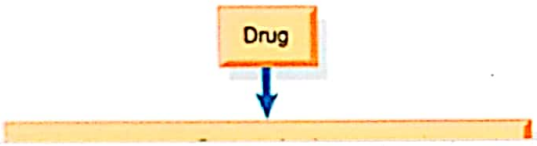
aggressive cancer. Genetic testing helps clinicians to provide personalized care and the most effective treatment based on the genetic signature of the tumor treatment, called *targeted therapy,* tries to match the treatment to the specific malfunctioning genes expressed in the tumor, or to selectively inhibit genetic factors that promote cancer growth (Genetests, 2015b).

Pharmacogenomics

The difference between genetics and genomics, described earlier in this chapter, corresponds to the terms *pharmacogenetics* and *pharmacogenomics,* which combine pharmacology and genetics or genomics. Pharmacogenetics refers to the study of the effect of variations in a single gene on drug response and toxicity. The field of pharmacogenetics has evolved so that it has become a broader genomic-based approach that recognizes the interaction of multiple genes and the environment on drug response. Pharmacogenomics refers to the study of the combined effect of variations in many genes on drug response and toxicity and involves methods that rapidly identify which genetic variations influence a drug's effect. Pharmacogenomics involves the search for genetic variations associated with medication metabolism and efficacy, with the goal of tailoring treatment to each individual's genomic makeup (NLM, 2015d).

It has long been known that patients differ in their response to medications. The genetic and genomic variations in drug metabolism account largely for the differences in drug response and drug-related toxicities. Drug metabolism involves genetically controlled protein/enzyme activity for absorption, distribution, drug–cell interaction, inactivation, and excretion—metabolic processes that are known as pharmacokinetics. The cytochrome *P450* (CYP) genes play a key role in the pharmacokinetic process of drug metabolism (Johnson, 2013). Once a drug reaches its target cell, other genes such as those regulating cell receptors and cell signaling control the drug's effect. This process is known as pharmacodynamics. Single genes may affect drug response. More commonly, drug response involves the interaction of multiple genes, the host, and the effects of other drugs. Figure 8-12 is a schematic display of the genetic and genomic influences on drug metabolism and treatment effect.



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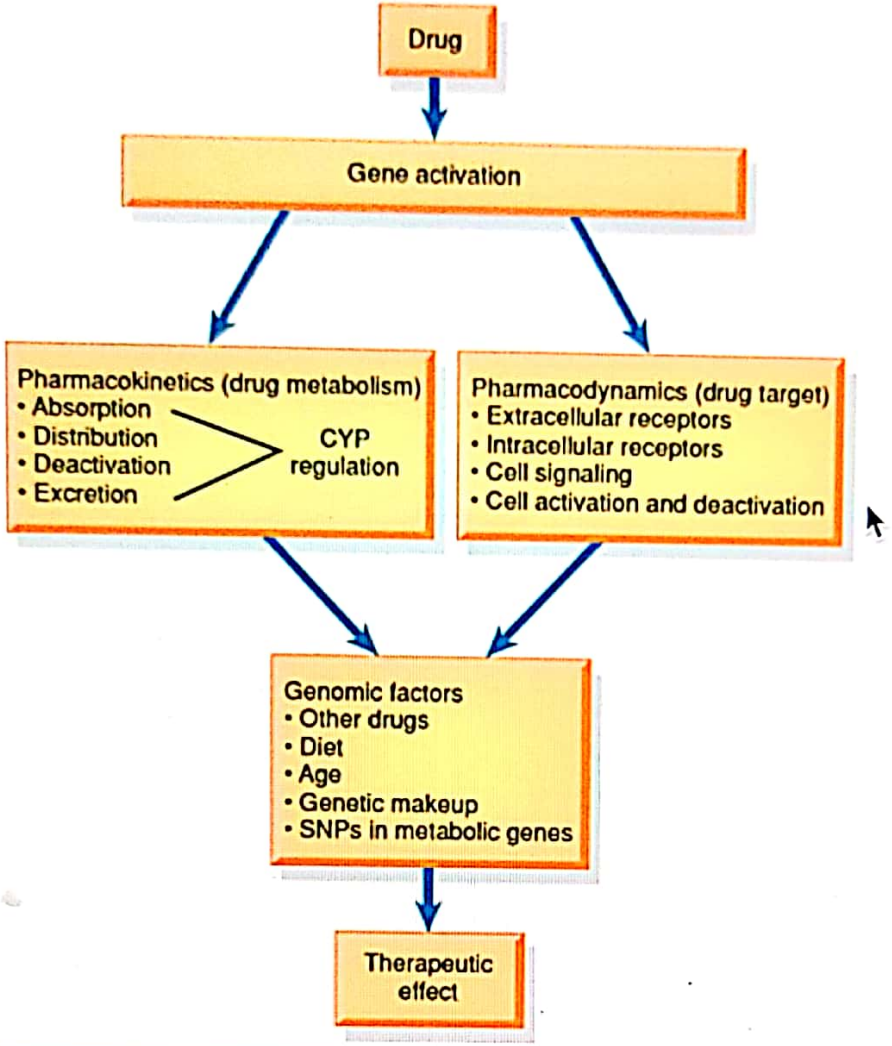

