International Journal of Molecular Medical Science, 2024, Vol.14, No.2, 61-68
http://medscipublisher.com/index.php/ijmms

Research Report Open Access

Optimizing Drug Therapy Using Genomic Information: A Pathway to Personalized Medicine

Shuyi Chen
Institute of Life Science, Jiyang College of Zhejiang A&F University, Zhuji, 311800, China
Corresponding author email: ssoy1@outlook.com

International Journal of Molecular Medical Science, 2024, Vol.14, No.2 doi: 10.5376/ijmms.2024.14.0009
Received: 01 Mar., 2024
Accepted: 02 Apr., 2024
Published: 12 Apr., 2024

Preferred citation for this article:
Chen S.Y., 2024, Optimizing drug therapy using genomic information: a pathway to personalized medicine, International Journal of Molecular Medical Science, 14(2): 61-68 (doi: 10.5376/ijmms.2024.14.0009)

Abstract This article explores the utilization of genomic information to optimize drug treatment, aiming to achieve personalized healthcare. As an emerging medical model, personalized healthcare aims to develop precise treatment plans based on patients' genomic information, thereby enhancing treatment outcomes and minimizing side effects. Initially, the importance of genomic information in personalized healthcare is introduced, encompassing its application in precise drug development and preventive medicine. The article then analyzes successful cases and challenges in the practical application of personalized healthcare, discussing technical limitations and cost issues in acquiring and analyzing Genomic data. Furthermore, ethical, privacy, and regulatory considerations in personalized healthcare are explored, along with suggestions and strategies to promote its development. Additionally, the future trends of genomic information in optimizing drug treatment and personalized healthcare are predicted, emphasizing the significance of interdisciplinary collaboration and technological innovation. Through comprehensive analysis and outlook, this article aims to provide beneficial insights and directions for the advancement of personalized healthcare.

Keywords Genomic information; Drug therapy; Personalized medicine; Drug development

In today's medical field, the concept of personalized medicine has gradually emerged and become an important direction to promote medical progress (Lai et al., 2020). Personalized medicine, in short, refers to providing patients with tailor-made treatment plans based on individual differences such as genetic characteristics, physiological status, and environmental factors. This medical model emphasizes the accuracy and effectiveness of treatment, aiming to improve patients' treatment effects and quality of life, reduce medical costs, and promote the rational allocation of medical resources.

The importance of personalized medicine is self-evident. By taking into account individual differences, personalized medicine can significantly improve treatment effects and reduce drug side effects, thereby improving patients' quality of life. Personalized medicine helps reduce health care costs. The traditional "one size fits all" treatment model often leads to waste and overuse of resources, while personalized medicine can reduce unnecessary medical expenditures through precise treatment (Salari and Larijani, 2017). Personalized medicine is also an inevitable trend in the development of medicine. With the rapid development of genomics, molecular biology and other disciplines, humans have a deeper and deeper understanding of individual differences, providing strong technical support for personalized medicine.

In the practice of personalized medicine, genomic information plays a crucial role. Genome is the carrier of genetic information of an organism and contains key information that determines individual physiological characteristics, disease susceptibility, and drug response. By analyzing genomic information, we can gain a deeper understanding of an individual's genetic background and predict their response and efficacy to specific drugs, thereby providing a scientific basis for personalized treatment. This study aims to deeply explore the role of genomic information in optimizing drug treatment and how to use this information to achieve personalized medicine (Yang et al., 2021).

1 Association between Genomic Information and Drug Treatment

1.1 How genomic information affects drug response and efficacy

Genomic information is the core of personalized medicine, which profoundly affects the response and efficacy of drugs in an individual. Each person's genome is unique, which determines the differences in the body's absorption, distribution, metabolism and excretion of drugs. Therefore, genomic information is crucial for predicting and optimizing drug treatment regimens. Genomic information has great potential in optimizing drug treatments through strategies such as genome-guided drug discovery and development, drug dosage adjustment, and drug combination and optimization of treatment regimens. Better use of genomic information to develop personalized treatment plans, improve treatment effectiveness and reduce the risk of side effects.

