The ghost of personalized medicine
Drug therapies tailored to the DNA profiles of individual patients could change the face of medicine, but such treatments aren’t commonly used in the clinic
By Bob Grant | June 14, 2011

The US Food and Drug Administration recommends that doctors genotype patients before prescribing more than 70 commonly-used medications for specific genetic biomarkers. These tests, the agency suggests, can help physicians identify those in which the drug is less efficacious, poorly metabolized, or dangerous. But medicine is still far from a day when drugs and treatment regimes are fitted precisely to a patient’s genomic profile.

According to a 2008 survey conducted by the American Medical Association (AMA) and Medco Research Institute, even though 98 percent of physicians agreed that the genetic profiles of their patients may influence drug therapy, only 10 percent believed they were adequately informed about how to test their patients for biomarkers that may predict the safety and/or efficacy of a particular drug.

“Less than 1 percent of all opportunities are being realized with respect to genetic testing,” said Felix Frueh, president and head of genomics initiatives at Medco. “There’s a long way until this new technology is going to see the translation.”

Indeed, while new biomarkers are identified everyday, and researchers are continuing to collect more and more information about genetic variants that confer some amount of disease risk or predict a specific response to a treatment, that information has yet to be widely implemented in the clinic. The AMA states on its website that physicians today can use more than 1,200 genetic tests for more than 1,000 different diseases to help diagnose and treat their patients, but only 13 percent of the 10,000 doctors who responded to the survey had ordered a genetic test for a patient in the preceding 6 months.

But while physicians by in large have been slow to adopt the practice of screening patients to search for genetic information of relevance to drug treatments, known as pharmacogenomics, neither research nor regulation has stalled, as evidenced by the FDA’s relabeling of dozens of approved drugs with biomarkers that affect their safety or efficacy in specific patient populations. “Pharmacogenomics is probably an area where personalized medicine is really able to deliver,” Frueh said, “and it is able to do so because those are tests that can be clearly associated with a particular therapy.”
In some cases, testing patients for the labeled pharmacogenomic markers has become critical. For example, the FDA strongly recommends that doctors prescribing the HIV drug abacavir test their patients for HLA-B*5701 allele. Individuals carrying that allele who take abacavir could become hypersensitive to the drug, which can lead to a systemic, potentially fatal flu-like illness. A 2008 study in the *New England Journal of Medicine* found that testing for the presence of HLA-B*5701 in HIV patients taking abacavir eliminated hypersensitivity reactions. “Abacavir is a black and white example,” Frueh said. “You know that if you don’t do genetic testing, you’re omitting something that’s clearly a standard of care today.”

“But,” he added, “we have to be careful that we’re not overstating what’s possible.” Other pharmacogenomic biomarkers, while helpful, aren’t as cut-and-dried. Studies have yielded mixed results, for example, about whether genetic testing for different *CYP2C19* alleles in patients taking the anticoagulant drug Plavix can indicate proper dosing schedules to improve how the drug is metabolized. Similarly, identifying single nucleotide polymorphisms in two genes, *CYP2C9* and *VKORC1*, in patients taking another blood thinner, warfarin, can help guide optimum dosing to prevent over anticoagulation, but the markers’ predictive ability varies widely across races, according to a 2008 *Pharmacogenomics* study.

Still, recent results suggest that genotyping patients who are receiving warfarin can improve health outcomes. A 2010 nationwide study that compared the effectiveness of warfarin among different patient populations, conducted by Medco and the Mayo Clinic of Rochester, Minnesota, found that patients receiving the drug who had been genotyped to determine their *CYP2C9* and *VKORC1* status were hospitalized about 30 percent less than patients whose genotypes were unknown. Remarkably, Frueh noted, only a handful of physicians out of the thousands contacted for the study were even aware that a genetic test existed that could potentially improve warfarin dosing in patients.

According to Vance Vanier, CEO of personal genetic analysis company Navigenics, this lack of implementation is one reason why personalized medicine is not yet a widespread clinical reality—a barrier that Vanier calls the “adoption gap” between advances in the lab and benefits in the clinic. “The world is awash in biomarker content,” Vanier said. “The key question is, ‘What is the most effective mechanism to drive awareness among the primary care physician base?’”

Part of the problem, he suggested, is that physicians underestimate the predictive power of genetic risk factors for certain diseases or treatment outcomes. For example, he said that when he asks physicians in training to state the relative risks of classical predictors of heart disease, such as cigarette smoking or diabetes, he consistently hears figures like “10 to 15 times.” In fact, Vanier said, most of those predictors only have relative risks of around 1.8 to 2 fold, similar to some of the more robustly linked genetic markers of disease or drug effectiveness. If doctors are made aware of the fact that certain genetic biomarkers can be just as powerful as traditional predictors, they may be more inclined to use them to help personalize treatment regimes.

Frueh agreed that there’s a problem with clinical uptake of new genomic tools and biomarkers, adding that researchers also need to do a better job of demonstrating the clinical utility of such advances. “There is a paucity of data that we can point to and talk to physicians and practitioners about the clinical effectiveness of these tools,” he said. “That has something to do with the lack of uptake as well.”

Furthermore, with the sheer volume of new genomic information coming out of labs across the globe, it’s difficult for physicians to stay abreast of the latest advances that could improve the way they treat their patients, Frueh said. “The ‘build it and they will come’ approach to personalized medicine is not going to work,” he said. “If you’re not actively reaching out to the people who are practicing, nobody is going to come.”
Correction (June 14): The original version of this article included incorrect figures for the relative risks of traditional vs. genetic predictors of disease and/or drug effectiveness. The mistake has been corrected, and The Scientist regrets the error.