FACT SHEET

NATIONAL INSTITUTES OF HEALTH

From Genes to Personalized Medicines

Yesterday

- Most doctors used a "one-size-fits-all" approach to prescribing medicines. They usually started with standard doses, and then observed how patients responded. If necessary, doctors changed the doses or drugs by a "trial and error" process.
- No one understood the biochemical reasons why certain medicines did not work for a small percentage of people or why some patients experienced serious adverse side effects.
- Although scientists and doctors suspected that a person's genes could play a role in the response to medicines, genetic technology was not advanced enough to reveal which genes — and which variations of those genes — were relevant.

Today

- Doctors are increasingly aware that genetic variations can cause different patients to respond in different ways to the same medication. The study of how genes affect the way a person responds to medicines is called pharmacogenetics or pharmacogenomics.
- Advances in understanding the genetic basis of individual drug responses come from the NIH Pharmacogenomics Research Network (PGRN) (http://www.nigms.nih.gov/Initiatives/PGRN). Since its founding in 2000, this nationwide alliance of research groups has studied genes and medications relevant to a wide range of diseases.
- Scientists have identified more than 3 million genetic variations, many of which may relate to disease risk or drug responses. Researchers are starting to use this information to predict whether a medicine might be effective, ineffective, or toxic in certain individuals. For example, researchers recently linked a common gene variant to poor effectiveness of an anti-clotting medicine, Plavix.
- Thanks to the work of PGRN researchers and others, several pharmacogenetic tests are now available. These tests can help doctors design the best treatment for patients with childhood leukemia, breast cancer, and heart disease. More tests are expected in the future, including those for drugs to treat asthma and depression.
- Scientists are also beginning to understand the combined actions of two or more drugs. One PGRN researcher found that tamoxifen (Nolvadex®), which is commonly used to treat breast cancer, is less effective in women who also take fluoxetine (Prozac®) to treat hot flashes caused by the anticancer drug.
- In a few cases, doctors analyze selected genes from patients before prescribing medication. For example, some research hospitals routinely examine groups of genes in children with leukemia before treating them. Different versions of these genes can result in dramatically different responses to antileukemia treatments. Based on the results of these genetic tests, doctors can prescribe the safest and most effective drug regimen for each child.
- The U.S. Food and Drug Administration has modified the labels of more than a dozen medicines to include pharmacogenetic information. This ensures that the drugs are as safe as possible and helps doctors customize doses for individual patients. Examples of drugs whose labels have changed are irinotecan (Camptosar®), used to treat colorectal cancer, mercaptopurine (Purinethol®), used to treat inflammatory bowel disease and childhood leukemia, and the blood thinner warfarin (Coumadin®), used to prevent heart attacks and strokes.
- A key component of the PGRN is the Pharmacogenomics Knowledge Base (PharmGKB) (http://www.pharmgkb.org/), a shared online resource that is freely available to the entire scientific community. By organizing and analyzing information about genes, drugs, and diseases, PharmGKB is speeding research progress toward a complete understanding of individual drug responses. To ensure privacy, the database does not include identifying information about research subjects.

Tomorrow

NIH-supported pharmacogenomics researchers are making steady progress towards understanding how genes influence drug responses. These findings will improve doctors' ability to personalize treatment by predicting an individual's response to a drug regimen and pre-empting problems, promising a future of:

- **More Accurate Dosing**

  Instead of basing a starting dose only on characteristics like weight and age, doctors will use a patient's genetic profile to determine the best drug and the optimal dose.

- **New, More Targeted Drugs**

  Pharmaceutical companies will be able to develop and market drugs for people with specific genetic profiles. Testing a drug candidate only in those likely to benefit from it could streamline clinical trials and speed the process of getting a drug to market.

- **Improved Health Care**

  Doctors will be able to prescribe the right dose of the right medicine the first time for everyone. This means that patients would receive medicines that are safer and more effective for them, speeding recovery, avoiding adverse reactions, and improving health care overall.

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