In 2017, a survey by Giacomini and others found that genomic information can reveal an individual's response mechanism to drugs. Certain genetic variations may lead to changes in drug targets, thereby affecting the efficacy of drugs. Genomic information can also help understand the metabolic pathways and speeds of drugs in the body, which is important for adjusting drug dosage and avoiding side effects caused by drug accumulation (Giacomini et al., 2017).

Yang et al. (2021) systematically analyzed the relationship between genomic information and drug response to reveal the key factors affecting drug treatment effects, providing new perspectives and methods for drug development and treatment strategies. It is also hoped that this research can promote the development of personalized medicine and bring better treatment effects and quality of life to patients.

Huang et al. (2016) found that the bioavailability and metabolism of PPIs are mainly affected by the drug metabolizing enzyme CYP2C19 and partly affected by CYP3A4. The differences in CYP3A4 and CYP2C19 enzyme activities caused by individual genetic factors are the molecular mechanisms responsible for the differences in PPI efficacy. one. Mutations in the CYP2C19 encoding gene can cause changes in the metabolic activity of the CYP2C19 enzyme, resulting in differences in blood drug concentrations and even different clinical reactions in different patients after taking drugs with CYP2C19 as the key metabolic enzyme. In addition, non-genetic factors such as concomitant medication and diet are also important factors affecting the efficacy of PPIs.

1.2 Effects of genetic polymorphisms, mutations and expression levels on drug response

Gene polymorphisms, mutations, and expression levels are three important aspects of genomic information that all have a significant impact on drug response. Gene polymorphism refers to the presence of multiple alleles at the same genetic locus. These alleles may contribute to individual differences in response to and efficacy of drugs. For example, certain genetic polymorphisms are related to the activity of drug-metabolizing enzymes, which in turn affects the concentration and efficacy of drugs in the body.

Min et al. (2015) used a clinical prospective randomized controlled study method to randomly divide 149 patients with extensive burns into a control group and an experimental group. The control group was given opioids in the normal mode, and the experimental group was given opioids based on the patient's genetic testing results. The patients' pain assessment scores at different time points were recorded. The results showed differences in the patient's genotype. The dosage of opioids was adjusted and individualized administration was performed. The design of drug regimen can save the dosage of opioids, increase the analgesic effect, and reduce the incidence of adverse reactions.

Barton et al. (2015) found that gene expression level refers to the degree to which a gene is transcribed into mRNA and translated into protein. Differences in gene expression levels may lead to changes in the quantity or activity of drug targets, thereby affecting the efficacy of the drug. By analyzing gene expression levels, we can better understand the mechanism of action of drugs in an individual and optimize treatment options accordingly.

Wu et al. (2015) took the Chinese Mongolian population as the research object, used the PCR-RFLP method to analyze CYP2D6 genotypes, and grouped them according to genotypes: CYP2D6*1/*1, CYP2D6*1/*10 and

CYP2D6*10/*10. Blood samples were dynamically collected to measure codeine and its metabolites morphine, morphine3 -glucuronide (M-3-G), and morphine-6-glucuronide from subjects who took a single oral administration of codeine. (morphine 6-glucuronide, M-6-G) plasma concentration. Although there is no significant difference in the pharmacokinetic parameters of codeine in subjects with different genotypes, there are significant differences in Cmax and the area under the drug-time curve of morphine, M-3-G, and M-6-G between groups ($P< 0.05$).

1.3 Application of genomic information in predicting drug responses and side effects

Genomic information has important application value in predicting drug responses and side effects. By parsing an individual's genomic information, it is possible to predict their response and efficacy to specific drugs, thus avoiding unnecessary drug trials and potential side effects. Genetic variations are associated with drug resistance, meaning some patients may not respond to certain drugs. (Xu et al., 2019). In this case, predicting drug response through genomic information can help doctors choose more effective treatments for patients. Genomic information can also be used to predict the side effects a drug may cause. By identifying genetic variants associated with drug side effects, doctors can assess patients' risk before administering the drug and take appropriate preventive measures.

