PHARMACOTHERAPY

EDITORIAL

Precision Pharmacotherapy Enables Precision Medicine

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At the heart of precision medicine lies the goal of optimizing care to ensure that the "right treatments are delivered to the right patient at the right time." Precision pharmacotherapy is an important component of precision medicine and is the focus of this special issue. Components of precision medicine related to pharmacotherapy may include: -omic approaches to identifying optimal drug therapies for patients based on molecular (DNA, RNA, protein) profiles, treatments targeting specific molecular components of disease pathology, and personalized dosing using individual kinetic profiles which are the combination of physiological, environmental, and genetic characteristics of a patient. As highlighted in this special issue, a call for contributions in the area of "precision medicine" resulted in great interest focusing on the -omics (pharmacogenomics, metabolomics) aspects of precision medicine.

Looking at precision medicine with a broader lens, many would say that the personalized medicine mantra has been a key component of clinical pharmacology since its inception the difference now being that scientific discovery has allowed for pharmacotherapy optimization in many new and exciting ways based on the integration of new technologies. An example of this is that the U.S. Food and Drug Administration (FDA) now lists more than 160 medications that contain specific pharmacogenomic information within their package inserts.[1, 2] As highlighted in this issue, approximately 100 of these medications possess potentially "actionable" pharmacogenomic information.[3] Notable challenges about how to put this into practice have informed study designs moving forward with an increasing number of drugs approved with companion diagnostic tests.

Now that we are more than 10 years beyond completion of the Human Genome Project, current work focusing on the optimization of treatment for a specific patient's illness is really building on the foundation started by the field of pharmacogenomics.[4] While there are some examples in which a few genetic variants have been deemed essential in determining drug response, this has become the exception rather than the rule, and as such the field has begun to evolve toward using a more-comprehensive approach, one that includes more than genomics, and as of late has been coined "precision medicine" or "precision health." Therefore, in this special issue of *Pharmacotherapy*, our goal has been to broadly represent work being done, which can be seen by the broad depth of articles we have chosen for inclusion.

This evolution from pharmacogenomics to precision medicine has been driven by advancements in our knowledge of disease mechanisms that have improved treatments for complex illnesses. These advances have been supported by a general research-sharing infrastructure provided by the National Institutes of Health (NIH). In 2000, the NIH supported the creation of the Pharmacogenomics Knowledge Base (PharmGKB) and the Pharmacogenomics Research Network (PGRN), which currently still serves as a primary resource for pharmacogenomic information. In fact, the partnership between PharmGKB and the PGRN has resulted in the establishment of the Clinical Pharmacogenomics Implementation Consortium (CPIC), which provides clinical practice guidelines for the interpretation of pharmacogenomic results, as it recognized early that guidelines were needed to help clinicians make rational prescribing decisions based on pharmacogenomic information.[5] Recently, work has described that one of

four pharmacogenomics test results had a potential clinically actionable outcome, which shows the possible impact on patient care.[6] Currently, there are more than 43 gene–drug pairs for which CPIC has provided guidelines. However, there are many more gene–drug pairs that are either in progress or may benefit from a consensus evaluation (https://cpicpgx.org/genes-drugs/). Internationally, other organizations are also working to advance clinically relevant pharmacogenomic knowledge; these include the Dutch Pharmacogenomics Working Group (https://www.pharmgkb.org/page/dpwg) and the European Pharmacogenomics Implementation Consortium (http://www.eu-pic.net/), which also provide pharmacogenomics resources and guidelines.

Advancing pharmacotherapy aspects of precision medicine requires research across the translational spectrum. Our goal in assembling this special issue was to present diverse examples of this work. Discovery research that identifies and characterizes gene–drug relationships provides a scientific foundation for clinical advancements. Examples in this issue include discovery metabolomics research in sepsis, the identification genetic loci related to drug sensitivity reactions, and characterizing the clinical pharmacology implications of drug metabolism genetics. Identifying available studies and harmonizing results from differing populations in study designs are essential parts of advancing the field. Highlighted in this issue are therapeutically relevant reviews related to antidepressants, antiretrovirals, statins, diabetes, opioids, and cancer treatments that provide comprehensive updates of pharmacogenomic information in areas where clinical tests are now available but have largely not yet been evaluated by guideline groups.

The "Holy Grail" of the Human Genome Project has long been to directly advance patient care. However, the evolution of knowledge about the human genome to pharmacology-related discovery and finally to clinical application has taken longer than originally expected. The successful implementation of precision medicine in the clinic requires thoughtful, multidisciplinary research. Importantly, this takes collaboration and the sharing of knowledge and resources. The PGRN freely disseminates numerous online educational resources related to the principles behind pharmacogenomics, as well as additional implementation resources. The CPIC group has developed a software tool to extract all CPIC guidelines gene variants from a genetic data set, interpret the alleles, and generate output for clinical decision support. Consortia such as the Electronic Medical Records and Genomics (eMERGE) and Implementing Genomics In Practice (IGNITE), as well as others provide research and resources related to clinical practice. Clinically relevant research and perspectives are also highlighted in this special issue. Examples include important information on how to choose a clinical laboratory for pharmacogenomic testing and using pharmacogenomic information to select novel therapies for tumors.

It is important to note that the science of precision medicine does not stop at the implementation of this work. Research examining the best way to use this information within clinical practice is desperately needed, along with data identifying the best way to educate patient populations, as well as the providers using pharmacogenomics as a "tool" within practice for the first time. Perhaps the biggest misconception about pharmacogenomics is that the "answers" provided by testing results are simple, when in fact this is not often the case. Therefore, it is critical for every health care provider using pharmacogenomics within the practice understand the nuances of this work and be aware of all available resources as we usher in new practices in regard to patient care.[7]

While this is an exciting time for the field of precision health, more work being done by the NIH will hopefully propel us into the next stage of understanding the impact of precision medicine in practice through the creation of the "All of Us" program, which "will enable a new era of medicine in which researchers, health care providers, and patients work together to develop individualized care" (https://allofus.nih.gov/about/about-all-us-research-program). By recruiting and analyzing samples from more than 1 million individuals within the United States, this participant-engaged and data-driven research may just usher in the next generation of "precision health." Therefore, as previously stated, the overall goal of pharmacogenomics and precision medicine is simple – provide the "right drug to the right patient at the right time." By working together, we can make this vision a reality, as the practice of pharmacogenomics or precision medicine or precision health becomes the standard of care.

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