Spring 2025, Volume 10, Issue 37 (39- 47) DOI: 10.22034/pmj.2025.2049550.1050

Personalized & Precision Medicine Journal

Homepage: www.pmjournal.ir

Pharmacogenomics: Unlocking the Future of Personalized Medicine and Precision Drug Development

Sanaz Khosravi Ghareh Cheh [1,*]

[1]Assistant doctor, Neurology Department, 93413 Cham, Germany.

ARTICLE INFO

Paper Type: Review Article

Submitted: 2025-01-22
Accepted: 2025-05-18

Keywords:
Pharmacogenomics
Personalized medicine
Drug development
Adverse drug reactions
Genomic profiling

Corresponding author:
Sanaz Khosravi Ghareh Cheh, Assistant doctor, Neurology Department, 93413 Cham, Germany. Email: sanazkhosravigharehcheh@gmail.com.

ABSTRACT

Pharmacogenomics is a relatively new subject that utilizes genomics and pharmacology to investigate how genetic variants influence individual responses to treatment with pharmaceuticals. A departure from the conventional "one-size-fits-all" treatment strategy is marked by the advent of pharmacogenomics, which makes it possible to tailor pharmacological regimens to the specific genetic profile of an individual. This domain can lead to significant improvements in pharmacological efficacy, reductions in adverse drug reactions (ADRs), and assistance in developing drugs that are both safe and effective for a wide range of conditions. The purpose of this study is to investigate the prospective results of pharmacogenomics, with a particular emphasis on its function in the process of drug development and its incorporation into personalized medicine. The purpose of this study is to investigate the genetic characteristics that influence the metabolism, efficacy, and toxicity of drugs, as well as to investigate the regulatory framework that is associated with pharmacogenomics testing. This paper summarizes the key genes related to pharmacogenomic responses and discusses the possible challenges in using them in practice, along with the expected advancements in this field of study.

How to Cite this Article:
S. Khosravi Ghareh Cheh . "Pharmacogenomics: Unlocking the Future of Personalized Medicine and Precision Drug Development" Personalized & Precision Medicine Journal, Vol. 10, no. 37, pp. 39- 47

INTRODUCTION

The field of pharmacogenomics is a relatively new field that combines genomics and pharmacology to shed light on the relationship between genetic variation and drug response (1). The human genome has a large number of genetic variants, each of which has the potential to affect how an individual reacts to drugs. There is a correlation between these genetic polymorphisms and the metabolism of drugs, the efficiency of treatments, and the likelihood of adverse drug reactions (ADRs) (2). Through the incorporation of pharmacogenomics data into clinical decision-making, medical professionals can optimize pharmaceutical therapy for specific patients, thereby tailoring therapies to the genetic profiles of those patients (3).

The conventional approach to the production of medications has generally adhered to a uniform strategy, in which a single medicine or dose regimen is delivered to all patients (4). This technique does not take into account genetic variances, which can have a significant impact on an individual's response to medication and how those medications are metabolized (5). Genetic differences in enzymes that help break down drugs, like cytochrome P450, can lead to either weaker effects of the medication or unwanted side effects in patients (6). The goal of personalized medicine, which is driven by pharmacogenomics, is to address these issues by ensuring that patients receive the most effective pharmaceuticals at the optimal dosages that are matched to their genetic profiles (7). When genetic features that influence medication responsiveness are identified, it has the potential to change both the

process of developing new drugs and clinical practice. Pharmacogenomics testing is the examination of several genetic markers to shed light on the ways in which the genetic profile of an individual can influence the effectiveness of a specific pharmacological treatment (8). Practitioners can give more accurate therapies that reduce risks and boost therapeutic effectiveness when they incorporate this knowledge into common practices in the healthcare industry (9). The purpose of this review article is to provide a comprehensive analysis of pharmacogenomics, with the main objective being to investigate its significance in the process of drug discovery, its incorporation into personalized medicine, and its potential for future developments. During the course of the project, genetic mechanisms that influence pharmaceutical responses will be investigated, critical pharmacogenomics genes will be investigated, and clinical applications in a variety of therapeutic spaces will be evaluated (8).

The Role of Pharmacogenomics in Drug Development

Pharmacogenomics is essential in contemporary drug research, informing the creation of safer and more efficacious drugs (9). Integrating genetic data into medication discovery and development enables pharmaceutical companies to enhance the identification of appropriate therapeutic candidates and diminish the probability of clinical trial failures (10). This section examines the influence of pharmacogenomics on drug development, especially regarding personalized medicine.

The Shift toward Personalized Medicine

Pharmacogenomics is essential in contemporary drug research, informing the creation of safer and more efficacious drugs. Bringing genetic information into the process of finding and developing new medications helps drug companies better identify suitable treatment options and reduce the chances of clinical trial failures (10). This section examines the influence of pharmacogenomics on drug development, especially regarding personalized medicine.

