Understanding pharmacogenomics: Clinician resources and references

Misty L. Gonzalez, PharmD, BCPP[1]
Jeffrey R. Bishop, PharmD, MS, BCPP[2]

[1]SIUE School of Pharmacy
[2]UIC College of Pharmacy

This issue of the Mental Health Clinician is dedicated to Pharmacogenomics in Clinical Practice and Research. Pharmacogenomics is a rapidly advancing field of interest for clinicians, patients, and government initiatives. Pharmacists, as drug information experts, are uniquely equipped to incorporate pharmacogenomic information into clinical practice to keep pace with growing interest in personalized medicine. Provided below are key resources clinicians may reference for more information on basics and advances in pharmacogenomics (Table 1). Also provided is a table of definitions of common terminology which may aid clinicians in understanding and interpreting literature or tests (Table 2).

Table 1. Helpful resources for further information*

Website or reference and description of the resource
http://www.ncbi.nlm.nih.gov/About/primer/index.html National Center for Biotechnology Information (NCBI) science primer site with links to basic reviews of some concepts presented in this lesson.
http://ghr.nlm.nih.gov/ National Library of Medicine Genetics reference site with links to basic genetics information and glossary of genetic terms.
http://www.genome.gov/10002096 National Human Genome Research Institute glossary of genetic terms.
http://www.pharmgkb.org/ The Pharmacogenomics knowledgebase (PharmGKB): contains information on how drugs and genetic polymorphisms affect clinical outcomes. The search engine is easy to use and gives annotated results with more details if desired.
http://www.pharmgkb.org/search/geneticTestList.action PharmGKB list of pharmacogenetic testing kits or devices.
http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm083378.htm Summary of FDA-approved medications with pharmacogenetics information in the product labeling.
http://guideline.gov/content.aspx?f=rss&id=15665 Agency for Healthcare Research and Quality link to current pharmacogenetic testing recommendations.
http://www.egappreviews.org/resources/links.htm The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) working group website which provides a systematic, evidence-based review of genetic tests.

*Information contained in this table is not for promotional purposes. Websites and resources are included that allow pharmacists rapid access to references or product/test information sheets.

Table 2. Pharmacogenomics Glossary

Term	Definition
Allele	One of the variant forms of a gene at a particular locus, or location, on a chromosome. Different alleles produce variation in inherited characteristics such as hair color or blood type. In an individual, one form of the allele (the dominant one) may be expressed more than another form (the recessive one).
Autosome	Any chromosome other than a sex chromosome. Humans have 22 pairs of autosomes.
Codon	Three bases in a DNA or RNA sequence which specify a single amino acid.
Exon	The region of a gene that contains the code for producing the gene's protein. Each exon codes for a specific portion of the complete protein. In some species (including humans), a gene's exons are separated by long regions of DNA (called introns or sometimes "junk DNA") that have no apparent function.
Epigenetics	The study of heritable changes in gene expression due to differences in methylation or histone deacetylation. DNA is organized into protein packages called histones. The structure of this packaging may make DNA more or less accessible for transcription in a given part of the body and is a source of genetic "variability" that is not dependent on the sequence of DNA.
Extensive metabolizer	An individual who has at least one full functioning allele of a gene coding for a drug metabolizing enzyme.
Gene	A functional and physical unit of inherited deoxyribonucleic acid (DNA) sequence that encodes the information for production of a functional polypeptide chain or a ribonucleic acid (RNA) molecule.
Genotype	The genetic identity of an individual at a given genetic location. The combination of alleles at a given locus.

Term	Definition
Haplotype	Multiple genetic variations in a given gene (i.e., more than one polymorphism) that are inherited as a single unit.
Heterozygous	Possessing two different copies of a particular gene, one allele inherited from each parent.
Homozygous	Possessing two identical copies of a particular gene, one allele inherited from each parent.
Intermediate metabolizer	An individual with genotypes coding for no enzyme function from one allele and reduced activity from the other allele.
Intron	A noncoding sequence of DNA that is initially copied into RNA but is cut out of the final RNA transcript.
Locus	The place on a chromosome where a specific gene is located, a kind of address for the gene.
Microarray (DNA)	A way of characterizing large numbers of genetic polymorphisms simultaneously. The method uses a robot to precisely apply tiny droplets containing small sequences of DNA with known genetic variations to glass slides. Researchers then attach fluorescent labels to DNA fragments from the sample being studied. The labeled probes are allowed to bind to complementary DNA strands on the slides. The slides are put into a scanning microscope that can measure the brightness of each fluorescent dot; brightness reveals how much of a specific DNA fragment is present, an indicator of whether a polymorphism is present in a given individual.
Mutation	A permanent structural alteration in DNA. In most cases, DNA changes either have no effect or cause harm, but occasionally a mutation can improve an organism's chance of surviving and passing the beneficial change on to its descendants.
Nucleotide	One of the structural components, or building blocks, of DNA and RNA. A nucleotide consists of a base (one of four chemicals: adenine, thymine, guanine, and cytosine) plus a molecule of sugar and one of phosphoric acid.
Pharmacogenetics	The study of how genetic variation in a gene affects an individual's outcome from drug therapy.
Pharmacogenomics	The study of how genetic variation in many genes affects an individual's outcome from drug therapy.

Term	Definition
Phenotype	The observable traits or characteristics of an organism, for example hair color, weight, or the presence or absence of a disease. Phenotypic traits are not necessarily genetic.
Polymorphism	A common variation in the sequence of DNA among individuals. Generally defined as a variant which is present in at least 1% of the population.
Poor metabolizer	An individual with genotypes coding for no or very little enzyme function from both alleles
Sex Chromosome	The X and Y sex chromosomes.
Single Nucleotide Polymorphism (SNP)	Common variations that occur in human DNA at a frequency of about one every 1,000 bases. They involve the alteration of single bases (i.e., insertion of an extra base, deletion of a base, substitution of a base). SNP is pronounced "snip".
Transcription	The process of converting DNA to RNA.
Translation	The process of protein production using an RNA transcript as a template.
Ultra rapid metabolizer	An individual who has excess enzymatic activity due to multiple copies (3-13) of functional alleles from gene duplication (most commonly seen with CYP2D6)

Tables recreated with permission of Jeffrey R. Bishop, PharmD, MS, BCPP.

How to cite this editor-reviewed article
Gonzalez ML, Bishop JR. Understanding pharmacogenomics: Clinician resources and references. Ment Health Clin [Internet]. 2012;1(9):205-6. Available from: http://dx.doi.org/10.9740/mhc.n99194.