Pharmacogenomics Gene Function

GENE	GENE FUNCTION	HEALTH CONDITIONS
ANKK1	Antipsychotic agents have been associated with hyperprolactinemia and tardive dyskinesia (TD). Patients with the AA genotype may have increased risk of side effects including hyperprolactinemia and weight gain, but decreased risk of tardive dyskinesia, during treatment with antipsychotic drugs as compared to patients with the AG or GG genotype. Dopamine, a key neurotransmitter that controls cognition, emotion, locomotor activity, and other endocrine functions, exerts its action by binding to five different receptors, including the dopamine D2 receptor (DRD2). Dysregulation of dopaminergic signal transmission is found in many pathological conditions such as Parkinson's disease and schizophrenia, and compounds that act as DRD2 agonists or antagonists are used to treat these conditions. Therapeutic and adverse events of several antipsychotics both result from their high affinity to antagonize DRD2. Within the several genetic variants of DRD2 that are relevant to disease susceptibility and therapeutic response, the Taq1A (32806C>T; rs1800497) is one of the most studied.	• Psychiatry
APOE	The APOE gene provides instructions for making a protein called apolipoprotein E. This protein combines with fats (lipids) in the body to form molecules called lipoproteins. Lipoproteins are responsible for packaging cholesterol and other fats and carrying them through the bloodstream. Maintaining normal levels of cholesterol is essential for the prevention of disorders that affect the heart and blood vessels (cardiovascular diseases), including heart attack and stroke. There are at least three slightly different versions (alleles) of the APOE gene. The major alleles are called e2, e3, and e4. The most common allele is e3, which is found in more than half of the general population.	• Alzheimer Disease • Age-Related Hearing Loss • Age-Related Macular Degeneration • Cardiovascular Diseases
COMT	The COMT gene provides instructions for making an enzyme called catechol-O-methyltransferase. In the brain, catechol-O-methyltransferase helps break down certain chemical messengers called neurotransmitters. These chemicals conduct signals from one nerve cell to another. Catechol-O-methyltransferase is particularly important in an area at the front of the brain called the prefrontal cortex, which organizes and coordinates information from other parts of the brain. This region is involved with personality, planning, inhibition of behaviors, abstract thinking, emotion, and working (short-term) memory. To function efficiently, the prefrontal	• 22q11.2 Deletion Syndrome • Alcohol Use Disorder • Fibromyalgia • Opioid Addiction • Schizophrenia • Bipolar Disorder • Panic Disorder • Anxiety

	cortex requires signaling by neurotransmitters such as dopamine and norepinephrine. Catechol-O-methyltransferase helps maintain appropriate levels of these neurotransmitters in this part of the brain.	• Obsessive-Compulsive Disorder (OCD), • Eating Disorders • Attention-Deficit/Hyperactivity Disorder (ADHD)
CYP1A2	The cytochrome P450 1A2 (CYP1A2) is responsible for metabolizing 8-10% of commonly used drugs as well as natural compounds such as caffeine. More than 20 different alleles have been characterized for the CYP1A2 gene, and some have been shown to affect enzyme activity and its sensitivity towards inducers. Individuals are predicted to have CYP1A2 normal, intermediate, or poor metabolic capacity, with high, possible, or low inducibility depending on their genotype. CYP1A2 genotype can help identify patients with high or low sensitivity to inducing agents, especially those released during smoking. The clinical relevance of this sensitivity becomes important in patients who are smokers or who have quit smoking. Drugs used in the management of pain and various psychiatric conditions are metabolized extensively by CYP1A2 and are sensitive to its function.	• Psychiatry • Pain Management
CYP2B6	CYP2B6 encodes a member of the cytochrome P450 superfamily of enzymes. The cytochrome P450 proteins are monooxygenases which catalyze many reactions involved in drug metabolism and synthesis of cholesterol, steroids and other lipids. This protein localizes to the endoplasmic reticulum and its expression is induced by phenobarbital. The enzyme is known to metabolize some xenobiotics, such as the anti-cancer drugs cyclophosphamide and ifosphamide. A cytochrome P450 monooxygenase involved in the metabolism of endocannabinoids and steroids (PubMed:21289075, PubMed:12865317).	• Opioid Addiction • Efavirenz Response
CYP2C8	The cytochrome P450 proteins are monooxygenases which catalyze many reactions involved in drug metabolism and synthesis of cholesterol, steroids and other lipids. This protein localizes to the endoplasmic reticulum and its expression is induced by phenobarbital. The enzyme is known to metabolize many xenobiotics, including the anticonvulsive drug mephenytoin, benzo(a)pyrene, 7-ethyoxycoumarin, and the anti-cancer drug taxol. A cytochrome P450 monooxygenase involved in the metabolism of various	• Drug Metabolism