The Shift toward Personalized Medicine

Traditionally, the objective of medication research was to construct therapies that would serve the broader population, frequently neglecting the genetic variability within patients (11). The universal approach has resulted in various issues, such as poor treatments for certain individuals and adverse drug reactions (ADRs) in others. Pharmacogenomics mitigates these constraints by facilitating personalized treatment options, wherein medications and dosages are customized according to an individual's distinct genetic profile (12). The transition to customized medicine signifies a fundamental transformation in the delivery of healthcare. Pharmacogenomics testing offers critical insights into how an individual's genetic composition influences their reaction to specific medications (13). For instance, certain genetic differences can cause a medicine to either digest too quickly, limiting its effectiveness, or too slowly, increasing the risk of toxicity (14). By finding genetic differences early, doctors can make better choices about which drugs to use and how much to give, reducing the chances of bad reactions and improving treatment results. With the increasing prevalence of customized medicine, the emphasis is transitioning from creating pharmaceuticals for the "average" patient to formulating drugs tailored to the "specific" patient, informed by their genetic data (15). This change can significantly improve how well medications work and how safe they are, while also reducing healthcare costs by avoiding the guesswork in prescribing drugs.

Early Integration of Pharmacogenomics in Drug Discovery

Pharmacogenomics is influencing clinical decision-making and is being included in the initial phases of drug research (16). In conventional drug development, researchers frequently perform clinical trials with diverse patient populations, presuming that the majority will exhibit comparable responses to a specific medication (17). This assumption can lead to drug candidates being unsuccessful in later stages of clinical development, particularly when the drugs cause unwanted side effects or do not work well for certain groups of patients (18). Pharmacogenomics addresses this difficulty by facilitating the identification of genetic biomarkers that might forecast a patient's reaction to a certain medication. Genomic profiling of patients participating in clinical trials can identify genetic variants that influence medication metabolism, efficacy, and safety (19). By incorporating pharmacogenomics data early in drug discovery, researchers can predict which patient populations are most likely to benefit from a treatment, helping to influence clinical trial design and lower the likelihood of trial failure (20).

The early incorporation of pharmacogenomics in drug research facilitates the identification of genetic variables that lead to treatment resistance. Certain alterations in cancer cells can render malignancies resistant to chemotherapy agents (21). By detecting these mutations promptly, researchers can create tailored treatments that particularly tackle these genetic modifications, enhancing therapeutic efficacy (22).

Regulatory Approaches to Pharmacogenomics

With the expansion of pharmacogenomics, regulatory bodies such as the U.S. Food and Drug Administration (FDA) have acknowledged its

significance in enhancing drug safety and efficacy (23). The FDA has actively formulated guidelines for integrating pharmacogenomics data into drug labeling, assisting doctors in making educated decisions based on patients' genetic profiles (24).

Pharmacogenomics labeling offers critical insights into the influence of genetic differences on medication metabolism, efficacy, and safety. Pharmacogenomics labels on medications such as warfarin, clopidogrel, and abacavir assist healthcare providers in determining the suitable treatment for patients according to their genetic profiles (25). Patients with certain genetic variations in the CYP2C9 gene might need a lower dose of warfarin because they are more sensitive to it, while those with a variant of the HLA-B gene may be at a higher risk of allergic reactions to abacavir (26). Regulatory agencies are helping to include genetic testing in regular medical practice by supporting pharmacogenomics labels for more and more medications. This regulatory initiative is facilitating the wider implementation of pharmacogenomics, which could substantially enhance patient outcomes (27).

Genetic Variation and Drug Response

Genetic variations are a crucial factor in determining individual responses to drugs. These changes can happen in genes that affect how drugs are processed, moved around, and how they interact with their targets, leading to differences in how well medications work, their safety, and their potential side effects (28). This section will look at the two main parts of pharmacogenomics pharmacokinetics and pharmacodynamics and explore how genetic differences affect how people respond to medications.

Pharmacokinetics: How Genetic Variation Affects Drug Metabolism

Pharmacokinetics refers to the mechanisms via which the body absorbs, distributes, metabolizes, and eliminates medicines (29). Genetic differences that impact how the body handles medications are mostly found in genes responsible for drug-metabolizing enzymes, drug transporters, and drug receptors. Genetic differences can lead to markedly divergent medication reactions among individuals, influencing the efficacy and safety of treatment (30). Pharmacogenomics has facilitated the comprehension of these differences and their implications for personalized medicine, allowing for the customization of medication therapy according to an individual's genetic profile (31). Genetic factors that influence pharmacokinetics can change how quickly a drug is absorbed, how it spreads in the body, how fast the liver breaks it down, and how well the kidneys remove it (32). These processes eventually govern the drug concentration at the site of action, which influences the therapeutic impact and the probability of adverse drug reactions (33).

Cytochrome P450 (CYP450) Enzyme Family

The cytochrome P450 (CYP450) enzyme family is a key component in pharmacokinetics. These enzymes facilitate the oxidative metabolism of several therapeutic pharmaceuticals, encompassing those utilized for pain management, depression, cardiovascular disorders, and cancer treatment. The CYP450 family plays a crucial role in phase I drug metabolism, wherein pharmaceuticals undergo modification via oxidation, reduction, or hydrolysis, typically enhancing their water solubility and facilitating excretion (34). Genetic differences in these enzymes can result in modified drug metabolism, which influences individual drug processing. The CYP450 enzyme family comprises more than 50 members, with CYP2D6, CYP2C19, CYP2C9, and CYP3A4 being the most clinically significant. The functional differences in these enzymes can lead to diverse metabolic phenotypes, from poor metabolizers (PMs) to ultra-rapid metabolizers (UMs) (35).

