

Pharmacogenetics Factors its Applications in Drug Development

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DESCRIPTION

Pharmacogenetics is a field of study that explores the connection between an individual's genetic makeup and their response to drugs. This emerging branch of genetics has the potential of personalized medicine, where treatments and medications are specifically developed to a patient's genetic profile. By understanding how genetic variations influence drug metabolism, efficacy, and safety, pharmacogenetics has the potential to revolutionize healthcare, making treatments more effective and safer for each patient.

Pharmacogenetics is rooted in the principle that genetic differences among individuals can significantly impact how their bodies metabolize drugs. Genes encode enzymes and proteins responsible for drug Absorption, Distribution, Metabolism, and Excretion (ADME). Variations in these genes can affect drug pharmacokinetics, leading to differences in how individuals respond to medications.

One of the most well-known examples of pharmacogenetics is the gene *CYP2D6*, which encodes an enzyme responsible for metabolizing a wide range of drugs, including antidepressants and opioids. Some individuals have a functional *CYP2D6* gene, allowing them to metabolize these drugs rapidly, while others carry non-functional variants, leading to slower metabolism and potentially increased drug concentrations in their bodies. Understanding these genetic differences helps healthcare providers adjust drug dosages to match a patient's metabolic capacity, optimizing treatment outcomes while minimizing side effects.

Pharmacogenetics has Several Clinical Applications:

Oncology: In cancer treatment, pharmacogenetics can help identify the most effective chemotherapy agents for a specific patient's tumor based on their genetic profile. This approach, known as precision oncology, can lead to more targeted and less toxic therapies.

Cardiology: Genetic variations can influence an individual's response to cardiovascular medications. Pharmacogenetics is used to determine the optimal dosages of drugs like clopidogrel, which prevents blood clots, and warfarin, a widely used anticoagulant.

Psychiatry: Psychiatric medications, such as Selective Serotonin Reuptake Inhibitors (SSRIs) and antipsychotics, often require careful dosing adjustments based on a patient's genetic makeup. Understanding a patient's genetic predisposition can help avoid adverse reactions and improve treatment outcomes.

Anaesthesiology: The response to anaesthetics, muscle relaxants, and pain medications can vary based on genetic factors. Pharmacogenetics in anaesthesiology can contribute to safer and more effective perioperative care.

Infectious diseases: The effectiveness of antiviral and antibacterial drugs can be influenced by genetic factors. Identifying these variations is crucial in optimizing treatment for infectious diseases.

Pharmacogenetics mainly focuses on drug metabolism, which encompasses two primary phases: Phase I and Phase II.

Phase I metabolism: This phase involves the alteration of the drug's chemical structure to facilitate excretion. Cytochrome P450 (CYP) enzymes, encoded by various genes, play a pivotal role in Phase I metabolism. Genetic variations in these genes can lead to rapid or slow metabolism of specific drugs, affecting their efficacy and toxicity.

Phase II metabolism: Phase II metabolism involves the conjugation of drugs with small molecules, making them more water-soluble and ready for excretion. Genetic variations in genes like *UGT1A1*, which encodes an enzyme responsible for bilirubin metabolism, can impact the metabolism of drugs like irinotecan, used in cancer therapy.

CYP2C9 and warfarin: The anticoagulant warfarin is notorious for its narrow therapeutic window. Genetic variations in the *CYP2C9* gene and the *VKORC1* gene, which encodes the warfarin target, can significantly influence a patient's response to the drug. Developing the warfarin dosage based on a patient's genetic profile can help maintain the right level of anticoagulation without an increased risk of bleeding.

TPMT and Thiopurines: Thiopurine drugs, such as azathioprine and mercaptopurine, are used in autoimmune conditions and some cancers. Genetic variations in the TPMT gene can lead to the rapid metabolism of these drugs, increasing the risk of myelosuppression. Patients with TPMT variants may require lower doses to avoid severe side effects.

HER2 and Trastuzumab: Trastuzumab is an effective targeted therapy for breast cancer. However, its success depends on the presence of the HER2 gene. Patients with HER2-positive breast cancer respond well to trastuzumab, while those without this genetic marker may not benefit from the treatment.

While the potential of pharmacogenetics is immense, several challenges need to be addressed for its widespread implementation:

Genetic diversity: The genetic basis of drug responses is highly diverse, and not all genetic variants have been identified. Comprehensive databases and research efforts are required to catalog and understand the myriad genetic influences on drug metabolism.

Clinical integration: The incorporation of pharmacogenetics into clinical practice remains a challenge. Healthcare providers need adequate training and resources to interpret genetic test results and

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Received: 29-Sep-2023, Manuscript No. Jbclinphar-23-117803, Editor
Assigned: 02-Oct-2023, Pre QC No. Jbclinphar-23-117803 (PQ), **Reviewed:**
16-Oct-2023, QC No. Jbclinphar-23-117803, **Revised:** 23-Oct-2023, Manuscript
No. Jbclinphar-23-117803 (R), **Published:** 30-Oct-2023, DOI:10.37532/0976-
0113.14(5).312

Cite this article as: Tongi J. Pharmacogenetics Factors its Applications in
Drug Development. J Basic Clin Pharma.2023,14(5):312-313.

make informed treatment decisions.

Data privacy and ethics: As genetic information becomes more integrated into healthcare, issues of data privacy and ethical considerations must be carefully managed to protect patient confidentiality and rights.

Cost and accessibility: Genetic testing can be expensive and may not be accessible to all patients. Reducing costs and expanding access to pharmacogenetic testing is essential for its broader utilization. Despite

these challenges, the future of pharmacogenetics is potential. As technology advances and our understanding of genetics grows, we are moving closer to a healthcare model where medications and treatments are personalized to each patient's unique genetic makeup. This individualized approach to make medicine safer and more effective, with fewer adverse reactions and improved therapeutic outcomes. In the coming years, pharmacogenetics is expected to revolutionize how we approach healthcare, making treatments more targeted and efficient while minimizing the implications in drug therapy.