Tsigelny (2019) By in-depth understanding of how genomic information affects drug response and efficacy, as well as the impact of genetic polymorphisms, mutations, and expression levels on drug response, we can better predict and adjust drug treatment plans and achieve the goal of personalized medicine.

Wu et al. (2015) observed the impact of different CPY2D6*10 genotypes on the use of fentanyl for postoperative analgesia in Chinese gastric cancer patients after surgery, and also obtained similar findings, which confirmed the above results, that is, the postoperative mutant type (m/m The cumulative opioid consumption of patients in the) group increased significantly; at the same time, no significant difference in adverse reactions was observed among the groups ($P>0.05$). Therefore, CPY2D6*10 gene polymorphism can affect patients' postoperative response to opioid analgesia.

2 Strategies for Optimizing Drug Treatment using Genomic Information

2.1 Genome-oriented drug discovery and development process

The genome-directed drug discovery and development process is a revolutionary approach that uses genomic information to guide drug development, resulting in more efficient and precise treatments. This process begins with genomic research on specific diseases, which provides important clues for the screening of drug targets by identifying gene variations and expression patterns related to the occurrence and development of the disease.

After obtaining potential drug targets, researchers will use genomic information to design and optimize drug candidates (Yang et al., 2021). This includes using genomic data to predict the ability of drugs to bind to targets, and to evaluate the efficacy and side effects of drugs. In addition, genomic information can help researchers identify potential safety risks in the early stages of drug development, thereby avoiding failures in later clinical trials.

Cancer treatment based on gene technology allows cancer to be prescribed from "seeing the doctor" to "prescribing medicine based on the person". This is the first time that humans have begun human trials using gene-edited T cells to treat cancer. It can be said that this is also a leap forward in the development of personalized cancer treatment. As the official press release of Nature magazine pointed out, this is the first intersection of the two hot fields of personalized gene editing and anti-cancer cell therapy, which is expected to have a profound impact on cancer treatment. Antoni Ribas, the corresponding author of the study, also said: This is a major leap forward in personalized cancer treatment using isolated immune receptors to specifically recognize patients' own cancer mutations (Foy et al., 2023).

Nielsen et al. (2016) tested the influence of multiple genes on pain sensitivity in healthy subjects. Experimental tests included thermal cutaneous pain stimulation, muscle and bone stimulation, mechanical, electrical and

thermal visceral stimulation and cold pressure test. The results showed that COMT The V108/158M genotype is associated with pain sensitivity. Other studies have found that the COMT V108/158M gene polymorphism is associated with postoperative opioid consumption.

2.2 Introduction to genome-guided drug dose adjustment strategies

Drug dosage is a key factor affecting treatment efficacy and side effects. Traditional drug dose adjustment is mainly based on the patient's general physiological characteristics such as weight, age, and renal function, but this method often fails to fully consider the impact of individual differences on drug response (Figure 1). Genome-guided drug dosage adjustment strategies can more accurately optimize drug dosage based on individual genomic information.

Li et al. (2018) analyzed the patient's genomic information to understand their metabolism rate, clearance rate and possible side effects sensitivity to drugs. This information can help doctors develop personalized drug dosage regimens for patients to ensure optimal drug concentration in the body, thereby improving treatment effectiveness and reducing the risk of side effects.

Genome-guided drug dose adjustment strategies can also help doctors adjust drug doses in a timely manner during treatment (Wang Panfei, 2021, https://zhuanlan.zhihu.com/). When a patient develops drug resistance or side effects, doctors can adjust the drug dosage or change drugs based on the patient's genomic information to avoid unnecessary treatment failures and side effects.