CYP2D6: A Key Enzyme in Drug Metabolism

CYP2D6 is one of the most extensively researched enzymes in pharmacogenomics, metabolizing a diverse range of medications, such as antidepressants, antipsychotics, opioids, and beta-blockers (36). Genetic variation in the CYP2D6 gene can produce varying amounts of enzyme activity, resulting in diverse metabolic phenotypes:
• Suboptimal Metabolizers (SMs): People with less active or non-working versions of the CYP2D6 gene may have lower enzyme activity, which can make it harder for their bodies to process certain drugs. Individuals with poor metabolisms of CYP2D6 substrates may exhibit elevated plasma drug concentrations, thereby heightening the risk of drug toxicity and adverse consequences (37). A poor metabolizer of codeine may not achieve pain relief since CYP2D6 is essential for turning codeine into its active metabolite, morphine. Antidepressants such as paroxetine and fluoxetine may accumulate in the body, resulting in adverse effects including nausea, dizziness, and serotonin syndrome (38).

•Ultra-Rapid Metabolizers (UMs) are people who have multiple copies of the CYP2D6 gene or specific gene variations that make them process drugs much faster. These individuals demonstrate heightened enzyme activity, resulting in accelerated drug metabolism (39). Consequently, therapeutic medication concentrations may remain unattainable due to rapid metabolism and clearance of the drug. People who metabolize tamoxifen very quickly might not get enough benefits from the treatment because the drug needs to be

changed into its active form (endoxifen) by CYP2D6 to work effectively against cancer (40). Due to the considerable heterogeneity in CYP2D6 activity, pharmacogenomics testing can assist doctors in identifying suitable medication and dosage for each patient. Testing for CYP2D6 can help doctors select the right antidepressant or opioid and adjust the dosages based on a person's metabolism, which can reduce the chances of side effects or not getting enough benefit from the treatment (41).

CYP2C19 and Clopidogrel

A notable instance of genetic diversity in drug metabolism pertains to the CYP2C19 enzyme, essential for the metabolism of clopidogrel, an antiplatelet medication commonly employed to avert blood clots, particularly in individuals at risk of myocardial infarctions and cerebrovascular accidents (42). Clopidogrel requires metabolism by the CYP2C19 enzyme to become active and produce its therapeutict (43).
• Diminished Enzyme Activity: Individuals possessing specific CYP2C19 polymorphisms, notably the CYP2C19*2 allele, demonstrate diminished or nonexistent CYP2C19 activity (44). This leads to a reduced activation rate of clopidogrel, making the medication less efficacious in preventing thrombotic incidents such as myocardial infarctions or cerebrovascular accidents. These individuals may face an elevated risk of cardiovascular events owing to the insufficient antiplatelet efficacy of clopidogrel (45). Conversely, individuals possessing the CYP2C19*17 allele, associated with heightened enzyme activity, may encounter an augmented antiplatelet impact, hence elevating the chance of bleeding problems (46).

To lower these risks, it is recommended to test for CYP2C19 gene variations, particularly for people using clopidogrel after being diagnosed with coronary artery disease or having a stent placed (47). For those with weak metabolism, prasugrel or ticagrelor may be safer and more effective than drugs that depend on CYP2C19 for activation. Pharmacogenomic testing can detect these patients and inform therapy choices to enhance clinical outcomes (48).

CYP2C9 and Warfarin

A key example of how drug processing can vary among individuals involves the enzyme CYP2C9, which is important for breaking down warfarin, a commonly used blood thinner. Warfarin is utilized to avert deep vein thrombosis, pulmonary embolism, and stroke in individuals with atrial fibrillation (49). The dosage of warfarin requires meticulous monitoring due to its narrow therapeutic index; insufficient dosage may result in thrombosis, while excessive dosage may cause hemorrhage. Variations in CYP2C9 markedly influence warfarin metabolism and the necessarye (50).

•CYP2C9 Polymorphisms: Individuals possessing specific polymorphisms in the CYP2C9 gene, such as CYP2C9*2 or CYP2C9*3, exhibit a reduced metabolic rate for warfarin compared to individuals with the wild-type allele. These individuals necessitate reduced doses of warfarin to attain the equivalent therapeutic benefit. Failure to appropriately regulate the dosage increases the risk of bleeding problems resulting from excessive anticoagulation (51).

•VKORC1 and Warfarin Sensitivity: In addition to CYP2C9, the VKORC1 gene, which makes the enzyme vitamin K epoxide reductase (52), also plays a role in how sensitive someone is to warfarin. Genetic differences in VKORC1 can also change how much warfarin a person needs, so testing for both CYP2C9 and VKORC1 can help doctors give the right amount of warfarin for better treatment. Pharmacogenomic-guided dosing helps doctors reduce risks by adjusting warfarin treatment based on each person's genetic makeup (53).