	endogenous substrates, including fatty acids, steroid hormones and vitamins (PubMed:7574697, PubMed:11093772, PubMed:14559847, PubMed:15766564, PubMed:19965576).	
CYP2C9	The CYP2C9 gene provides instructions for making an enzyme that is found in a cell structure called the endoplasmic reticulum, which is involved in protein processing and transport. The CYP2C9 enzyme breaks down (metabolizes) compounds including steroid hormones and fatty acids. The CYP2C9 enzyme also plays a major role in breaking down the drug warfarin, which thins the blood and prevents blood clots from forming. This enzyme also assists in metabolizing other drugs such as ibuprofen, which reduces inflammation.	• Warfarin Sensitivity
CYP2C19	The CYP2C19 enzyme plays a role in the processing or metabolizing of at least 10 percent of commonly prescribed drugs, including a drug called clopidogrel (also known as Plavix). Clopidogrel is an antiplatelet drug, which means that it prevents blood cell fragments called platelets from sticking together (aggregating) and forming blood clots. The CYP2C19 enzyme converts clopidogrel to its active form, which is necessary for the drug to function in the body. The active drug then stops (inhibits) a receptor protein known as P2RY12 that is found on the surface of platelets. During clot formation, the P2RY12 receptor protein helps platelets cluster together to form a clot in order to seal off damaged blood vessels and prevent blood loss.	• Clopidogrel Resistance • Cardiovascular Disease • Psychiatric Disorders • Seizure Disorders
CYP2D6	This protein localizes to the endoplasmic reticulum and is known to metabolize as many as 25% of commonly prescribed drugs. Its substrates include antidepressants, antipsychotics, analgesics and antitussives, beta adrenergic blocking agents, antiarrythmics and antiemetics. The gene is highly polymorphic in the human population; certain alleles result in the poor metabolizer phenotype, characterized by a decreased ability to metabolize the enzyme's substrates. Some individuals with the poor metabolizer phenotype have no functional protein since they carry 2 null alleles whereas in other individuals the gene is absent. This gene can vary in copy number and individuals with the ultrarapid metabolizer phenotype can have 3 or more active copies of the gene.	• Disorder due cytochrome p450 CYP2D6 variant
CYP3A4	The cytochrome P450 3A4 and 3A5 (CYP3A4 and CYP3A5) account for 40-80% of total CYP in human liver and intestine, respectively. Most importantly, CYP3A enzymes metabolize 50% of commonly used drugs. The CYP3A4*1 B variant is the most studied, and results in an enzyme with a moderately decreased activity. It occurs in	• Pain Management • Psychiatric Conditions • Cardiovascular Disease

	50% of African- Americans, 3-5% of Caucasians, and <1% of Asians. The CYP3A4*2, *3, *12, and *17 are also considered decreased activity alleles. The CYP3A4 *22 allele has been characterized as a decreased function allele that can be clinically relevant and associated with a decreased clearance of certain substrates.	
CYP3A5	The cytochrome P450 proteins are monooxygenases which catalyze many reactions involved in drug metabolism and synthesis of cholesterol, steroids and other lipids. The encoded protein metabolizes drugs as well as the steroid hormones testosterone and progesterone. Expression of this gene is widely variable among populations, and a single nucleotide polymorphism that affects transcript splicing has been associated with susceptibility to hypertensions.	• Pain Management • Psychiatric Conditions • Cardiovascular Disease
Factor II	The F2 gene provides instructions for making a protein called prothrombin (also called coagulation factor II). Coagulation factors are a group of related proteins that are essential for normal blood clotting (hemostasis). After an injury, clots protect the body by sealing off damaged blood vessels and preventing further blood loss. Thrombin is also thought to be involved in cell growth and division (proliferation), tissue repair, and the formation of new blood vessels.	• Prothrombin Deficiency • Prothrombin Thrombophilia
Factor V	The F5 gene provides instructions for making a protein called coagulation factor V. Coagulation factors are a group of related proteins that make up the coagulation system, a series of chemical reactions that form blood clots. After an injury, clots seal off blood vessels to stop bleeding and trigger blood vessel repair.	• Rare Bleeding Disorder Called Factor V Deficiency • Factor V Leiden Thromobophilia
Factor VII	The F7 gene provides instructions for making a protein called coagulation factor VII. Coagulation factors are a group of related proteins that are involved in the coagulation system, which is a series of chemical reactions that form blood clots. After an injury, clots seal off blood vessels to stop bleeding and trigger blood vessel repair.	• Factor VII Deficiency Almost 300 mutations in the F7 gene have been found to cause a rare bleeding disorder called factor VII deficiency. This disorder commonly causes nosebleeds, easy bruising, bleeding of the gums, and prolonged or excessive bleeding following surgery or physical injury. In severe cases, life-