2.3 Genome-guided drug combinations and optimized treatment options

Genome-directed drug combinations and optimized treatment regimens are one approach that leverages genomic information to develop comprehensive treatment plans. It takes into account the impact of multiple genetic variations in a patient on drug response and aims to maximize treatment effectiveness and minimize side effects by combining multiple drugs.

In November 2022, researchers from the University of California and an immuno-oncology therapy company used CRISPR-Cas9 gene editing technology to modify T cells so that they could specifically recognize cancer cells and launch concentrated attacks, and launched the first human clinical trial (Foy et al., 2023). Each of the 16 subjects was infused with genetically engineered T cells with up to three different targets. The researchers then found that these edited cells began to circulate in the subjects' blood, and the concentrations around the tumors were greater than the concentration of non-edited cells before treatment. One month after treatment, five subjects were in stable condition, indicating that their tumors were not growing. Only two people experienced adverse reactions that may have been caused by the activity of these edited T cells.

In other words, researchers can use CRISPR gene editing technology to modify immune cells so that these cells can recognize individual-specific mutant proteins in tumor patients (Scott et al., 2023). When these cells are injected into a patient, the gene-edited T cells preferentially flow to the site of cancer cells to eliminate them.

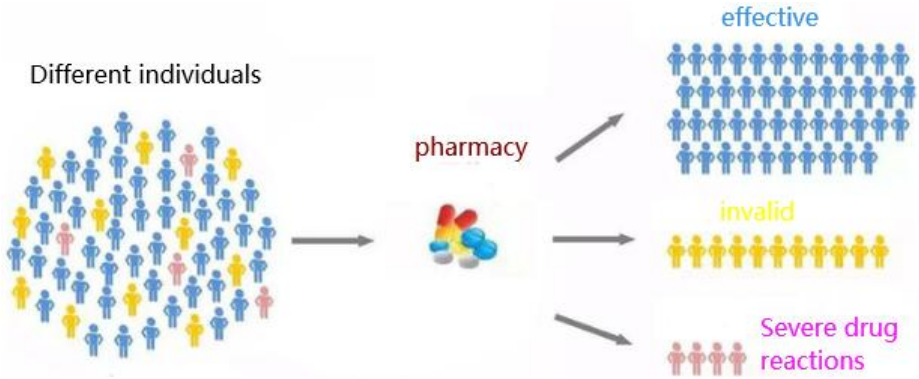

Figure 1 Traditional drug doses has different efficacy for different individuals (https://zhuanlan.zhihu.com/p/439470102)
Note: The effect of different individuals is different, and some individuals may even have severe drug reactions

3 Practice and Challenges of Personalized Medicine

3.1 Successful cases and challenges of personalized medicine in practical applications

Personalized medicine, as the forefront of today's medical field, has demonstrated its huge potential and value in practice. In practical applications, personalized medicine has achieved many successful cases. For example, a study by Columbia University proved that cancers need to be classified, but they are not all different, but can be identified as certain types. That is, all cancers can be divided into 112 subtypes, and there are 24 unique ones. The main module (Master regulatory protein) with higher correlation is controlled (https://www.thepaper.cn/newsDetail_forward_22490453). In this way, new drugs targeting master regulatory proteins can be developed to treat more patients with similar cancers (Goetz and Schork, 2018). Some patients with hereditary cancer have discovered specific gene mutations through genetic testing, and thus received targeted drug treatment, which significantly improved the treatment effect and quality of life. Personalized treatment plans for rare disease patients have also achieved remarkable results. Due to their special conditions, traditional treatment methods are often ineffective for these patients, and personalized medicine provides them with hope.

Personalized medicine also faces many challenges in practice, and the maturity and popularity of the technology is an important issue (Matheur and Sutton, 2017). Although genome sequencing technology has made great progress, its cost, accuracy, and accessibility still limit the widespread application of personalized medicine. Secondly, the allocation of medical resources is also a challenge. Personalized medicine requires more investment in medical resources, including advanced medical equipment, professional doctors and researchers, which is a huge challenge for many developing countries and regions.

