

Personalized Medicine



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Pharmaco-What?

Introducing Personalized Medicine –
Part of the Genetic Science Learning Center at the University of Utah, this module provides an overview of the impact of personalized medicine on drug development and dosing.

ageofpersonalizedmedicine.org

The Age of Personalized Medicine –
Developed by the Personalized Medicine Coalition (HudsonAlpha is a member), this site includes a portfolio of drugs and diagnostic tests that comprise the first wave of personalized medicine and a series of case studies highlighting personalized medicine in action.

Personalized Medicine – What you need to know:

- Genes are specific segments of DNA that contain the instructions for creating proteins.
- Different versions of a gene (called polymorphisms) may lead to slight differences in the proteins.
- These genetic differences contribute to the variation found in human hair and eye color, body size and shape and risk of developing various disease.
- Genetic differences also influence how our body processes medication, impacting proper dosage, effectiveness and the presence of potential harmful side effects.
- Personalized medicine is an attempt to identify the genetic variation present in a patient and identify their risk for certain disease and response to various types of medication.
- Personalized medicine offers the promise of customizing disease management, treatment and possibly even prevention, by identifying the genetic and environmental risks present for a patient.

Imagine, in the not-to-distant future, sitting in the doctor's office for an annual physical. Your doctor draws a blood sample and adds a panel of genetic markers to the usual list of tests. Some of these tests search for genetic sequences in your DNA that alter the risk of developing specific diseases. Others predict how you will respond to certain medications, identifying those that will be most effective and those with harmful side effects. Based upon the results, the doctor designs an individualized plan of diet, lifestyle changes and medication to treat or

minimize the impact of disease. Although it sounds like science fiction, this scenario is the realm of personalized medicine, a field that is beginning to yield some promising early results.

What is it?

At its core, personalized medicine uses information about a person's genetic makeup to tailor strategies for the detection, treatment or prevention of disease. This may include genetic screening tests to identify susceptibility to disease or more precisely pinpoint existing conditions. It may also be used to guide pharmaceutical choices, highlighting the brand and dose of medication best suited for a patient. The goal of personalized medicine is to help physicians and their patients identify the best course of action to prevent or manage a disease based upon the patient's genetic and environmental profile.

Drawing an analogy from the world of fashion, personalized medicine is the equivalent of a custom-made suit or outfit, designed with an individual's unique body measurements. This type of tailored approach provides a much better fit than purchasing something off the rack.

Background

People vary from one another in many ways – what they eat, their lifestyle, the environmental factors they are exposed to and variations in their DNA. The Human Genome Project showed that we humans are 99.9% similar at the level of our DNA. However, that remaining 0.1% makes us unique - not only in our appearance and behavior, but also in our risk to develop certain diseases and our response to different types of medication. Some portion of this natural variation (called DNA polymorphisms), influences our risk of getting

What types of diseases are we talking about?

Rarely, a single polymorphism is responsible for a specific genetic disorder like Huntington's, cystic fibrosis, or sickle cell anemia. The majority of human disease is caused by a combination of several mild polymorphisms present in a number of genes, together with a susceptible environment. It is believed that diseases such as diabetes, asthma, Alzheimer's, Parkinson's, coronary artery disease, schizophrenia, rheumatoid arthritis, and many forms of cancer occur as a result of these complex interactions between genetic and environmental risks. Singularly, each polymorphism is not sufficient to cause the disease – it is rather the accumulation of many genetic and lifestyle risks that leads to onset of symptoms.

or avoiding specific diseases. Certain polymorphisms also influence the course of disease, impacting the age of onset for symptoms or the speed of progression. This variation, coupled with environmental factors (like diet, exercise and exposure to various chemicals or harmful settings), has a strong influence on the likelihood an individual will develop a given disease, as well as the most effective method of treatment.

Genetic variation also contributes to differences in how drugs are absorbed and used by the body. This is part of the reason why one drug may work spectacularly in one individual, not at all for another and produce harmful side effects in a third. For example, variation in the *CYP2C9* and *VKORC1* genes impact whether someone is likely to develop a dangerous reaction to warfarin, a blood-thinning medication often prescribed for people at risk for blood clots or heart attacks. A genetic test that identifies the susceptible changes has now been developed to help doctors adjust warfarin doses based

on each patient's genetic profile.

Personalized medicine hopes to understand the role of genetic polymorphisms in disease development and treatment, allowing physicians to determine which groups of individuals are at greatest risk for a given disease and identify the lifestyle changes or treatments that will best delay the onset of the disease or reduce its impact.

Why Now?

Until recently, identifying genetic polymorphisms and markers correlated with various disease states was time-consuming and expensive. The large-scale studies required to pinpoint susceptible variation was simply not practical. Today, new technologies such as microarrays

Personalized medicine at HudsonAlpha

A number of HudsonAlpha associates are positioned along the cutting edge of personalized medicine. A sampling of those companies includes:

Applied Genomics, Inc. (www.applied-genomics.com) is developing novel tools for the detection and classification of human cancers to clinical variation among patients useful in planning treatment options.

Conversant Healthcare Systems, Inc. (www.conversanthcs.com) provides human cancer blood specimens to researchers seeking genetic and other biomarker information in the development of diagnostic tests, prognostic indicators and therapeutic treatments.

Microarrays Inc. (www.microarrays.com) develops prefabricated and custom DNA microarrays which can be used to identify genetic polymorphisms that influence disease risk.

Theragnostix Reference Laboratories is developing a series of molecular diagnostic tests to determine an infection's cause and its associated drug resistance so doctors can choose the best treatment.

(described in the Spring 2007 issue, available online) and rapid DNA sequencing systems are making genetic screening faster and more affordable. For example, the cost to determine one base (A,T,C,G) of the DNA sequence has plummeted from \$10 in 1990 to less than one-third of a penny today. This technology shift allows researchers to sequence tens of thousands of bases per person in a rapid and cost-effective fashion. The variation present across thousands of individuals can be compared to identify changes that impact the cause, progression and ideal treatment of a disease. In the same way, different responses to drugs can be linked to genetic polymorphisms to classify which DNA changes influence treatment success.

The promise of personalized medicine

Driven by the findings of researchers, this newfound knowledge is rapidly moving into the clinical setting. At the forefront are a series of drugs such as Gleevec, Herceptin, and Iressa that are known to be most effective in people with a specific genetic profile. Straightforward genetic tests are performed to identify who will benefit from these medications. At the same time, more precise diagnostic tests are in development that better classify disease subtypes or progression. One of the "holy grails" in personalized medicine is the so-called \$1,000 genome – the ability to sequence a human's genetic information at an economically feasible price. The information identified in our genome will help develop a lifelong plan of health maintenance tailored to our unique genetic polymorphisms. As sequencing technology continues to advance, this dream becomes more and more a reality. ■

– Dr. Neil Lamb

director of educational outreach
HudsonAlpha Institute for Biotechnology

