol. 56, no. 1, p. e70115, Jan 2026, doi: 10.1111/eci.70115.

[39] M. Jinks, E. C. Davies, B. A. Boughton, S. Lodge, and G. L. Maker, "(1)H NMR spectroscopic characterisation of HepG2 cells as a model metabolic system for toxicology studies," (in eng), Toxicol In Vitro, vol. 99, p. 105881, Aug 2024, doi: 10.1016/j.tiv.2024.105881.

[40] S. Kant, Deepika, and S. Roy, "Integrative Multi-Omics and Artificial Intelligence: A New Paradigm for Systems Biology," (in eng), Omics, vol. 29, no. 12, pp. 576-587, Dec 2025, doi: 10.1177/15578100251392371.

[41] K. Mokbel, M. Weedon, R. Daniels, V. Moye, and L. Jackson, "Evaluating genotype-treatment interactions for high-risk medications in British general practice: a retrospective cohort study using UK Biobank," (in eng), Br J Gen Pract, vol. 76, no. 763, pp. e163-e174, Feb 1 2026, doi: 10.3399/bjgp.2024.0806.

[42] R. Zhang, H. Wen, Z. Lin, B. Li, and X. Zhou, "Artificial Intelligence-Driven Drug Toxicity Prediction: Advances, Challenges, and Future Directions," (in eng), Toxics, vol. 13, no. 7, Jun 23 2025, doi: 10.3390/toxics13070525.

[43] Q. S. Sheng et al., "Revolutionizing toxicological risk assessment: integrative advances in new approach methodologies (NAMs) and precision toxicology," (in eng), Arch Toxicol, vol. 99, no. 12, pp. 4697-4707, Dec 2025, doi: 10.1007/s00204-025-04169-y.

[44] A. A. Bagdasaryan et al., "Pharmacogenetics of Drug Metabolism: The Role of Gene Polymorphism in the Regulation of Doxorubicin Safety and Efficacy," (in

eng), Cancers (Basel), vol. 14, no. 21, Nov 4 2022, doi: 10.3390/cancers14215436.

[45] M. B. Black et al., "Biological system considerations for application of toxicogenomics in next-generation risk assessment and predictive toxicology," (in eng), Toxicol In Vitro, vol. 80, p. 105311, Apr 2022, doi: 10.1016/j.tiv.2022.105311.

[46] J. Su, L. Yang, Z. Sun, and X. Zhan, "Personalized Drug Therapy: Innovative Concept Guided With Proteoformics," (in eng), Mol Cell Proteomics, vol. 23, no. 3, p. 100737, Mar 2024, doi: 10.1016/j.mcpro.2024.100737.

[47] D. Morales Castro, L. Dresser, J. Granton, and E. Fan, "Pharmacokinetic Alterations Associated with Critical Illness," (in eng), Clin Pharmacokinet, vol. 62, no. 2, pp. 209-220, Feb 2023, doi: 10.1007/s40262-023-01213-x.

[48] S. M. Alnasser, "Revisiting the approaches to DNA damage detection in genetic toxicology: insights and regulatory implications," (in eng), BioData Min, vol. 18, no. 1, p. 33, May 6 2025, doi: 10.1186/s13040-025-00447-8.

[49] H. M. Nafchi, H. Solatzadeh, E. Hajimaghsoudi, and E. Babakhanzadeh, "Personalizing cancer therapy: the role of pharmacogenetics in overcoming drug resistance and toxicity," (in eng), Mol Biol Rep, vol. 52, no. 1, p. 785, Aug 2 2025, doi: 10.1007/s11033-025-10887-4.

[50] L. A. Saarimäki et al., "Toxicogenomics Data for Chemical Safety Assessment and Development of New Approach Methodologies: An Adverse Outcome Pathway-Based Approach," (in eng), Adv Sci (Weinh), vol. 10, no. 2, p. e2203984, Jan 2023, doi: 10.1002/advs.202203984.

[51] T. Xiang et al., "Disinfection Byproducts Confirmed over 50 Years: Systematic Curation, Modes of Toxic Action, and Toxicogenomics," (in eng), Environ Sci Technol, vol. 59, no. 42, pp. 22334-22350, Oct 28 2025, doi: 10.1021/acs.est.4c13900.

[52] Á. González-Domínguez, N. Estanyol-Torres, C. Brunius, R. Landberg, and R. González-Domínguez, "QComics: Recommendations and Guidelines for Robust, Easily Implementable and Reportable Quality Control of Metabolomics Data," (in eng), Anal Chem, vol. 96, no. 3, pp. 1064-1072, Jan 23 2024, doi: 10.1021/acs.analchem.3c03660.

[53] J. Portugal, S. Mansilla, and B. Piña, "Perspectives on the Use of Toxicogenomics to Assess Environmental Risk," (in eng), Front Biosci (Landmark Ed), vol. 27, no. 10, p. 294, Oct 28 2022, doi: 10.31083/j.fbl2710294.

[54] T. Hartung and C. Rovida, "Mechanistic read-across comes of age: a comparative appraisal of EFSA 2025 guidance, ECHA's RAAF, and good read-across practice," (in eng), Front Toxicol, vol. 7, p. 1690491, 2025, doi: 10.3389/ftox.2025.1690491.

[55] A. S. Jwa and R. A. Poldrack, "Addressing privacy risk in neuroscience data: from data protection to harm prevention," (in eng), J Law Biosci, vol. 9, no. 2, p. lsac025, Jul-Dec 2022, doi: 10.1093/jlb/lsac025.

[56] I. García-García, E. Seco-Meseguer, A. M. Borobia, and A. J. Carcas-Sansuán, "Implementing pharmacogenetics in clinical trials: considerations about current methodological, ethical, and regulatory challenges," (in eng), Expert Rev Clin Pharmacol, vol. 17, no. 1, pp. 1-10, Jan 2024, doi: 10.1080/ 17512433. 2023.2293999.