Pharmacodynamics: Genetic Variation in Drug Targets

Pharmacodynamics pertains to the effects of medicine on the body, and genetic differences in drug targets can markedly change drug response. Pharmacological targets include receptors, enzymes, and transporters, and genetic differences in these targets can cause variations in how well medications work and their side effects (54). Variations in the human leukocyte antigen (HLA) gene family are linked to hypersensitivity reactions to specific medications. A prominent example is the correlation between the HLA-B57:01 allele and abacavir hypersensitivity. Individuals possessing this genetic variant face a markedly elevated risk of severe allergic reactions to abacavir, an antiretroviral treatment for HIV. Conducting pharmacogenomic testing for HLA-B57:01 before initiating abacavir medication can avert potentially fatals (55).

Another instance of genetic diversity in pharmacological targets is the occurrence of mutations in the EGFR gene in non-small cell lung carcinoma (NSCLC). These mutations correlate with a heightened probability of responding to EGFR-targeted treatments, such as erlotinib or gefitinib. Genetic testing for EGFR mutations helps doctors identify patients who are most likely to benefit from specific treatments, improving results and reducing side effects (56).

Key Genes in Pharmacogenomics

Numerous essential genes significantly impact pharmacogenomics by affecting medication metabolism, effectiveness, and safety. This section offers a summary of key genes in pharmacogenomics and their influence on drug therapy (57).

Cytochrome P450 Enzymes

The CYP450 enzyme family facilitates the metabolism of numerous frequently prescribed medications. Changes in the CYP450 genes can lead to differences in how drugs are processed in the body, which can affect how well they work and their side effects. CYP2D6, CYP2C19, and CYP2C9 are among the most extensively researched CYP450 enzymes. Variations in the CYP2D6 gene influence the metabolism of medications such as tamoxifen, utilized in breast cancer therapy (58). Certain individuals possess genetic variations that render them inefficient metabolizers of tamoxifen, hence diminishing the drug's efficacy (59). Pharmacogenomics testing for CYP2D6 can help doctors decide how to give tamoxifen and other drugs that are processed by this enzyme.

The CYP2C19 gene has a role in the metabolism of clopidogrel, an anticoagulant drug. Genetic testing for CYP2C19 differences can help determine if a patient will benefit from clopidogrel or if they should consider other treatment options (60).

Human Leukocyte Antigen (HLA) Genes

The HLA genes play a crucial role in the immune system's capacity to identify and react to exogenous stimuli. Polymorphisms in specific HLA alleles correlate with drug-induced hypersensitivity reactions (61). The HLA-B57:01 variant is linked to a higher chance of having a bad reaction to abacavir, while the HLA-B15:02 allele is associated with a greater risk of Stevens-Johnson syndrome in people taking carbamazepine (62). Genetic testing for these alleles can assist doctors in refraining from providing medications that may elicit adverse reactions in vulnerable patients (63).

VKORC1 and TPMT

The VKORC1 gene plays a role in the metabolism of warfarin, a widely utilized anticoagulant. Variations in VKORC1 can influence a patient's susceptibility to warfarin, necessitating modifications to the medicine dosage. The TPMT gene affects how the body processes thiopurines, which are a type of medicine used to suppress the immune system in treating leukemia and autoimmune diseases. Genetic testing for VKORC1 and TPMT helps doctors adjust medicine dosages and avoid problems that can happen from taking too much or too little (64).

Applications of Pharmacogenomics in Therapeutic Areas

Pharmacogenomics has important implications for various therapeutic domains, including cardiology, cancer, and psychiatry. This section examines the application of pharmacogenomics across several medical disciplines to enhance patient outcomes (65).

Cardiovascular Drugs

Cardiovascular disorders rank among the foremost causes of mortality globally, and pharmacogenomics possesses the capacity to revolutionize the treatment of these ailments. Numerous cardiovascular medications, including anticoagulants and antiplatelet medicines, are processed by enzymes belonging to the CYP450 family (66). Genetic testing for CYP2C19 polymorphisms can inform the administration of clopidogrel in people predisposed to cardiovascular events. Similarly, pharmacogenomics testing for warfarin sensitivity can assist in establishing the correct dosage for individual patients, minimizing the risk of bleeding problems (66).

Oncology

In oncology, pharmacogenomics facilitates the creation of targeted medicines tailored to specific genetic abnormalities in malignancies. Targeted therapies, such as trastuzumab for breast cancer with HER2 positivity and erlotinib for non-small cell lung cancer with EGFR mutations, offer more effective treatments with fewer side effects compared to traditional chemotherapy (67). Integrating pharmacogenomics testing into standard cancer care enables physicians to discern patients who are most likely to benefit from these medications, hence enhancing survival rates and minimizing needless treatments (68).

Psychiatry

Pharmacogenomics is increasingly essential in the management of psychiatric diseases. Numerous psychiatric medicines, such as antidepressants and antipsychotics, are processed by CYP450 enzymes. Genetic testing for polymorphisms in these enzymes helps identify the most effective drugs for particular patients, hence enhancing therapeutic success and minimizing adverse effects (69). Moreover, pharmacogenomic testing can forecast drug resistance in psychiatric patients, facilitating more precise treatment methods.