3.2 Technical limitations and cost issues in obtaining and analyzing genomic information

The acquisition and analysis of genomic information is a key step in achieving personalized medicine, but currently this field still faces technical limitations and cost issues. In terms of technical limitations, although genome sequencing technology has made great progress, its accuracy and stability still need to be improved. At the same time, the analysis and interpretation of genomic data is also a huge challenge, requiring professional bioinformatics knowledge and skills (Williams, 2020). The acquisition and analysis of genomic information also faces challenges in ethics and privacy. How to ensure the security and privacy of data is an urgent problem that needs to be solved.

In terms of cost issues, the cost of genome sequencing and data analysis is still high, which limits the widespread application of personalized medicine (Lorenzo-Luaces et al., 2021). Although sequencing costs have declined in recent years as technology advances and market competition intensifies, it remains a heavy burden for many patients and families. Therefore, how to reduce the cost of obtaining and analyzing genomic information is the key to realizing the widespread application of personalized medicine.

3.3 Impact of ethics, privacy and regulations on personalized medicine

Ethics, privacy and regulations are important factors affecting the development of personalized medicine. In terms of ethics, personalized medicine involves the in-depth exploration and utilization of human genetic information, which requires a balance between medical progress and human dignity. Privacy protection is another key issue. Genome information is one of the most private information of an individual, and its leakage may cause a great invasion of personal privacy (Salari and Larijani, 2017). In the process of promoting personalized medicine, a sound privacy protection mechanism must be established to ensure the security of personal genomic information. The regulatory environment also has a profound impact on the development of personalized medicine. Different countries and regions have different regulatory environments and regulatory policies for personalized medicine. This provides both diversity and complexity for the development of personalized medicine. How to promote the development of personalized medicine while complying with regulations is currently an important issue.

Guan (2022) survey shows that the core of personalized medicine is "patient-centered" and various attributes related to personal rights and interests and their environment must be considered. From the perspective of ethical governance, it is more about guiding smart medical services through ethical norms, leveraging modern science and technology, and providing fast, safe, scientific and professional medical services with limited medical resources to maximize welfare.

4 Conclusion and Outlook

4.1 Importance of genomic information applications

Genomic information plays a crucial role in optimizing drug treatment and achieving personalized medicine (Giacomini et al., 2017). By using genomic information, we can gain a deeper understanding of the pathogenesis and individual differences of diseases, and provide more precise and personalized guidance for drug development and treatment plans. The Human Genome Project found that the genetic sequence difference between people is only one thousandth, containing about 3 million variations, and every 500 to 1 in the genome There is a variation in 0,000 bases, called a polymorphism, and these differences create different genotypes that determine people's different risks of disease and different responses to drugs (Figure 2).

The application of genomic information can also help improve treatment effects, reduce the risk of side effects, and reduce the waste of medical resources, which has important clinical and social significance (https://zhuanlan.zhihu.com/p/439470102). We should continue to strengthen the research and application of genomics and related technologies, promote the development of personalized medicine, and make greater contributions to human health.

4.2 Application prospects of new technologies and methods in personalized medicine

New technologies and methods have broad prospects for application in personalized medicine. For example, gene editing technologies such as CRISPR-Cas9 provide new possibilities for the treatment of genetic diseases (Helle and Steele, 2021). New genomic technologies such as single-cell sequencing technology and liquid biopsy will enable this research to gain a deeper understanding of the pathogenesis and individual differences of the disease and provide richer information for personalized medicine. With the integrated analysis of multi-omics data, a more comprehensive understanding of the patient's disease status and treatment response can be provided, providing a more solid foundation for precise treatment.

