THE DAWN OF PERSONALIZED MEDICINE: THE ROLE OF THE PHARMACIST

Imagine a trip to the pharmacy to fill a prescription for a blood pressure or cholesterol medication and leaving with a medication tailor-made just for you with a decrease in concerns for adverse drug reactions, side effects, or whether the medicine will work. Such a day is not too far off. This is the promise of pharmacogenomics, the study of how a person's genetic makeup may determine the effectiveness of a drug. Using the ever-increasing amounts of healthcare and 'omics data (e.g., clinical, genomic, and family history) collected from large populations, researchers today better understand how an individual's genetic makeup influences responses to disease, medical conditions, and drugs to treat them.

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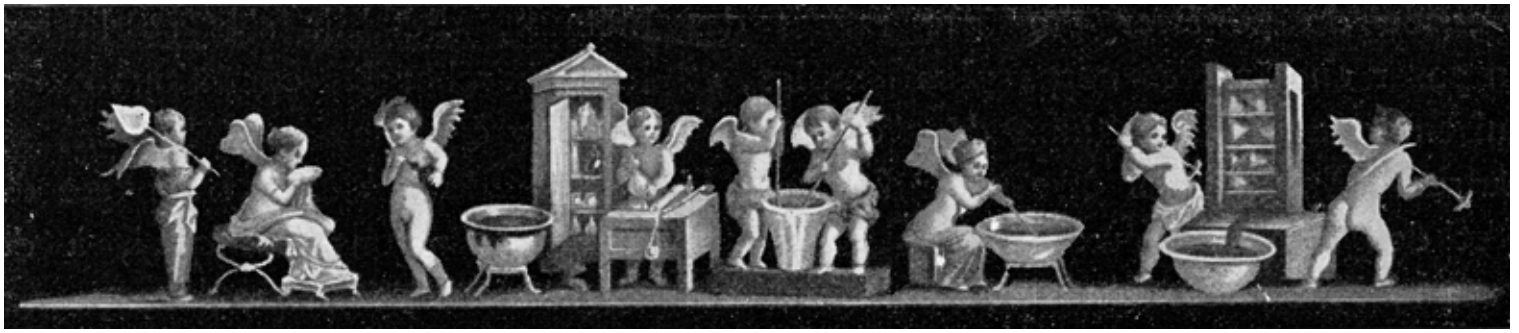

As a result, the field of pharmacogenomics has emerged as one of the keys to discover and develop novel drug therapies that promise an entirely new, personalized approach to medicine. This new field of science is expected to alter dramatically what medications we take as well as how to select the right medications; to reduce trial-and-error in prescribing medications; and to provide pharmacotherapy guidelines to clinicians to optimize patient care. Pharmacogenomics and the resulting personalized medicine approach are producing greater adherence to treatment compliance by patients; lowering costs; and expanding the role of both pharmacy practice and education; we provide more detail on these points in Sections B and C.

A

Beginnings of Personalized Medicine

Building on 70 years of research and technology, an international consortium of government agencies and academic centers pooled resources to complete the "Human Genome Project (HGP)," the DNA sequence of the entire human genome. The HGP has given rise to a medical revolution, yielding fruit such as the identification of 1,800 genes associated with various diseases; two thousand genetic tests now available for diagnostic applications; and more than 350 biotechnology products currently in clinical trials.

Pharmacogenomics, the convergence of pharmacology and genomics, has emerged as a field that can lead to safer and more efficacious drugs by considering the genetic variations of a patient population. Pharmacogenomic testing provides information about the potential of patients to respond to a drug (efficacy) or have an adverse response (safety) depending on the populations genetic profile. The future of medicine is moving to analyses based on each person's genome, leading to discovery of powerful precision medicines that would be tailored to each person by a healthcare provider – the genesis of personalized medicine.

B

Economic Benefits of Personalized Medicine

Personalized medicine has many benefits, a key one being the lowering of costs associated with treating and long-term management of diseases. New technologies like genetic testing are expected to improve patient outcomes and lower expenses in broad-based clinical settings by informing a healthcare provider as to which drug(s) would be the safest and most efficacious for his/her patient. Several studies have clearly demonstrated that a pharmacogenomic-informed treatment strategy using these technologies is indeed cost-effective. Administration of medications such as azathioprine, clopidogrel, abacavir, carbamazepine, irinotecan, and clozapine benefit from the use of pharmacogenomic testing by allowing the physician to prescribe the optimal drug and dose based on the patient's unique genomic profile. A detailed analysis of the cost savings resulting from incorporating pharmacogenomics testing for patients with depression, reported annual savings of $3,962 per patient.[1] As the cost of genetic testing decreases, pharmacogenomic testing clearly has the potential to be a cost-effective intervention.