Challenges and Future Directions

Pharmacogenomics holds exciting promise, but its wider application in clinical practice requires the resolution of a few challenges. The problems encompass the expense of genetic testing, the absence of defined protocols for pharmacogenomics testing, and ethical issues about genetic privacy (70).

Ethical Considerations and Access to Pharmacogenomics Testing

The growing accessibility of pharmacogenomics tests prompts significant ethical concerns about genetic privacy and the risk of hereditary discrimination. Securing patients' genetic information and ensuring its

responsible utilization will be key to building public trust and promoting the extensive implementation of pharmacogenomics testing (71).

Cost and Accessibility

Even though the cost of genetic testing has significantly decreased over the past few years, it continues to be a barrier to its widespread adoption. Access to these treatments is made more difficult for a significant number of people because there are no standardized reimbursement regulations in place for pharmacogenomics testing (72).

Future Directions in Pharmacogenomics

The future of pharmacogenomics relies on improving our understanding of how genes influence how people respond to medications, making genetic testing more accessible, and better using pharmacogenomic information in medical decisions. With the advancement of genetic technology, pharmacogenomics will increasingly influence personalized medicine and precision drug development (73).

CONCLUSION

Pharmacogenomics indicates a paradigm change in drug discovery and clinical treatment. By integrating genetic data, pharmacogenomics is revolutionizing pharmaceutical therapy. The process facilitates more precise and effective therapies, hence improving patient outcomes by enhancing efficacy and reducing side effects. Pharmacogenomics possesses the capacity to transform medicine development and patient treatment worldwide, and this capacity is expanding as research in this domain progresses. In summary, pharmacogenomics is revolutionizing healthcare by facilitating more personalized and precise therapies that enhance drug efficacy, minimize adverse effects, and optimize patient outcomes. The continuous advancement of research indicates that pharmacogenomics has significant potential to transform pharmaceutical development and patient care.

Pharmacogenomics has the chance to transform medicine by transcending broad treatments and integrating genetic data into clinical decision-making, fostering a genuinely individualized and precision-oriented practice. As this domain advances, it will unveil new prospects for enhancing the safety, efficacy, and efficiency of healthcare, establishing personalized medicine as a fundamental aspect of contemporary medical practice.

Authors' Contribution

Sanaz Khosravi Ghareh Cheh was involved in the conceptualization, design and writing of the manuscript draft. The author read and confirmed the final manuscript.

Funding

Not applicable.

Availability of data and materials

All data are obtainable after an appeal from the corresponding author.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1.Davis BH, Limdi NA. Translational Pharmacogenomics: Discovery, Evidence Synthesis and Delivery of Race-Conscious Medicine. Clinical pharmacology and therapeutics. 2021;110(4):909-25.
2.Gummadi AC, Guddati AK. Genetic Polymorphisms in Pharmaceuticals and Chemotherapy. World journal of oncology. 2021;12(5):149-54.
3.Behdani AM, Lai J, Kim C, Basalelah L, Halsey T, Donohoe KL, et al. Optimizing pharmacogenomic decision-making by data science. PLOS digital health. 2024;3(2):e0000451.
4.Tyson RJ, Park CC, Powell JR, Patterson JH, Weiner D, Watkins PB, et al. Precision Dosing Priority Criteria: Drug, Disease, and Patient Population Variables. Frontiers in pharmacology. 2020;11:420.
5.Su J, Yang L, Sun Z, Zhan X. Personalized Drug Therapy: Innovative Concept Guided With Proteoformics. Molecular & Cellular Proteomics. 2024;23(3):100737.
6.Hossam Abdelmonem B, Abdelaal NM, Anwer EKE, Rashwan AA, Hussein MA, Ahmed YF, et al. Decoding the Role of CYP450 Enzymes in Metabolism and Disease: A Comprehensive Review. Biomedicines [Internet]. 2024; 12(7).
7.Sadee W, Wang D, Hartmann K, Toland AE. Pharmacogenomics: Driving Personalized Medicine. Pharmacological reviews. 2023;75(4):789-814.
8.Qahwaji R, Ashankyty I, Sannan NS, Hazzazi MS, Basabrain AA, Mobashir M. Pharmacogenomics: A Genetic Approach to Drug Development and Therapy. Pharmaceuticals [Internet]. 2024; 17(7).
9.Javaid M, Haleem A, Singh RP. Health informatics to enhance the healthcare industry's culture: An extensive analysis of its features, contributions, applications and limitations. Informatics and Health. 2024;1(2):123-48.
10.Qahwaji R, Ashankyty I, Sannan NS, Hazzazi MS, Basabrain AA, Mobashir M. Pharmacogenomics: A Genetic Approach to Drug Development and

