

# Pharmacogenomics: Applications to Patient Care

## Learning Objectives

### Module 1

#### Principles of Genetic Medicine

Authors, Ronald G. Davidson and Joseph D. McInerney

1. Discuss the central assumptions of genetics and genetic medicine.
2. Recognize and apply the basic vocabulary of genetics and the basic principles of inheritance.
3. Describe and apply the basic principles of molecular biology as they relate to genetic medicine.
4. Explain how to access new genetic technologies as appropriate.
5. Identify the ethical, legal and social issues that arise from the application of genetic knowledge and technology.

#### Applied Molecular and Cellular Biology

Author, Taimour Y. Langaee

1. Define the cellular functions of the nucleus and cytoplasmic organelles.
2. Describe the effects of regulatory sequences and proteins on transcription.
3. Study a timeline of the events in RNA processing and mRNA translation.
4. Identify the role of cell signaling molecules, receptors, and intracellular signaling in cell signal transduction.
5. Apply molecular and cellular biology principles to explain the possible genetic basis of variability in drug responses.

#### Analysis of the Human Genome and Proteome

Author, H. Trent Spencer

1. Explore the technology and methodology driving nucleic acid- and protein-based discoveries and understand the potential impact of these discoveries on drug therapy.
2. Identify the technologies driving advances in the field of gene therapy.
3. Apply new deoxyribonucleic acid-based methodology to the analysis of specific disease states.
4. Describe the realized versus potential benefits of genome and proteome analysis.

#### Bioinformatics

Author, Austin L. Hughes

1. Determine the major resources and methods in bioinformatics.
2. Explore the kinds of questions that can be addressed by bioinformatics studies.
3. Explain how bioinformatics studies apply to pharmacogenomics.
4. Explain how bioinformatics studies apply to pharmacology in general.
5. Analyze studies that apply basic bioinformatics techniques.

#### Applications of Genomics to Health Care

Authors, Daren L. Knoell and Wolfgang Sadee

1. Distinguish how independently occurring polymorphisms could result in development of a complex disease.
2. Explore how individual patient genomic information will change the way pharmacists diagnose, classify, and treat a common disease such as hypertension.
3. Identify three major areas where pharmacists would be involved in using genomic screening to help patients.

Ethical Issues in Genomics

Author, William L. Allen

1. Identify the historical roots and dangers of genetic discrimination, which in part explain the anxiety associated with ethical issues arising from advances in genetic science and technology.
2. Explain how the traditional obligations of medical ethics, such as informed consent and confidentiality, are applied in the context of clinical genetics.
3. Discuss what new ethical, legal, and social challenges are posed by the development of functional genomics ensuing from the Human Genome Initiative.
4. Assess the risks of genetic discrimination.
5. Examine the scope and limitations of current regulatory protections against genetic discrimination and the professional obligation to inform patients of the risks of genetic discrimination that may result from submitting to a genetic test.

## **Module 2**

Pharmacogenetics: A Historical Perspective

Author, Werner Kalow

1. Recognize the historical background of pharmacogenetics.
2. Understand why some early observations created pharmacogenetics as a new science.
3. Understand how can one relate "phenotypes" and "genotypes."
4. Compare old and contemporary discoveries in pharmacogenetics.

Pharmacogenetics of Oxidative Drug Metabolism and Its Clinical Applications

Author, Reginald Frye

1. Apply knowledge to explain or predict the role of genetic variability in drug targets on drug efficacy and toxicity.
2. Demonstrate an understanding of the complexity of most drug responses (i.e. the drug response cascades), and the influence this has on the contribution of genetic variability to drug response.
3. Evaluate the current and future potential applications of drug target pharmacogenetics to individualization of drug therapy.

Phase II Drug Metabolism Pharmacogenetics and Its Clinical Implications

Author, Reginald Frye

1. Understand the role of genetic variability in phase II metabolizing enzymes on drug pharmacokinetics, efficacy, and toxicity.
2. Describe the molecular basis for a genetic variation influencing the functional activity of phase II metabolizing enzymes.
3. Identify the areas of current and future potential applications of phase II metabolizing enzyme pharmacogenetics to tailor drug therapy.

Drug Transporter Pharmacogenetics

Author, Deanna L. Kroetz

1. Discuss the cellular and intracellular localization, substrate specificity and proposed role of transporters in the absorption, distribution and elimination of drugs.
2. Describe clinical data supporting a role for efflux transporters in bioavailability, CNS exposure and tumor resistance.
3. Discuss the importance of neurotransmitter transporters as drug targets.
4. Describe the degree of genetic variation in drug transporters.
5. Discuss the functional implications of genetic variation in drug transporters and how this might affect the efficacy and safety of drugs.
6. Discuss the potential for prediction of altered drug response based on drug transporter genotypes.