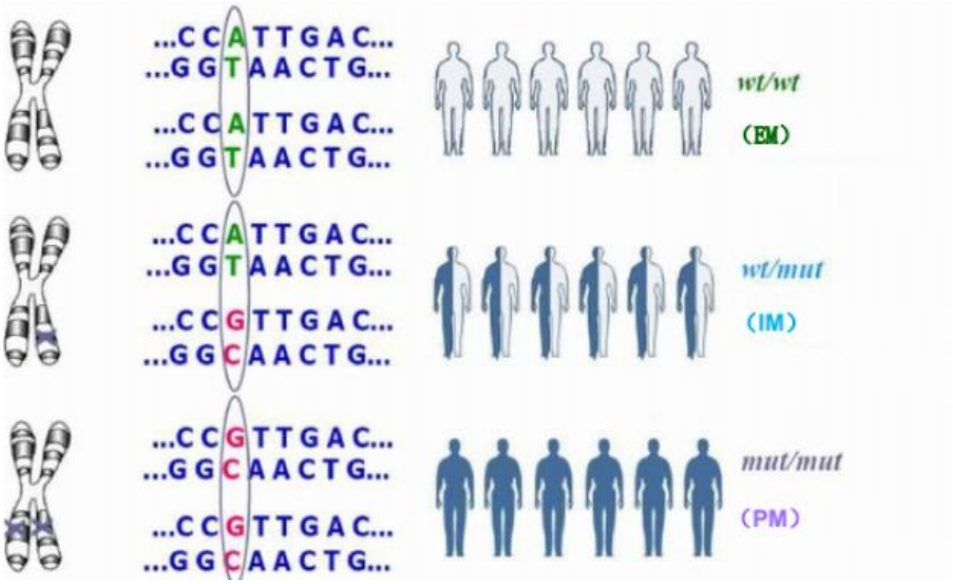

Figure 2 Individuals with different genotypes have different drug responses (https://zhuanlan.zhihu.com/p/439470102)
Note: The gene sequence contains about 3 million variants, with one variation for every 500~1 000 bases in the genome, and these differences form different genotypes that determine people at different risk of disease and different responses to drugs

As genomic information is increasingly used in the medical field, related ethical, privacy and regulatory issues will also receive more attention. We look forward to the continuous improvement of relevant regulations to ensure the safe, legal and compliant use of genomic information and protect patients' rights. Privacy and rights (Blobel et al., 2016). The future development trend of genomic information in optimizing drug treatment and personalized medicine is full of potential and opportunities. With the continuous advancement of technology and the strengthening of interdisciplinary cooperation, it is expected to achieve more accurate, safe and effective personalized medicine in the future, making greater contributions to human health and well-being.

4.3 Put forward suggestions and strategies to promote the development of personalized medicine

In order to promote the development of personalized medicine, we must first continue to strengthen the research and development of genomics and related technologies, improve their maturity and promote popularization, so as to ensure that a wider range of patients can benefit from them. It is crucial to establish a sound genomic information database and sharing platform, which will help promote the openness and sharing of data and provide researchers with abundant resources.

The training and education of medical personnel cannot be ignored. By improving their knowledge of genomics and personalized medicine, treatment options can be ensured to be more accurate and effective (Lai et al., 2020). Formulating and improving relevant regulations and policies is also the key to ensuring the legality and safety of personalized medicine. It is also necessary to strengthen communication and education with patients, improve their awareness of personalized medicine, and encourage them to actively participate in the treatment process, which will help promote the overall development of personalized medicine.

4.4 Future development trends

With the continuous innovation of science and technology, genomic information will play an increasingly important role in optimizing drug treatment and personalized medicine. Looking into the future, it is expected that genomic information will promote the development of precision drugs. By in-depth understanding of the molecular mechanisms of diseases, precision drugs can be developed that target specific genetic variations to improve treatment effects and reduce side effects. Genomic information will also assist preventive medicine, improving patient health by predicting disease risk and enabling early intervention and preventive treatment.