Therapy. Pharmaceuticals (Basel, Switzerland). 2024;17(7).
11.Shea L, Pesa J, Geonnotti G, Powell V, Kahn C, Peters W. Improving diversity in study participation: Patient perspectives on barriers, racial differences and the role of communities. Health expectations : an international journal of public participation in health care and health policy. 2022;25(4):1979-87.
12.Micaglio E, Locati ET, Monasky MM, Romani F, Heilbron F, Pappone C. Role of Pharmacogenetics in Adverse Drug Reactions: An Update towards Personalized Medicine. Frontiers in pharmacology. 2021;12:651720.
13.Su J, Yang L, Sun Z, Zhan X. Personalized Drug Therapy: Innovative Concept Guided With Proteoformics. Molecular & cellular proteomics : MCP. 2024;23(3):100737.
14.Marques L, Costa B, Pereira M, Silva A, Santos J, Saldanha L, et al. Advancing Precision Medicine: A Review of Innovative In Silico Approaches for Drug Development, Clinical Pharmacology and Personalized Healthcare. Pharmaceutics [Internet]. 2024; 16(3).
15.Raijada D, Wac K, Greisen E, Rantanen J, Genina N. Integration of personalized drug delivery systems into digital health. Advanced Drug Delivery Reviews. 2021;176:113857.
16.Ahsani-Estahbanati E, Sergeevich Gordeev V, Doshmangir L. Interventions to reduce the incidence of medical error and its financial burden in health care systems: A systematic review of systematic reviews. 2022;9.
17.Abad-Santos F, Aliño SF, Borobia AM, García-Martín E, Gassó P, Maroñas O, et al. Developments in pharmacogenetics, pharmacogenomics, and personalized medicine. Pharmacological Research. 2024;200:107061.
18.Sun D, Gao W, Hu H, Zhou S. Why 90% of clinical drug development fails and how to improve it? Acta pharmaceutica Sinica B. 2022;12(7):3049-62.
19.Hippman C, Nislow C. Pharmacogenomic Testing: Clinical Evidence and Implementation Challenges. Journal of personalized medicine. 2019;9(3).
20.Duan X-P, Qin B-D, Jiao X-D, Liu K, Wang Z, Zang Y-S. New clinical trial design in precision medicine: discovery, development and direction. Signal Transduction and Targeted Therapy. 2024;9(1):57.
21.Marcu LG, Marcu DC. Pharmacogenomics and Big Data in medical oncology: developments and challenges. Therapeutic advances in medical oncology. 2024;16:17588359241287658.
22.Garg P, Malhotra J, Kulkarni P, Horne D, Salgia R, Singhal SS. Emerging Therapeutic Strategies to Overcome Drug Resistance in Cancer Cells. Cancers [Internet]. 2024; 16(13).
23.Kabbani D, Akika R, Wahid A, Daly AK, Cascorbi I, Zgheib NK. Pharmacogenomics in practice: a review and implementation guide. 2023;14.
24.Kabbani D, Akika R, Wahid A, Daly AK, Cascorbi I, Zgheib NK. Pharmacogenomics in practice: a review and implementation guide. Frontiers in pharmacology. 2023;14:1189976.
25.Omran S, Leong SL, Blebil A, Mohan D, Teoh SL. Effectiveness of pharmacogenomics educational interventions on healthcare professionals and health professions students: A systematic review. Research in Social and Administrative Pharmacy. 2023;19(11):1399-411.
26.Kloypan C, Koomdee N, Satapornpong P, Tempark T, Biswas M, Sukasem C. A Comprehensive Review of HLA and Severe Cutaneous Adverse Drug Reactions: Implication for Clinical Pharmacogenomics and Precision Medicine. Pharmaceuticals [Internet]. 2021; 14(11).
27.Scott SA. Personalizing medicine with clinical pharmacogenetics. Genetics in Medicine. 2011;13(12):987-95.
28.Jmel H, Sarno S, Giuliani C, Boukhalfa W, Abdelhak S, Luiselli D, et al. Genetic diversity of variants involved in drug response among Tunisian and Italian populations toward personalized medicine. Scientific Reports. 2024;14(1):5842.
29.Kaye AD, Koress CM, Novitch MB, Jung JW, Urits I, Viswanath O, et al. Pharmacogenomics, concepts for the future of perioperative medicine and pain management: A review. Best Practice & Research Clinical Anaesthesiology. 2020;34(3):651-62.
30.Li Y, Meng Q, Yang M, Liu D, Hou X, Tang L, et al. Current trends in drug metabolism and pharmacokinetics. Acta pharmaceutica Sinica B. 2019;9(6):1113-44.
31.Amaro-Álvarez L, Cordero-Ramos J, Calleja-Hernández M. Exploring the impact of pharmacogenetics on personalized medicine: A systematic review. Farmacia hospitalaria : organo oficial de expresion cientifica de la Sociedad Espanola de Farmacia Hospitalaria. 2024;48(6):299-309.
32.Bansal N, Momin S, Bansal R, Gurram Venkata SKR, Ruser L, Yusuf KJPM. Pharmacokinetics of drugs: newborn perspective. 2023. 2023;7.
33.Galeano D, Li S, Gerstein M, Paccanaro A. Predicting the frequencies of drug side effects. Nature Communications. 2020;11(1):4575.
34.Iacopetta D, Ceramella J, Catalano A, Scali E, Scumaci D, Pellegrino M, et al. Impact of Cytochrome P450 Enzymes on the Phase I Metabolism of Drugs. Applied Sciences [Internet]. 2023; 13(10).
35.Zhao M, Ma J, Li M, Zhang Y, Jiang B, Zhao X, et al. Cytochrome P450 Enzymes and Drug Metabolism in Humans. International journal of molecular sciences. 2021;22(23).

