



Drug–Gene Interactions: Genetic Variation and Its Influence on Medication Response

Daniel Morgan *

Department of Pharmacogenomics, University of Toronto, Toronto, Canada

DESCRIPTION

Drug-gene interactions describe the relationship between genetic variation and the way an individual responds to a medicine. Differences in Deoxyribonucleic Acid (DNA) can affect drug absorption, distribution, metabolism, elimination, target binding, therapeutic activity and adverse reactions. Two patients receiving the same medicine at an identical dose may therefore experience different outcomes. Pharmacogenomics examines these genetic differences and provides information that can support appropriate medication selection and dosing. Genes involved in drug metabolism are among the most important factors in drug-gene interactions. The human body contains several enzyme systems that chemically modify medicines before they are eliminated. *Cytochrome P450* enzymes are particularly important because they metabolize a large number of pharmaceutical compounds. Genetic variants in *Cytochrome P450 2D6*, *CYP2C19*, *CYP2C9* and other genes can alter enzyme activity. Depending on the medication, reduced or increased enzyme activity may lead to higher or lower drug concentrations.

CYP2D6 is responsible for the metabolism of numerous medicines used in psychiatry, cardiology, neurology and pain management. Individuals may carry genetic variants associated with absent, reduced, normal, or increased enzyme activity. A person with very low *CYP2D6* activity may accumulate higher concentrations of a medicine that depends on this enzyme for clearance. In contrast, increased enzyme activity can result in faster removal and potentially lower exposure. *CYP2C19* also has important clinical relevance. This enzyme participates in the metabolism of several medicines, including certain antiplatelet agents and proton pump inhibitors. Genetic variation can influence the conversion of some medicines into active metabolites or affect their elimination. Genetic information may therefore be useful when selecting an appropriate medication in situations where established pharmacogenomic recommendations are available.

Drug transporters represent another important category of genes. Transport proteins regulate movement of medicines across cell membranes and influence intestinal absorption, tissue distribution and renal or hepatic elimination. Variants in transporter genes can modify the amount of a medicine reaching its intended site of action. Differences in transporter activity may consequently contribute to variation in treatment response or unwanted effects. Genes encoding drug targets can also influence medication outcomes. Medicines commonly act by binding to receptors, enzymes, ion channels, or signaling proteins. A genetic alteration that changes the structure or quantity of such a target can modify drug binding or downstream cellular responses. In oncology, genomic characteristics of tumor cells are frequently considered when selecting medicines directed against specific molecular targets.

Drug-gene interactions are particularly relevant to adverse drug reactions. Certain genetic variants are associated with an increased likelihood of serious reactions to specific medicines. One example involves Human Leukocyte Antigen (HLA) related genetic variation and selected immune-mediated reactions. Testing for relevant genetic markers before treatment can help identify individuals who may require an alternative medicine when clinical guidelines recommend such testing. Warfarin provides another well-known example of genetic influence on medication response. Variants in Vitamin K Epoxide Reductase Complex Subunit 1 (*VKORC1*) can affect sensitivity to warfarin, while *CYP2C9* variants can influence its metabolism. Other clinical factors, including age, diet, concurrent medicines and health status, also affect the appropriate dose. Genetic information can therefore form one part of a broader approach to dose selection.

Drug-gene interactions may also affect the activation of prodrugs. Some medicines are administered in a relatively inactive form and require enzymatic conversion into an active compound. If a genetic variant reduces the activity of the enzyme responsible for this conversion, the medicine may produce less

Correspondence to: Daniel Morgan, Department of Pharmacogenomics, University of Toronto, Toronto, Canada, E-mail: daniel.morgan@pharmgen.ca

Received: 30-May-2025, Manuscript No. JPP-25-32573; **Editor assigned:** 02-Jun-2025, PreQC No. JPP-25-32573 (PQ); **Reviewed:** 16-Jun-2025, QC No. JPP-25-32573; **Revised:** 23-Jun-2025, Manuscript No. JPP-25-32573 (R); **Published:** 30-Jun-2025, DOI: 10.35248/2153-0645.25.16.135

Citation: Morgan D (2025). Drug-Gene Interactions: Genetic Variation and Its Influence on Medication Response. J Pharmacogenom Pharmacoproteomics. 16:135.

Copyright: © 2025 Morgan D. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

therapeutic effect. Conversely, increased enzymatic activity may produce greater amounts of the active compound. Pharmacogenomic testing can be performed using different laboratory methods. Targeted genotyping can identify selected variants, while sequencing methods can examine larger regions of DNA. Genotyping arrays can assess numerous variants simultaneously. The appropriate method depends on the medicine, clinical purpose, number of variants involved, laboratory resources and required reporting time.

Interpreting genetic results requires careful consideration of the specific variant and medicine. A genetic change does not automatically indicate that a treatment will fail or cause toxicity.

Its clinical meaning depends on the gene, variant type, drug mechanism, patient's phenotype and available clinical evidence. Pharmacogenomic guidelines and curated databases can assist healthcare professionals in connecting genetic findings with medication recommendations. Drug-gene interactions are also influenced by factors outside the genome. Age, body composition, liver and kidney function, diet, smoking, alcohol consumption, disease conditions, adherence and interactions between medicines can alter drug exposure. Genetic information should therefore be considered together with these clinical factors rather than used as the only basis for treatment decisions.