

Personalized Medicine: An Introduction

Summary

Personalized medicine is the use of new methods of molecular analysis to better manage a patient's disease or predisposition toward a disease. It aims to achieve optimal medical outcomes by helping physicians and patients choose the disease management approaches likely to work best in the context of the patient's unique genetic and environmental profile. Such approaches may include genetic screening programs that more precisely diagnose diseases and their sub-types, or help physicians select the type and dose of medication best suited to a certain group of patients.

People vary from one another in many ways — what they eat, the types and amount of stress they experience, exposure to environmental factors, and their DNA. Many of these variations play a role in health and disease. For example, the natural variations found in our genes could influence our risk of developing a certain disease, and the degree to which it progresses. Variations in several genes can influence how well a patient might respond to a particular drug.

Personalized medicine hopes to use these variations to develop new safe and effective treatments for genetically defined sub-groups of patients. Treatments may include administration of drug therapy as well as recommendations for lifestyle changes that can delay onset of a disease or reduce its impact.

Personalized medicine stands poised to transform healthcare over the next several decades. New diagnostic and prognostic tools will increase our ability to predict the likely outcomes of drug therapy, while the expanded use of “biomarkers” – biological molecules that are associated with a particular disease state – could result in more focused and targeted drug development. Personalized medicine also offers the possibility of improved health outcomes and has the potential to make healthcare more cost-effective.

Though sometimes described as a phenomenon of the future, personalized medicine is already having an impact on patient treatments. Molecular testing is being used to identify those breast cancer and colon cancer patients likely to benefit from new treatments, and newly diagnosed patients with early stage invasive breast cancer can now be tested for the likelihood of recurrence. In another example, a genetic test for patients with an inherited cardiac condition can help their physicians determine which course of hypertension treatment to prescribe in order to maximize benefit and minimize serious side effects.

Personalized medicine promises many medical innovations, and has the potential to change the way treatments are discovered and used. But the pathway to the development of personalized medicine is marked by the need to identify and address a range of public policy issues. The implications for current systems, such as healthcare payer and physician incentives, medical records privacy and clinical trial ethics, must be explored by all stakeholders, who will need to reach agreement on what modifications should be made. The way such issues are managed will affect the evolution of personalized medicine and shape its ability to prevent, diagnose and manage disease.

The Coalition seeks to serve as a source of information on public policy matters that will affect the realization of the promise of personalized medicine.

The membership of the PMC is open, with the goal of attracting universities and academic medical centers, non-profit research entities, relevant trade associations, patient organizations, government officials (*ex-officio*), healthcare organizations, healthcare providers, information technology companies, and research-based commercial companies that offer an array of products and services including research tools, diagnostic technologies and products, screening services, and therapeutic interventions.

The paradigm of personalized medicine can be illustrated as follows:



This arrow reflects the current and anticipated flow of healthcare services, and changing points of intervention, as medicine becomes more personalized. Early detection testing will continue based on large population risk (e.g., mammograms), while new forms of risk assessment will be incorporated (e.g., determining which women carry the genetic variation that increases their risk for developing cancer). Though true prevention must occur before disease symptoms are present, better risk assessment enables more targeted monitoring (e.g., women with the genetic variation should have more frequent mammograms); followed by symptom-driven diagnosis, in which molecular monitoring could possibly identify disease subtypes that cannot be clinically determined. Such diagnosis may or may not lead to targeted therapy, but in either event we may also benefit from improvements in monitoring a patient's response to a particular therapy.

The Science

Humans are unique individuals. With the exception of identical twins, our genomes are unique as well. Though all of us are genetically very similar, there are small differences in our DNA that are unique — and which make us unique in terms of health, disease and our response to certain treatments.

The natural variations (DNA polymorphisms) found in our genes play a role in our risk of getting or not getting certain diseases. The combination of these variations across several genes — along with numerous external factors such as environment, diet and exercise — affect each individual's risk. Natural genetic variations also are part of the reason that the same drug works well in one individual and not another. Variations in DNA can lead to differences in how drugs are absorbed, metabolized and used by the body. Understanding these genetic variations and their interactions with environmental factors will help researchers produce better diagnostics and drugs, and will help physicians better select treatments and dosing based on individual need.

The vast majority of genes function exactly as intended: giving rise to proteins that play key roles in biological processes and allow a person to grow and live in his/her environment. In rare instances, one single mutated or malfunctioning gene leads to a distinct genetic disease or syndrome. The most familiar of these rare disorders include sickle cell anemia and cystic fibrosis. Such disorders are termed “monogenic” because a single gene is responsible for their occurrence. But multiple genes acting together can also influence the development of many common and complex diseases, as well as our response to the pharmaceuticals designed to treat them. The contribution of several genes to these complex disorders is termed “polygenic.”

Often as a result of this complexity, what may appear to be one disease on a clinical level could, on a molecular level, be reclassified as several different diseases, each of which might respond to a different treatment. Such disease complexity exists for asthma and many forms of cancer. Through molecular analysis of “biomarkers” — biological molecules that are associated with a particular disease state — scientists can identify these sub-types within a disease. Biomarker analysis can also help classify sub-groups of patients who have the same molecular variation of the disease, enabling one to monitor its progression, select appropriate treatments, and measure the patient's response to medication.