36.Gopisankar MG. CYP2D6 pharmacogenomics. Egyptian Journal of Medical Human Genetics. 2017;18(4):309-13.
37.Vaidya F, Chhipa A, Mishra V, Gupta V, Rawat S, Kumar A, et al. Molecular and cellular paradigms of multidrug resistance in cancer. Cancer Reports. 2020;5.
38.Nahid NA, Johnson JA. CYP2D6 pharmacogenetics and phenoconversion in personalized medicine. Expert opinion on drug metabolism & toxicology. 2022;18(11):769-85.
39.Zanger UM, Schwab M. Cytochrome P450 enzymes in drug metabolism: Regulation of gene expression, enzyme activities, and impact of genetic variation. Pharmacology & Therapeutics. 2013;138(1):103-41.
40.He W, Grassmann F, Eriksson M, Eliasson E, Margolin S, Thorén L, et al. CYP2D6 Genotype Predicts Tamoxifen Discontinuation and Prognosis in Patients With Breast Cancer. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2020;38(6):548-57.
41.Hines LJ, Wilke RA, Myers R, Mathews CA, Liu M, Baye JF, et al. Rationale and design for a pragmatic randomized trial to assess gene-based prescribing for SSRIs in the treatment of depression. Clinical and Translational Science. 2024;17(6):e13822.
42.Ellithi M, Baye J, Wilke RA. CYP2C19 genotype-guided antiplatelet therapy: promises and pitfalls. Pharmacogenomics. 2020;21(12):889-97.
43.Mirabbasi SA, Khalighi K, Wu Y, Walker S, Khalighi B, Fan W, et al. CYP2C19 genetic variation and individualized clopidogrel prescription in a cardiology clinic. Journal of community hospital internal medicine perspectives. 2017;7(3):151-6.
44.Shubbar Q, Alchakee A, Issa KW, Adi AJ, Shorbagi AI, Saber-Ayad M. From genes to drugs: CYP2C19 and pharmacogenetics in clinical practice. 2024;15.
45.Squizzato A, Bellesini M, Takeda A, Middeldorp S, Donadini MP. Clopidogrel plus aspirin versus aspirin alone for preventing cardiovascular events. The Cochrane database of systematic reviews. 2017;12(12):Cd005158.
46.Lee CR, Thomas CD, Beitelshees AL, Tuteja S, Empey PE, Lee JC, et al. Impact of the CYP2C19*17 Allele on Outcomes in Patients Receiving Genotype-Guided Antiplatelet Therapy After Percutaneous Coronary Intervention. Clinical pharmacology and therapeutics. 2021;109(3):705-15.
47.Pereira NL, Rihal CS, So DYF, Rosenberg Y, Lennon RJ, Mathew V, et al. Clopidogrel Pharmacogenetics. Circulation Cardiovascular interventions. 2019;12(4):e007811.
48.Shubbar Q, Alchakee A, Issa KW, Adi AJ, Shorbagi AI, Saber-Ayad M. From genes to drugs: CYP2C19 and pharmacogenetics in clinical practice. Frontiers in pharmacology. 2024;15:1326776.
49.Ageno W, Gallus AS, Wittkowsky A, Crowther M, Hylek EM, Palareti G. Oral anticoagulant therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e44S-e88S.
50.Tatarunas V, Lesauskaite V, Veikutiene A, Grybauskas P, Jakuska P, Jankauskiene L, et al. The effect of CYP2C9, VKORC1 and CYP4F2 polymorphism and of clinical factors on warfarin dosage during initiation and long-term treatment after heart valve surgery. Journal of thrombosis and thrombolysis. 2014;37(2):177-85.
51.Zhou X-Y, Lu X-R, Li Y-H, Ma Y-Q, Zhao S-W, Wang F, et al. Identification and Enzymatic Activity Evaluation of a Novel CYP2C9 Allelic Variant Discovered in a Patient. 2021;12.
52.Shaw K, Amstutz U, Kim R, Lesko L, Turgeon J, Michaud V, et al. Clinical Practice Recommendations on Genetic Testing of CYP2C9 and VKORC1 Variants in Warfarin Therapy. Therapeutic drug monitoring. 2015;37:428-36.
53.Azzam H, Elwakeel H, Awad I, El-farahaty R, El-Gilany A-H, El-Sharawy S. VKORC1 and CYP2C9 genotypes in Egyptian patients with warfarin resistance. Blood coagulation & fibrinolysis : an international journal in haemostasis and thrombosis. 2014;27.
54.Ahmed S, Zhou Z, Zhou J, Chen SQ. Pharmacogenomics of Drug Metabolizing Enzymes and Transporters: Relevance to Precision Medicine. Genomics, proteomics & bioinformatics. 2016;14(5):298-313.
55.Kolou M, Poda A, Diallo Z, Konou E, Dokpomiwa T, Zoungrana J, et al. Prevalence of human leukocyte antigen HLA-B*57:01 in individuals with HIV in West and Central Africa. BMC Immunology. 2021;22(1):48.
56.Harrison PT, Vyse S, Huang PH. Rare epidermal growth factor receptor (EGFR) mutations in non-small cell lung cancer. Seminars in cancer biology. 2020;61:167-79.
57.Hossam Abdelmonem B, Abdelaal NM, Anwer EKE, Rashwan AA, Hussein MA, Ahmed YF, et al. Decoding the Role of CYP450 Enzymes in Metabolism and Disease: A Comprehensive Review. Biomedicines. 2024;12(7).
58.Khan BA, Robinson R, Fohner AE, Muzquiz LI, Schilling BD, Beans JA, et al. Cytochrome P450 Genetic Variation Associated with Tamoxifen Biotransformation in American Indian and Alaska Native People. Clinical and translational science. 2018;11(3):312-21.
59.Mulder TAM, de With M, Del Re M, Danesi R, Mathijssen RHJ, van Schaik RHN. Clinical CYP2D6 Genotyping to Personalize Adjuvant