In terms of personalized treatment, genomic information will help doctors develop treatment plans that are more in line with the patient's individual characteristics (Sarvan and Nori, 2021). By analyzing a patient's genomic information, doctors can predict the patient's response to drugs and adjust drug dosage, combinations or treatment strategies to achieve truly personalized treatment. In the future, the application of genomic information will not only be limited to the field of genomics, but will also be deeply integrated with other disciplines such as medicine, bioinformatics, and computer science to promote interdisciplinary cooperation and technological innovation. This will accelerate the development of personalized medicine, promote progress in the medical field, and bring better treatment effects and quality of life to more patients.

References

CBarton J.C., Edwards C.Q., and Acton R.T., 2015, HFE gene: Structure, function, mutations, and associated iron abnormalities, Gene, 574(2): 179-192.
https://doi.org/10.1016/j.gene.2015.10.009
PMid:26456104 PMCid:PMC6660136

Blobel B., Lopez D.M., and Gonzalez C., 2016, Patient privacy and security concerns on big data for personalized medicine, Health and Technology, 6: 75-81.
https://doi.org/10.1007/s12553-016-0127-5

Foy S.P., Jacoby K., Bota D.A., Hunter T., Pan Z., Stawiski E., Ma Y., Lu W., Peng S., Wang C.L., Yuen B., Dalmas O., Heeringa K., Sennino B., Conroy A., Bethune M.T., Mende I., White W., Kukreja M., Gunturu S., Humphrey E., Hussaini A., An D., Litterman A.J., Quach B.B., Ng A.H.C., Lu Y., Smith C., Campbell K.M., Anaya D., Skrdlant L., Huang E.Y., Mendoza V., Mathur J., Dengler L., Purandare B., Moot R., Yi M.C., Funke R., Sibley A., Stallings-Schmitt T., Oh D.Y., Chmielowski B., Abedi M., Yuan Y., Sosman J.A., Lee S.M., Schoenfeld A.J., Baltimore D., Heath J.R., Franzusoff A., Ribas A., Rao AV., and Mandl S.J., 2023, Non-viral precision T cell receptor replacement for personalized cell therapy, Nature, 615(7953): 687-696.
https://doi.org/10.1038/s41586-022-05531-1
PMid:36356599 PMCid:PMC9768791

Giacomini K.M., Yee S.W., Mushiroda T., Weinshilboum R.M., Ratain M.J., and Kubo M., 2017, Genome-wide association studies of drug response and toxicity: an opportunity for genome medicine, Nature Reviews Drug Discovery, 16(1): 70-70.
https://doi.org/10.1038/nrd.2016.234
PMid:27885282 PMCid:PMC5443656

Goetz L.H., and Schork N.J., 2018, Personalized medicine: motivation, challenges, and progress, Fertility and sterility, 109(6): 952-963.
https://doi.org/10.1016/j.fertnstert.2018.05.006
PMid:29935653 PMCid:PMC6366451

Guan J., 2022, Ethical Issues in the Development of Smart Healthcare, Zhongguo Yixue Lunlixue (Chinese Medical Ethics), 35(4): 358-361.

Helle S., and Steele S., 2021, Cutting edge or ignored resource: assessing the uptake and content of the NHS e-Learning for healthcare on "identifying and supporting survivors of modern slavery", Journal of Public Health, 43(2): 413-419.
https://doi.org/10.1093/pubmed/fdz124
PMid:31735970

Huang W., Ji C.M., Guo M., Ni W.W., Meng L., Wei J.F., 2016, Pharmacogenomics of proton pump inhibitors, Shijie Huaren Xiaohua Zazhi (Shijie Huaren Xiaohua Zazhi), 24(33): 4458-4466.
https://doi.org/10.11569/wcjd.v24.i33.4458

Lai C.C., Wang J.H., Ko W.C., Yen M.Y., Lu M.C., Lee C.M., and Hsueh P.R., 2020, COVID-19 in long-term care facilities: an upcoming threat that cannot be ignored, Journal of microbiology, immunology, and infection, 53(3): 444.
https://doi.org/10.1016/j.jmii.2020.04.008
PMid:32303483 PMCid:PMC7153522

Li Y., Li X., Luo H., Sun L., Wang Y.Z., 2018, Research progress of the impact of gene polymorphisms in opioids pain treatment, Zhongguo Yiyuan Yaoxue Zazhi (Chinese Journal of Hospital Pharmacy), 38(2): 203-208.