Until recently, many technologies for examining DNA, proteins and other biomarkers were slow and expensive, which limited the scope and impact of molecular analysis. But new technologies, such as microarrays and protein arrays, are making biomarker detection much faster and more affordable. Future advances may make it feasible for physicians to screen patients for relevant molecular variations in the office prior to prescribing a particular drug.

The Promise

Personalized medicine has the potential to change the way we think about, identify and manage health problems. It is already having an exciting impact on both clinical research and patient care, and this impact will grow as our understanding and technologies improve.

It is already clear that personalized medicine promises three key benefits:

- Better diagnoses and earlier interventions. Molecular analysis could determine precisely which variant of a disease a person has, or whether an individual is susceptible to drug toxicities, to help guide treatment choices. For preventive medicine, such analysis could improve the ability to identify which individuals are predisposed to develop a particular condition — and guide decisions about interventions that might prevent it, delay its onset or reduce its impact.
- More efficient drug development. A better understanding of genetic variations could help scientists identify new disease subgroups or their associated molecular pathways, and design drugs that target them. Molecular analysis could also help select patients for inclusion in, or exclusion from, late stage clinical trials — helping gain approval for drugs that might otherwise be abandoned because they appear to be ineffective in the larger patient population.
- More effective therapies. Currently, physicians often have to use trial and error to find the most effective medication for each patient. As we learn more about which molecular variations best predict how a patient will react to a treatment, and develop accurate and cost-effective tests, doctors will have more information to guide their decision about which medications are likely to work best. Testing is already being used to find the one in four women likely to respond to a particular breast cancer drug. In the future, tests may help identify the one in ten patients who for tumor-specific molecular reasons will benefit from a new lung cancer drug. In addition, testing could help predict the best dosing schedule or combination of drugs for a particular patient.

The Challenge

As personalized medicine becomes more pervasive, a number of policy issues arise. A new healthcare paradigm with far-reaching implications, personalized medicine requires us to examine our current approaches to clinical trials, intellectual property rights, reimbursement policies and patient privacy and confidentiality. Given the array of issues, it is important that a broad spectrum of life science companies, healthcare providers, payers and policymakers participate in shaping the evolution of this new opportunity.

Some of the issues raised by personalized medicine include:

- Intellectual property. A strong intellectual property system is necessary to stimulate investment in innovation. It is essential that government patent systems offer protection for innovations relating to personalized medicine, as well as high quality patent examination that allows patents of appropriate scope and quality.
- Regulatory oversight. The U.S. Food and Drug Administration (FDA) is playing a key role in advancing personalized medicine, conducting discussions and convening debate about the implications for drug development and regulatory review. The FDA has been at the forefront of this issue, identifying emerging trends, and is in the process of developing guidelines for the submission of genetic data. Among the questions being considered: How narrowly should clinical trials be designed to include or exclude people based on the results of certain genetic screening tests? Should efficacy be defined in different ways for different genetic sub-groups? Regulators will need to answer these

and many other questions while working closely with academic and industrial scientists, professional associations and patient groups.

According to former FDA Commissioner Mark McClellan: “Pharmacogenomics [another name for personalized medicine] holds great promise to shed scientific light on the often risky and costly process of drug development, and to provide greater confidence about the risks and benefits of drugs in specific populations. Pharmacogenomics is a new field, but we intend to do all we can to use it to promise the development of medicines. By providing practical guidance on how to turn the explosion of pharmacogenomic information into real evidence on new drugs, we are taking an important step toward that goal.”

- Reimbursement. Personalized medicine will make it increasingly important for patients to have access to diagnostic and prognostic tests, as well as all appropriate medicines. As a result, public and private payers will need to grapple with new and complex questions, such as: Will therapies be reimbursed only for those patients who are identified, using whatever tests are available at the time, as likely to respond? Should all tests for all genetic traits that could pose serious safety issues be covered if they are available — or only if the trait is relatively common and the test relatively cost-effective? Should some demonstrated degree of efficacy in the general population be required to justify reimbursement for new therapies? Can insurance limit coverage to therapies that are effective only in populations of a certain size or prevalence? How should payment systems deal with testing and treatment for extremely rare conditions? How will the insurance concept of shared risk be affected by the increasing ability to individualize risk factors? Should improved medical education, new IT systems or patient education be covered?
- Privacy, confidentiality and patients' rights. Patient protection is clearly a critical issue, and one that must be addressed to build public confidence — without which it will be impossible to collect the molecular and clinical data that is the foundation of personalized medicine capability. Among the issues that must be addressed: the implications of being identified as predisposed to a certain condition or non-responsive to available treatments; the rights of non-consenting family members of the tested individuals; the implications for existing ethnic groups or as-yet-undefined genetic subgroups; and the psychological and social effects of genetic testing for the individual tested.

Pharmaceutical and biotech companies, diagnostics companies, researchers, medical educators, information technology managers, healthcare providers, laboratories, patient advocates, policymakers, payers and other stakeholders must all work together to carefully review the issues at hand and consider their interconnected implications. The common goal: an integrated policy framework that balances patient, industry and scientific interests without hindering advancement of this tremendously important sector. Through these efforts, we can help ensure that personalized medicine is able to fulfill its promise as rapidly as possible.

— END —

For references and additional sources of information, see www.personalizedmedicinecoalition.org “Resources”