Tamoxifen Treatment in ER-Positive Breast Cancer Patients: Current Status of a Controversy. Cancers. 2021;13(4).
60.Lopez J, Mark J, Duarte GJ, Shaban M, Sosa F, Mishra R, et al. Role of genetic polymorphisms in clopidogrel response variability: a systematic review. Open heart. 2023;10(2).
61.Deshpande P, Hertzman RJ, Palubinsky AM, Giles JB, Karnes JH, Gibson A, et al. Immunopharmacogenomics: Mechanisms of HLA-Associated Drug Reactions. Clinical pharmacology and therapeutics. 2021;110(3):607-15.
62.Kazaoka A, Fujimori S, Yamada Y, Shirayanagi T, Gao Y, Kuwahara S, et al. HLA-B*57:01-dependent intracellular stress in keratinocytes triggers dermal hypersensitivity reactions to abacavir. PNAS nexus. 2024;3(4):pgae140.
63.Molatefi R, Talebi S, Samei A, Roshanravan N, Manshouri S, Hashemi B, et al. Clues of HLAs, metabolic SNPs, and epigenetic factors in T cell-mediated drug hypersensitivity reactions. Heliyon. 2024;10(14):e33976.
64. Shalia K, Doshi S, Parikh S, Pawar P, Divekar S, Varma S, et al. Prevalence of VKORC1 and CYP2C9 gene polymorphisms in Indian population and its effect on warfarin response. The Journal of the Association of Physicians of India. 2012;60:34-8.
65.Shugg T, Tillman EM, Breman AM, Hodge JC, McDonald CA, Ly RC, et al. Development of a Multifaceted Program for Pharmacogenetics Adoption at an Academic Medical Center: Practical Considerations and Lessons Learned. Clinical Pharmacology & Therapeutics. 2024;116(4):914-31.
66.Mauriello A, Ascrizzi A, Molinari R, Falco L, Caturano A, D'Andrea A, et al. Pharmacogenomics of Cardiovascular Drugs for Atherothrombotic, Thromboembolic and Atherosclerotic Risk. Genes. 2023;14(11).
67.Sentana-Lledo D, Academia E, Viray H, Rangachari D, Kobayashi SS, VanderLaan PA, et al. EGFR exon 20 insertion mutations and ERBB2 mutations in lung cancer: a narrative review on approved targeted therapies from oral kinase inhibitors to antibody-drug conjugates. 2023. 2023;12(7):1590-610.
68.Weth FR, Hoggarth GB, Weth AF, Paterson E, White MPJ, Tan ST, et al. Unlocking hidden potential: advancements, approaches, and obstacles in repurposing drugs for cancer therapy. British Journal of Cancer. 2024;130(5):703-15.
69.Alchakee A, Ahmed M, Eldohaji L, Alhaj H, Saber-Ayad M. Pharmacogenomics in Psychiatry Practice: The Value and the Challenges. International journal of molecular sciences. 2022;23(21).
70.Floris M, Moschella A, Alcalay M, Montella A, Tirelli M, Fontana L, et al. Pharmacogenetics in Italy: current landscape and future prospects. Human Genomics. 2024;18(1):78.
71.Stratton TP, Olson AW. Personalizing Personalized Medicine: The Confluence of Pharmacogenomics, a Person's Medication Experience and Ethics. Pharmacy [Internet]. 2023; 11(3).
72.Buchanan J, Wordsworth S, Schuh A. Issues surrounding the health economic evaluation of genomic technologies. Pharmacogenomics. 2013;14(15):1833-47.
73.Oates JT, Lopez D. Pharmacogenetics: An Important Part of Drug Development with A Focus on Its Application. International journal of biomedical investigation. 2018;1(2).