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Introduction to the Symposium on Precision Medicine

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In his 2015 State of the Union speech, US President Barack Obama announced the Precision Medicine Initiative, now called the All of Us Research Program, with the mission to "enable a new era of medicine through research, technology, and policies that empower patients, researchers, and providers to work together toward development of individualized care."[1] Consonant with these values, in this issue of *Mayo Clinic Proceedings* we introduce a series of articles, representing diverse medical disciplines, with the goal of describing how precision medicine will change, and already is changing, the way patients, clinicians, and researchers view health and disease.

Precision or individualized medicine is, according to the National Institutes of Health, "an emerging approach for disease treatment and prevention that takes into account individual variability in environment, lifestyle and genes for each person."[2] Precision medicine uses as its foundation the individualized approach to patient care that physicians and researchers have traditionally used but provides added insight using new approaches and technologies such as genome sequencing. As a result, the approach to health care advancement is both evolutionary and revolutionary.

Precision medicine and genomics introduce new concepts and terminology. A human DNA sequence consists of approximately 3 billion base pairs that make up the almost 20,000 genes. Current sequencing technology, known as high-throughput or next-generation sequencing (to distinguish it from the Sanger sequencing technique used to sequence the first human genome), allows for rapid sequencing of DNA and RNA. For comparison, contemporary (circa January 2017) high-throughput sequencing requires 1 to 2 days and costs approximately $1000 to sequence the genome of a single human, in contrast to the 13 years and $2.7 billion required to sequence the first human genome using Sanger methodologies.[3] Not surprisingly, when used in various applications, high-throughput sequencing has revolutionized the field of personalized medicine.

Whole-genome sequencing uses high-throughput sequencing to read all of the genome, both the portions that encode for genes and the nonencoding portions, and is the tool used in the investigation of a genetic basis for rare diseases, often termed the *diagnostic odyssey*.[4] Whole-exome sequencing looks at only the DNA engaged in encoding genes, which comprises less than 1% of the total DNA sequence. Consequently, whole-exome sequencing is faster and cheaper than whole-genome sequencing and is often used to search for Mendelian disorders related to specific allelic variants in specific genes.[5] RNA sequencing allows study of the expression levels of genes.[6] Any of these technologies can be applied not just to humans but to the study and identification of commensal microbes (the microbiome) or the microbiome subsets that serve as human pathogens. Lastly, gene panel testing uses high-throughput sequencing to search for common sequence variations (known as single-nucleotide polymorphisms or SNPs) with greater sensitivity in a smaller number of specific genes such as those involved in cancer or metabolism of drugs.[7] Used alone or in combination,[8] these techniques have advantages and disadvantages in both cost and complexity of interpretation, many of which will be discussed throughout this symposium.

The *Mayo Clinic Proceedings* Symposium on Precision Medicine will consist of multiple articles spanning a wide range of topics in personalized medicine. The first article, which appears in this issue of the *Proceedings*,[9] addresses one of the most publically discussed aspects of this field: how whole-genome sequencing in *healthy* people is being used to help *diverse* human populations lead healthier lives. Numerous organizations, both commercial and academic, are already studying how to use the information gained from genome sequencing and, in many cases, are marketing

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testing kits not just to health care professionals and patients but also to healthy consumers. Many clinicians already face questions about direct-to-consumer testing, and this topic will be covered in-depth in an article in a future *Proceedings* issue. Other articles in this symposium will focus on how personalized medicine and genomics are impacting specific fields in medicine such as oncology, rheumatology, neurology, gastroenterology, cardiology, and pharmacology. In each article, experts in their fields will review the state-of-the-art of the science, discuss controversies head-on, and provide insights into how advancements in personalized medicine and genomics are changing their field now and in the future.

Gene sequencing is at the heart of these discussions on precision medicine. However, the clinical application of the knowledge learned from sequencing can be modified by factors such as a patient's environment, internal microbiota, and previous treatments. Thus, in actual practice, precision medicine involves much more than just the study and application of DNA data.

Some experts predict that by 2023, each patient will have his or her genome sequenced.[10] In just the past year, we have seen remarkable growth in the field of personalized medicine: advances in our understanding of the genomics of cancer,[11] characterization of the microbiome,[12] understanding of rare diseases,[4] and introduction of pharmacogenomics into daily prescribing.[13]

Research to identify genomic and proteomic information (which can be used to define disease risk and prognosis, as well as response to therapy) has already provided an enormous amount of data that must be assessed in the context of clinical trials and clinical care. These efforts will continue to grow and must be evaluated for their clinical utility. They will add to, and be tested as, decision tools. This process will not be straightforward and will require major efforts in interpretation of data and education of clinicians and patients in order to provide appropriate perspectives for the care of individual patients. Among the many issues to be addressed is how precision medicine evidence is validated, implemented, and assessed. Knowledge networks will need to be developed and with them, infrastructure for the regulation of data access, privacy, and security.[14] Cost issues, including novel innovation-oriented reimbursement and regulatory frameworks, and, importantly, efforts to strengthen engagement and public trust, will be needed to realize the potential of precision medicine.[14]

Although there are many outstanding questions regarding the evidence to support its use,[13] along with concerns regarding the ethical, legal, and social issues surrounding the knowledge it creates,[15] the era of precision medicine has arrived. By the end of this symposium, we aim to help readers—whether health care professionals or recipients—understand how clinical care already has been, and will increasingly be, impacted by the field of precision medicine.

Timothy B. Curry, MD, PhD
Center for Individualized Medicine
Department of Anesthesiology and Perioperative Medicine
Department of Physiology and Biomedical Engineering
Mayo Clinic
Rochester, MN

Eric L. Matteson, MD, MPH
Division of Rheumatology
Department of Internal Medicine
Division of Epidemiology
Department of Health Sciences Research
Mayo Clinic
Rochester, MN

A. Keith Stewart, MBChB, MBA, MRCP, FRCPC
Center for Individualized Medicine
Division of Hematology/Oncology
Department of Internal Medicine
Department of Clinical Genomics
Mayo Clinic
Rochester, MN

Correspondence: Address to Timothy B. Curry, MD, PhD, Center for Individualized Medicine, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (curry.timothy@mayo.edu).

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