		threatening episodes of bleeding inside the skull or gastrointestinal tract can occur. Some affected individuals have no bleeding problems.
HTR2A	This gene encodes one of the receptors for serotonin, a neurotransmitter with many roles. Mutations in this gene are associated with susceptibility to schizophrenia and obsessive-compulsive disorder, and are also associated with response to the antidepressant citalopram in patients with major depressive disorder (MDD). MDD patients who also have a mutation in intron 2 of this gene show a significantly reduced response to citalopram as this antidepressant downregulates expression of this gene.	• Alcohol Dependence • Schizophrenia • Obsessive-Compulsive Disorder • Major Depressive Disorder • Seasonal Affective Disorder • Anorexia Nervosa 1 • Fibromyalgia
HTR2C	HTR2C gene encodes a receptor that responds to the endogenous neurotransmitter serotonin. This serotonin receptor is a G protein-coupled receptor with wide distribution across the central and peripheral nervous systems in humans. It mediates excitatory neurotransmission via serotonin. Serotonin signaling regulates mood, anxiety, feeding, and many other behaviors, as well as dopamine and norepinephrine release in certain areas of the brain. Genetic variation in the HTR2C gene in known to be partially involved in pathogenesis of some psychiatric disorders and adverse effects of antipsychotic medications.	• Psychiatric Disorders
MTHFR	The MTHFR gene provides instructions for making an enzyme called methylenetetrahydrofolate reductase. This enzyme plays a role in processing amino acids, the building blocks of proteins. Methylenetetrahydrofolate reductase is important for a chemical reaction involving the vitamin folate (also called vitamin B9). Specifically, this enzyme converts a form of folate called 5,10-methylenetetrahydrofolate to a different form of folate called 5-methyltetrahydrofolate. This is the primary form of folate found in blood, and is necessary for the multistep process that converts the amino acid homocysteine to another amino acid, methionine. The body uses methionine to make proteins and other important compounds.	• Homocystinuria • Age-Related Hearing Loss • Alopecia Areata. • Anencephaly • Spina Bifida
OPRM1	The OPRM1 gene provides instructions for making a protein called the mu (μ) opioid receptor. Opioid receptors are part of the endogenous opioid system, which is the body's internal system for regulating pain, reward, and addictive behaviors.	• Alcohol Use Disorder • Opioid Addiction
RYR1	The RYR1 gene provides instructions for making a protein called ryanodine receptor 1.	• Central Core Disease (CCD)

	This protein is part of a family of ryanodine receptors, which form channels that transport positively charged calcium atoms (ions) within cells. Channels made with the ryanodine receptor 1 protein play a critical role in muscles used for movement (skeletal muscles).	• Congenital Fiber-Type Disproportion • Multiminicore Disease • Malignant Hyperthermia • Centronuclear Myopathy
SLCO1B1	The SLCO1B1 gene provides instructions for making a protein called organic anion transporting polypeptide 1B1, or OATP1B1. This protein is found in liver cells; it transports compounds from the blood into the liver so that they can be cleared from the body. For example, the OATP1B1 protein transports bilirubin, which is a yellowish substance that is produced when red blood cells are broken down. In the liver, bilirubin is dissolved in a digestive fluid called bile and then excreted from the body. The OATP1B1 protein also transports certain hormones, toxins, and drugs into the liver for removal from the body. Drugs transported by the OATP1B1 protein include statins, which are used to treat high cholesterol; heart disease medications; certain antibiotics; and some drugs used for the treatment of cancer.	• Rotor Syndrome • Reduced Ability To Process Certain Drugs, Including Statins
UGT1A1	The protein produced from the UGT1A1 gene, called the bilirubin uridine diphosphate glucuronosyl transferase (bilirubin-UGT) enzyme, is the only enzyme that glucuronidates bilirubin, a substance produced when red blood cells are broken down. This enzyme converts the toxic form of bilirubin (unconjugated bilirubin) to its nontoxic form (conjugated bilirubin), making it able to be dissolved and removed from the body.	• Warfarin Resistance • Crigler-Najjar Syndrome • Gilbert Syndrome • Jaundice In Newborns • Transient Familial Neonatal Hyperbilirubinemia
VKORC1	The VKORC1 gene provides instructions for making a vitamin K epoxide reductase enzyme. The VKORC1 enzyme helps turn on (activate) clotting proteins in the pathway that forms blood clots. Specifically, the VKORC1 enzyme converts one form of vitamin K into a different form of vitamin K that assists in activating clotting proteins.	• Warfarin Resistance • Warfarin Sensitivity