C

Impact of Pharmacogenomic Testing on Medication Adherence

In the U.S., approximately 30 to 50 percent of all patients do not take their medications as prescribed. Factors that influence this behavior include side effects; decreased or lack of ›

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efficacy; cost of treatment; lack of insurance coverage; and patient perceptions that the drug prescribed is ineffective.[2] Non-adherence to medication regimens is a significant economic and healthcare burden, estimated at approximately $300 billion in the U. S. annually – patients' health worsens causing extended or more intensive treatment.

Pharmacogenomic testing provides strong incentives for patients to adhere to medication instructions. The personal nature of becoming aware of one's genetic makeup, coupled with being informed about potential therapeutic possibilities for a disease, may remove a patient's hesitation and reluctance to follow through with a prescribed therapeutic regimen.

Evidence supporting a positive impact of pharmacogenomic testing on medication adherence has been reported with statin therapy. Patients who received genetic test results for the Solute Carrier Organic Anion Transporter Family Member lBl (SLCOlBl) gene that encodes for the organic anion transporting polypeptide C (OATlBl) associated

Table 1: Pharmacist Competencies in Pharmacogenomics

The competencies describe pharmacist-specific knowledge necessary to achieve the competencies outcomes and are focused in four key areas.

Basic Genetic Concepts	To demonstrate an understanding of the basic genetic/genomic concepts and nomenclature.
	To recognize and appreciate the role of behavioral, social, and environmental factors (lifestyle, socioeconomic factors, pollutants, etc.) to modify or influence genetics in the manifestation of disease.
	To identify drugs and diseases and associated genetic variations to facilitate development of prevention, diagnostic and treatment strategies; appreciate differences in testing methodologies and need to explore these differences in drug literature evaluation.
	To use family history (minimum of three generations) in assessing predisposition to disease and selection of drug treatments.
Genetics and Disease	To understand the role of genetic factors in maintaining health and preventing disease.
	To assess the difference between clinical diagnosis of disease and identification of genetic predisposition to disease (genetic variation is not strictly correlated with disease manifestation).
	To appreciate that pharmacogenomic testing may also reveal certain genetic disease predispositions (e.g., Apo E4 polymorphism).
Pharmacogenomics/ Pharmacogenetics	To demonstrate an understanding of how genetic variation in a large number of proteins (e.g., drug transporters, metabolizing enzymes, receptor targets) influence pharmacokinetics and pharmacodynamics related to pharmacologic effects and drug responses.
	To understand the influence of ethnicity in genetic polymorphisms and associations of polymorphisms with drug responses.
	Recognize the availability of evidence-based guidelines that synthesize information relevant to genomic/pharmacogenomic tests and selection of drug therapy (e.g. Clinical Pharmacogenetics Implementation Consortium).
Ethical, Legal and Social Implications	To understand the potential physical and/or psychosocial benefits, limitations and risk of pharmacogenomic/ pharmacogenetic information for individuals, family members and communities, especially with pharmacogenomic/ pharmacogenetic tests that may relate to predisposition to disease.
	To understand the increased liability that accompanies access to detailed genomic patient information and maintain the confidentiality and security of this information.
	To adopt a culturally sensitive and ethical approach to patient counseling regarding genomic/pharmacogenomic test results.
	To appreciate the cost, cost-effectiveness, and reimbursement by insurers relevant to genomic or pharmacogenomic tests, for patients and populations.
	Identifying when to refer a patient to a genetic specialist or genetic counselor.

with increased statin concentration, showed more improved adherence to the statin therapy.[3] Patients skipped far fewer days of medication, and a corresponding increase in the average length of time over which they continued to take their medications was reported.

D

Expanding Role of Pharmacy Practice

Educating pharmacists about pharmacogenomics opens important, new opportunities for pharmacists to expand their scope of practice, creating a new specialty area for the pharmacy profession as a whole. This is in keeping with the evolution of the pharmacy profession in general over the years, during which time pharmacists' roles have expanded and grown. Pharmacists are now integral members of inter-professional healthcare teams and participate in diverse, advanced patient-centered services, such as drug monitoring and disease management, multidisciplinary clinical care, and education of patients and other healthcare providers.