Lorenzo-Luaces L., Peipert A., De Jesus Romero R., Rutter L.A., and Rodriguez-Quintana N., 2021, Personalized medicine and cognitive behavioral therapies for depression: Small effects, big problems, and bigger data, International Journal of Cognitive Therapy, 14: 59-85.
https://doi.org/10.1007/s41811-020-00094-3

Mathur S., and Sutton J., 2017, Personalized medicine could transform healthcare, Biomedical Reports, 7(1): 3-5.
https://doi.org/10.3892/br.2017.922
PMid:28685051 PMCid:PMC5492710

Min Y.Y., Zhu S., Luo Y., and Xiong D.F., 2015, To explore effect of CYP3A4 gene polymorphism and genetic testing on the efficacy of fentanyl in patients with extensive burns, Zhongguo Shenghua Yaowu Zazhi (Chin J Biochem Med), 35(8): 86-88, 91.

Nielsen L.M., Olesen A.E., Sato H., Christrup L.L., and Drewes A.M., 2016, Association between gene polymorphisms and pain sensitivity assessed in a multi-modal multi-tissue human experimental model-an explorative study, Basic Clin Pharmacol Toxicol, 119(4): 360-366.
https://doi.org/10.1111/bcpt.12601
PMid:27061127

Salari P., and Larijani B., 2017, Ethical issues surrounding personalized medicine: a literature review, Acta Medica Iranica, (1): 209-217.

Sarvan M.S., and Nori L.P., 2021, Personalized medicine: a new normal for therapeutic success, Indian Journal of Pharmaceutical Sciences, 83: 3.
https://doi.org/10.36468/pharmaceutical-sciences.790

Scott E.C., Baines A.C., Gong Y., Moore J.R., Pamuk G.E., Saber H., Subedee A., Thompson M.D., Xiao W., Pazdur R., Rao V.A., Schneider J., and Beaver J.A., 2023, Trends in the approval of cancer therapies by the FDA in the twenty-first century, Nature Reviews Drug Discovery, 22: 625-640.
https://doi.org/10.1038/s41573-023-00723-4
PMid:37344568

Tsigelny I.F., 2019, Artificial intelligence in drug combination therapy, Briefings in Bioinformatics, 20(4): 1434-1448.
https://doi.org/10.1093/bib/bby004
PMid:29438494

Williams M.T., 2020, Psychology cannot afford to ignore the many harms caused by microaggressions, Perspectives on Psychological Science, 15(1): 38-43.
https://doi.org/10.1177/1745691619893362
PMid:31801042

Wu S.B., Cai L.N., Yang X.H., Fu H.G., Sun K., Yuan F., and Dong T.L., 2015, Impact of CYP2D6 polymorphisms on postoperative fentanyl analgesia in gastric cancer patients, Genet Test Mol Biomarkers, 19(5):248-262.
https://doi.org/10.1089/gtmb.2014.0318
PMid:25825958

Xu H., Hui X., Zhu H.J., Li D.Y., and Ge W.H., 2019, Application of pharmacogenomics in clinical medication, Yaoxue yu Linchuang Yanjiu (Pharmaceutical and Clinical Research), 27(1): 46-51.

Yang J., Song Y., Tang M.C., Li M., Deng J., Wong N.K., and Ju J., 2021, Genome-directed discovery of tetrahydroisoquinolines from deep-sea derived Streptomyces niveus SCSIO 3406, The Journal of Organic Chemistry, 86(16): 11107-11116.)
https://doi.org/10.1021/acs.joc.1c00123
PMid:33770435