Drug Target Pharmacogenetics and Pharmacogenomics

Author, Julie A. Johnson

1. Apply knowledge to explain or predict the role of genetic variability in drug targets on drug efficacy and toxicity.
2. Demonstrate an understanding of the complexity of most drug responses (i.e., the drug response cascades), and the influence this has on the contribution of genetic variability to drug response.
3. Evaluate the current and future potential applications of drug target pharmacogenetics to individualization of drug therapy.

Pharmacogenomics in Drug Discovery and Drug Development

Author, John M. Valgus

1. Describe the risks and values that genomic information brings to the drug discovery and development process.
2. Understand how pharmacogenomics and genomic technology will lead to an increased number of drug targets.
3. Identify how pharmacogenomics could be implemented and used in each phase of pre-clinical and clinical trials.
4. Identify key regulatory issues that pharmacogenomics raises in the drug development process.

Societal and Ethical Issues in Pharmacogenomics

Author, Pilar N. Ossorio

1. Understand that modern anthropology and genetics show that there are no genetically distinguishable human racial groups.
2. Realize race is relevant in biomedical research because the social interactions that create race can have profound affects on human health.
3. Discuss why several different conceptions of justice support the twin propositions that researchers should pay attention to race, and that researchers should be very careful about attributing observed differences in biomedical outcomes to genetic differences between races.
4. Understand that several different conceptions of justice, as well as the human subjects research regulations, generate ethical imperatives for researchers to conduct and report their research in a manner that minimizes harm to subjects.

### **Module 3**

Oncology/Hematology  
Author, Jill M. Kolesar

1. Describe the role of pharmacogenetics in carcinogenesis
2. Understand the role of genetic mutations in the diagnosis and prognosis of cancer and hematological disorders
3. Describe the clinical use of pharmacogenomics and pharmacogenetics in oncology pharmacotherapy
4. Assess the use of pharmacogenomics in developing in new antineoplastic agents

Infectious Diseases  
Author, P. David Rogers

1. Describe host genetic factors that contribute to susceptibility to infectious diseases.
2. Analyze the role of genomics in understanding the virulence of pathogenic organisms.
3. Recognize the contributions and utility of genomics to our understanding of the host-pathogen relationship.
4. Evaluate the application of genomics to the anti-infective-drug discovery and development process.
5. Discuss the potential clinical utility of pharmacogenomics in the management of infectious diseases.
6. Describe the role of genomics in vaccine development.

Cardiovascular  
Author, Larisa M. Humma

1. Apply clinical data to predict the effects of drug metabolizing, drug transporter, and drug target gene polymorphisms on cardiovascular drug responses.
2. Assess the potential impact of variations in genes influencing cardiovascular disease progression on responses to cardiovascular drugs.
3. Identify from the available literature how genetic variability might influence responses to cardiovascular drugs, including drugs that have not been specifically

studied.

4. Evaluate the ultimate effects of a combination of polymorphisms in drug metabolizing, drug transporter, drug target, and/or disease progression genes on cardiovascular drug response.
5. Explore the potential improvement in cardiovascular disease management that may arise from the application of pharmacogenomics.

#### Central Nervous System/Psychiatry

Authors, Vicki L. Ellingrod and Jeffrey R. Bishop

1. Discuss the role of pharmacogenetics in the treatment of patients with central nervous system disorders, including mental illness.
2. Describe how the use of DNA arrays can assist in the discovery and target selection of new drugs for the treatment of CNS disorders.

#### Respiratory

Author, John Lima

1. Characterize the pharmacogenetic influence on the bronchodilatory response.
2. Compare  $\alpha$ 1AT deficiency with other complex forms of COPD.
3. Describe why the  $\beta$ 2 adrenergic receptor haplotype may be more important than individual SNPs found in the gene.
4. Understand the contemporary gene therapy strategies designed to correct cystic fibrosis.

#### Transplants

Authors, Gilbert J. Burckart and HongXia Zheng

1. Describe the current understanding of clinical pharmacogenomics in the pharmacotherapy of transplant patients.
2. Describe the candidate genes, outcome markers, and analysis of this information in transplant patients.
3. Discuss the future use of clinical pharmacogenomic data in individualizing immunosuppressive therapy for transplant patients.