In addition to their traditional role, pharmacists can now administer vaccines and dispense certain medications in most states without a prescription. The pharmacists' role in the pharmaceutical industry has also evolved to encompass a wide array of clinical, medical, regulatory, and marketing functions.[4] Pharmacists provide unique value to the healthcare system by optimizing medication use to improve outcomes and decrease adverse events.[5] Pharmacists are among the most accessible healthcare professionals in the U.S. – a rare finding in the industry.[6] The pharmacists' scope of practice is continuously evolving and will expand further as technology and healthcare evolve.

E

An Era of Growth and Change: The Role of the Pharmacist in Precision Medicine

Pharmacists are uniquely qualified among healthcare professionals to play leading roles in the field of personalized healthcare. In addition, they can make important contributions to translational research and implementation.[7]

Application of pharmacogenomic information requires an understanding of how genetic variations impact pharmacokinetic and pharmacodynamic properties (how drugs move through the body and the effect drugs have on the body, respectively); patient populations; and knowledge of molecular pathways.[8] Pharmacists are experts in pharmacotherapy and have first-hand clinical knowledge of drug metabolizing enzymes, transporters, drug targets and how they relate to drug pathways (see **Table 1**). Pharmacists are well aware that not all drugs are created equal, and that "one size does not fit all".

Pharmacogenomics is an additional tool for pharmacists to use for individualized care. Services provided by pharmacists in hospitals include advising on dose adjustment (98 percent), providing drug information (93 percent), and pharmacokinetic analysis (92 percent). Additionally, pharmacists have always been on the front-line guiding patients about the appropriate use of medications. Because of their distinctive knowledge of pharmacology and pharmacotherapy, and accessibility to patients, pharmacists are ideally suited to champion clinical pharmacogenomics.[8]

F

Implementation in the Pharmacists' Practice

Pharmacists are beginning to be recognized as essential partners in implementing pharmacogenomics in the clinical setting. In a recent editorial issue of the American Journal of Medical Genetics, a physician noted that "pharmacogenomics may reside more comfortably in the pharmacotherapy purview of pharmacists rather than physicians, at least as far as programmatic development and leadership are concerned".[9] Similarly, in 2013, a pharmacogenomics commentary authored

by genetic counselors proposed a partnership model between pharmacists and genetic counselors. The authors highlighted pharmacists' unique knowledge and skills as complementary to other healthcare professionals, noting that a team-based approach could "enable the comprehensive delivery of services essential to the appropriate use of pharmacogenomic testing".[10] As an increasing number of pharmacists engage in clinical pharmacogenomics, their roles as practice-based leaders in pharmacogenomics is becoming more evident.[11]

G

Pharmacists as Rising Trailblazers in Pharmacogenomics

As mentioned above, pharmacists possess the unique expertise and competencies to excel in this growing field, and thus the importance of pharmacists' leadership in this arena is increasingly being noticed. Pharmacists are already engaged in some of these roles and are rapidly emerging as trailblazers in pharmacogenomics.[11]

H

Educating Pharmacists in Precision Medicine

National pharmacy organizations have recognized the importance of incorporating pharmacogenomics into daily patient care and have noted that pharmacists have a tremendous opportunity to lead precision medicine in clinical practice. According to the American Society of Health-System Pharmacists (ASHP), pharmacists require a basic understanding of clinical pharmacogenomics in order to provide patient care that incorporates pharmacogenomic recommendations, design drug-therapy regimens based on pharmacogenomic results, and communicate recommendations to healthcare teams.

ASHP believes that pharmacists have a responsibility to take prominent roles in the clinical application of pharmacogenomics to promote safe, effective, and cost-efficient medication practices.[12] In 2011, the American Pharmacist Association (APhA) issued a white paper encouraging the development and integration of pharmacogenomics into pharmacy practice through medication therapy management (MTM).[13] The Accreditation Council for Pharmacy Education (ACPE) and the American Association of Colleges of Pharmacy (AACP) both require colleges and schools of pharmacy to include pharmacogenomics in Doctor of Pharmacy curricula to prepare pharmacy students for the field of precision medicine.