SNPs, described earlier, are common genetic variations that occur most frequently throughout the human genome and often contribute to variations in enzymatic activity that affect drug metabolism. The CYPs, a family of enzymes, play a key role in the pharmacokinetic process of drug metabolism. More than 300 variations (SNPs) of genes that control CYP activation and deactivation have been identified. Researchers have created a catalog of CYP variations because of their role in drug metabolism (HUGO Gene Nomenclature Committee, 2015).

Four classes of CYP metabolic activity levels have been identified based on a person's CYP genotype and the corresponding drug response: (1) poor metabolizers, (2) intermediate metabolizers, (3) extensive metabolizers, and (4) ultrarapid metabolizers. Poor metabolizers have a specific SNP variation in a CYP gene that causes little or no function, resulting in very little or no drug metabolism and higher blood levels of active drug because the drug cannot be absorbed or excreted. Conversely, ultrarapid metabolizers have SNP variations that cause increased enzyme activity, resulting in rapid absorption, distribution, and excretion of a drug. Ultrarapid metabolizers have lower drug blood levels, usually with inadequate therapeutic response or longer treatment time to achieve therapeutic results. Both poor metabolizers and ultrarapid metabolizers are predisposed to adverse drug reactions. Poor metabolizers may have adverse effects or toxicities from high blood levels of drugs and need a lower dose, whereas ultrarapid metabolizers have inadequate treatment response because of lower drug blood levels and may need a higher dose or more frequent dosing. Table 8-6 shows examples of differences in drug response in poor versus ultrarapid metabolizers. Intermediate metabolizers have reduced enzyme activity levels and metabolize drugs at a slower than normal rate. Because intermediate metabolizers have some enzyme activity, they may have differences in treatment response. Extensive metabolizers have normal enzyme activity levels and normal drug metabolism. Differences in metabolism of other medications occur with other genetic variations.

TABLE 8-6 Examples of Clinical Effects of Cytochrome P450 Enzyme Variations

	Effects

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		Effects	
Enzyme	**Drug**	**Poor Metabolizer**	**Ultrarapid Metabolizer**
CYP2C9	Warfarin (Coumadin)	Bleeding	Longer treatment time to achieve stable dosing
	Phenytoin (Dilantin)	Ataxia	Not established
CYP2C19	Diazepam (Valium)	Sedation	Poor response
	Omeprazole (Prilosec)	Drug-induced side effects (e.g., taste perversion)	
CYP2D6	Tricyclic antidepressants	Cardiotoxicity	No response to recommended dose; need 10-fold increase in dose
	Selective serotonin reuptake inhibitors	Nausea	Not established
	Antipsychotics	Parkinson-like effects	Longer treatment time and higher drug costs

Adapted from Genetests. (2015a). Retrieved on 6/30/2015 at: www.genetests.org/; HUGO Gene Nomenclature Committee. (2015). *Cytochrome P450*. Retrieved on 7/9/2015 at: www.genenames.org/cgi-bin/search?search_type=all&search=cytochrome+P450&submit=Submit; Johnson, J. A. (2013). Pharmacogenetics in clinical practice: How far have we come and where are we going? *Pharmacogenomics*, 14(7), 835–843.

Nurses have traditionally monitored and reported drug response and drug adverse effects. Clinical guidelines for pharmacogenomic testing for several drugs, such as warfarin (Coumadin), abacavir (Ziagen), trastuzumab (Herceptin), mercaptopurine (Purinethol), and irinotecan (Camptosar), are currently being tested (NIH, 2014c). Pharmacogenomic testing offers patients and health care providers more information about drug dosage, time to achieve response, and risk

Selective serotonin reuptake inhibitors	Nausea	Recommended dose, need 10-fold increase in dose
Antipsychotics	Parkinson-like effects	Not established
		Longer treatment time and higher drug costs

Adapted from Genetests. (2015a). Retrieved on 6/30/2015 at: www.genetests.org/; HUGO Gene Nomenclature Committee. (2015). *Cytochrome P450*. Retrieved on 7/9/2015 at: www.genenames.org/cgi-bin/search?search_type=all&search=cytochrome+P450&submit=Submit; Johnson, J. A. (2013). Pharmacogenetics in clinical practice: How far have we come and where are we going? *Pharmacogenomics*, 14(7), 835–843.

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