# SYMPOSIUM

# Progress in Pharmacogenomics and Its Promise for Medicine

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**Pharmacogenomics addresses the impacts of diverse and multiple genes in populations as determinants of responses of individual patients to drugs. The field has its roots in basic science, and is pivotal in drug development, elucidation of therapeutic efficacy, and constraining the risks of adverse drug reactions. Regulatory agencies are relying increasingly on pharmacogenomics for identification of patients who are particularly likely to benefit from treatment with specific agents and exclusion of those at risk of adverse drug reactions. Practical applications of pharmacogenomics already abound particularly in the use of drugs acting on the central nervous system and on the cardiovascular system. The Society for Experimental Biology and Medicine (SEBM) is proud and pleased to have devoted its 2008 symposium, presented at the annual Experimental Biology meeting in San Diego on April 6, 2008, to advances in pharmacogenomics with emphasis on drug development, regulatory agency considerations, and clinical applications.** Exp Biol Med 233:1482–1483, 2008

**Key words:** pharmacogenetics; pharmacogenomics; single gene polymorphisms

Pharmacogenomics is an exploding field that promises to enhance health care in the 21st century. The word is derived from "pharmacology" and "genome." The focus of the field is the impact of an individual patient's genetic makeup on the response to pharmacologic agents.

Differences in the genome, especially the presence or absence of single nucleotide polymorphisms (SNPs), are being increasingly taken into account in drug development and selection of specific therapeutic interventions. Pharmacogenomics offers numerous potential benefits to pharmaceutical companies, physicians, patients, and society. Nevertheless, progress in pharmacogenomics is hampered by some constraints.

An individual's response to a drug may be positive, negative, or lacking. Its nature is determined in part by the expression of multiple genes. Pharmacogenomics encompasses the influence of all of an individual's genes, the genome, on the specific patient's response to a specific drug. Variations in the genome are often a function of SNPs. More than 10 million SNPs occur in humans (1). Even a single SNP can have substantial effects on an individual's response to a specific drug. Pharmacogenetics is the study of individual single gene polymorphisms on the drug response. However, the two terms, pharmacogenomics and pharmacogenetics, are often used interchangeably. An ultimate objective of pharmacogenomics is identification and characterization of all of the pertinent genes that influence the response to a specific drug. If this were to be accomplished, SNPs could be used to identify drugs with minimal toxicity and side effects with respect to treatment of individual patients. Thus, physicians would be better positioned to personalize treatment.

Successful applications of pharmacogenomics are likely to result in benefits at many levels of the health care system. Pharmaceutical firms that develop drugs and physicians who administer them comprise two. With the use of rational drug design, structural biology, and improved selection of subjects enrolled in clinical trials with the use of SNP

Support for the symposium and its publication was provided by the Society for Experimental Biology and Medicine.

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DOI: 10.3181/0806-S-208
1535-3702/08/23312-1482$15.00

screening, more powerful and effective drugs should become available in shorter intervals. As pharmacogenomics matures, physicians are likely to become more effective in reducing the incidence of adverse drug reactions and enhancing therapeutic efficacy. Patients treated with drugs selected in part based on their genotypes will be more likely to respond positively and metabolize the agents used effectively with minimal adverse drug reactions. Improved patient selection should contribute not only to better health for treated patients but also to diminished overall health care costs. Pharmaceutical firms will be more likely to bring effective drugs to market more rapidly and with less expense. In aggregate, these possibilities have great potential for improving the health care system.

Much is needed before the potential benefits of pharmacogenomics can be fully realized. Identification and analysis of millions of SNPs that might influence the response to a specific drug or class of drugs is complex. Even after SNPs of interest have been catalogued, drug companies may limit drug development to agents targeting treatment of those comprising large groups. Development of drugs anticipated to be effective in only small cohorts may lie fallow. Improved DNA microarray and related technologies are needed to expedite SNP screening in a timely and cost effective manner. Extensive training of physicians will be required. Diverse ethical and legal issues including ownership of rights to genetic information, privacy, and insurance implications require resolution.

The purpose of the SEBM symposium was to provide an overview of pharmacogenomics from the perspectives of authorities with diverse expertise. Its organizers and chairs were Burton E. Sobel, M.D. and Charles A. Blake, Ph.D. It comprised four presentations that are represented by the four peer-reviewed manuscripts that follow.

Randal J. Kirk, J.D., Scott R. Horner, Ph.D., and Jeffrey L. Hung, M.H.S., M.P.H. reviewed the history of pharmacogenomics and its tools in research, clinical trials, and clinical medicine. They discussed the economic, regulatory, and technological driving forces influencing adoption of phamacogenomics. They discussed impediments to its development affecting pharmaceutical companies including limitations in education of clinicians, required statistical methods, and the current intellectual property landscape.

Mary K. Pendergast, J.D., LL.M. focused on regulatory agency considerations pertinent to pharmacogenomics. She emphasized federal oversight of pharmacogenomic research and the challenges associated with its clinical validation and utility.

Meeta Patnaik, M.D. discussed the role of pharmacogenomics in the treatment of central nervous system disorders. She emphasized the power of pharmacogenetic testing to predict the likelihood of efficacy and minimize the likelihood of adverse reactions with drugs used for treatment of several central nervous system disorders.

Steven R. Goodman, Ph.D., Editor-in-Chief of the Society for Experimental Biology and Medicine's journal *Experimental Biology and Medicine*, highlighted the journal's publication of multidisciplinary research including pharmacogenomics. His research on pharmaco-proteomic approaches to elucidation of defective structural proteins and treatment of sickle cell disease is the focus of his manuscript.

The symposium and its publication proffers the promise of pharmacogenomics for medicine. The field has advanced markedly, and its potential is enormous. Though barriers must be overcome, progress is already profound.

1. Human Genome Project Information, http://www.ornl.gov/sci/techresources/Human_Genome/faq/snps.shtml