I

Challenges: Gaps in Knowledge and Resources

As a consequence of the advancement and rapid progress in pharmacogenomics, the pharmacy profession is now faced with significant challenges. Education and training are needed to equip pharmacists with the knowledge and skills to utilize pharmacogenomics and to support current patient care standards. Practicing pharmacists and many recent pharmacy school graduates have had limited exposure to pharmacogenomics, and their knowledge varies depending on the year of graduation and degree (PharmD vs. B.S.). It is crucial that pharmacists are prepared to use pharmacogenomic information to appropriately individualize medication therapy.[11]

Colleges and schools of pharmacy are responding to these needs through the development of innovative educational strategies to ensure graduates are prepared to apply pharmacogenomics to patient-centered care. Pharmacogenomics content in pharmacy education has increased over the last decade from 39 percent in 2005 to 89 percent in 2010.[14] The amount of pharmacogenomics content is likely to increase as requirements to incorporate pharmacogenomics into licensing exams are implemented.

Inclusion of pharmacogenomics material into existing curricula varies among institutions (14). Many include pharmacogenomics as an elective course while others integrate the content throughout other courses similar to pharmacotherapy. Even after the content is included, pharmacy students require additional knowledge and experience to address other components of precision medicine, such as bioinformatics, genetics, and the ethical, legal, social, and economic implications of pharmacogenomics.[15] After mastering the didactic portions, students still need experiential training environments, which are essential for any future clinical pharmacist to apply pharmacogenomics data.[15] Presently, a few sites exist for students to practice and apply pharmacogenomics in "real" patient care settings.

To overcome these challenges of implementation, a variety of pharmacogenomic education and training offerings that incorporate practice-based training are available for educators, practitioners, and new graduates. Traditional continuing education courses are also available, but are not sufficient to prepare practitioners for their roles.[15] For example, one study showed that a one-hour, case-based pharmacogenetics educational program increased participants' pre- and post-test pharmacogenomics knowledge scores by only seven percent. Many institutions have adopted a systematic approach to educating practitioners. These include St. Jude Children's Research Hospital, Vanderbilt University, Mayo Clinic, the UF Health Personalized Medicine Program at the University of Florida, and Touro College of Pharmacy-New York Medical College.

There are increasing numbers of residency and fellowship programs that offer practice-

based opportunities for pharmacists to expand their knowledge and skills to specialize in pharmacogenomics or focus on specific therapeutic areas, such as cardiology, psychiatry, or oncology.[15] Graduate programs in pharmacogenomics/genomic medicine are also available at the master's and doctoral levels.

The Road Ahead: The Only Constant is Change

Pharmacists have long been providing unique value in the healthcare system through optimizing medication use to decrease adverse events and improve treatment outcomes. New guidelines are being made available and national organizations are releasing statements emphasizing the pharmacist's role in utilizing pharmacogenomic data, as this is becoming the standard of care in many institutions. In fact, pharmacogenomics is gaining momentum more rapidly in patient care than initially projected. In a field primed for continued growth, tremendous opportunities await pharmacists where they can apply a variety of skill sets. In our ever-changing healthcare environment, pharmacists' roles will continue to evolve. This is an exciting time for the profession to embrace these new opportunities and to take prominent roles in incorporating pharmacogenomics into clinical practices. ■

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Dr. Chumki received her PharmD from Touro College of Pharmacy (New York, NY) and BS in Biology from St. John's University (New York, NY), and is a licensed pharmacist in New York and New Jersey. She is also certified in pharmacogenomics.

Dr. Chumki is the PharmD fellowship program director and coordinator of the PharmD internship program at Admera Health, which allows her to educate and contribute to the development of future pharmacists in the field of PGx. Through her work, she is committed to raising awareness of the impact of PGx in clinical practice and fostering increased incorporation of PGx expertise to broaden treatment options.

Brigitte Azzi received her B.S. in Biology from the George Washington University and is currently pursuing a Pharm.D. at the Touro College of Pharmacy in New York. She first became involved in research by presenting at the Academy of Managed Care Pharmacy (AMCP) 2018 Annual Meeting in which she was awarded the AMCP Foundation's Best Poster Award in the Student Pharmacist category. She later was accepted as a 2018-2019 PQA-CVS Health Foundation Scholar to elaborate on her project and to design and implement a quality-related initiative. Brigitte hopes to continue conducting impactful research that will improve the caliber of medicine and the quality of patient care.

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