Guest Editorial

Direct-to-Consumer Genetic Testing

Two Sides of the Coin

The complete sequencing of the human genome in 2003 was highly publicized; however, many people misinterpreted that milestone as the “complete understanding of everything in the human genome.” In actuality, our professional community’s great progress in molecular diagnostics has been tempered by the reality that we still have much to learn about the relationships between genes and disease. Recently, a set of commentaries in the *New England Journal of Medicine* reiterated just how elusive genotype/phenotype correlations, when applied to complex diseases, can be.^{1–3} Information culled from such genome-wide association studies is often repackaged using standard molecular diagnostic lab techniques, co-opted by direct-to-consumer (DTC) genomic testing companies, and sold to consumers. Is that information of value to the “patient” or is it merely recreational genomics?

Amid the seemingly incongruent mix of mature and clinically useful tests for some diseases and paucity of knowledge for others, DTC genomic testing companies have come to market offering testing for genetic markers for health and risk assessment. Certainly we can agree that people should be proactive in making their own health care decisions and have a right to information about their individual genomes; yet, the question remains whether DTC genomic tests are beneficial in making those decisions.

As with any retail commercial offering, there are different types of DTC genomic testing. One example is testing directed toward an individual with a family member affected by a specific disease, prompting worry of inheriting the same disease. An Internet search may uncover a laboratory that offers testing for that mutation without a doctor’s order. Whether the result is positive or negative has all manner of interpretation ramifications. Without a physician and/or (better yet) a genetic counselor in the mix to aid in interpretation, how useful to the lay “patient” is the test result?

There’s another type of DTC genomic testing that is equivalent to genetic fortune telling. Several companies now offer DNA analysis with a variety of claims ranging from determining ancestry to choosing cosmetics based on DNA sequence (the former is possible, but not the latter). These examples are fairly harmless, and if people choose to spend their money for these purposes, that’s

their prerogative. Indeed, some have termed this “recreational genomics,” and if one accepts that moniker, then caveat emptor. But what about companies that make broad claims regarding genetics and health? That’s more serious than whether one is descendant from royalty or has a skin DNA pattern that demands a certain moisturizer.

DTC for Specific Genes

The Internet provides easy access to information about diseases, which is, for the most part, a good thing. Some sites are peer-reviewed, frequently updated, and provide excellent information about diseases and diagnostics tests, eg, www.labtestsonline.org, www.WebMD.com. On the other hand, a University of Michigan study found that the information on Internet sites offering melanoma education contained wrong (14%), missing (62%), or misinterpreted (41%) information.⁴ If a patient has the misfortune of “Googling” the “wrong” site, they may not be able to overcome such an initial handicap. A motivated melanoma patient will likely find his or her way to good information eventually. It is questionable, however, whether people can ultimately come to the right conclusions regarding more complex genetic health information. The tests themselves can be imperfect, ie, not detect all possible mutations, the results can be subtle and/or difficult to interpret, and risk analysis may be taken out of proportion. Professional counsel is essential in the context of such examples. Further, the ability to interpret posted or referenced primary scientific data accurately and correctly is not within the skill set of most “surfing the Web.”

Whatever the motivation, even if an individual is well informed before considering or ordering a DTC genomic test, this is no guarantee that the individual can adequately understand the results for which they may pay hundreds or thousands of dollars. There are questions we in the molecular diagnostics community understand can have complicated answers: (i) what if the test result is negative and the patient develops symptoms anyway; (ii)

Adapted from *DNA From A–Z and Back Again*. CA Holland-Staley and DH Farkas. AAC Press, Washington, DC 2008.

Address correspondence to Daniel H. Farkas at dan@scmmlab.com.

what if there are other disease-associated genes or mutations not included in the ordered test; (iii) what if the test was performed incorrectly or performed in an unaccredited, uncertified lab; (iv) what if other factors play a role in disease development? These questions have complex answers; while the patient has the right to gain access to this information via DTC genomic testing, s/he may be doing themselves and their family members a disservice by acting in the absence of a physician's or genetics professional's input.

The Internet has marginalized the stock broker and the travel agent; in the same vein, patients from Gen X and Y to Baby Boomers can and do gather genetic/medical information about themselves that may prove useful to the physician who cares for them. Good quality information from empowered knowledgeable patients should be welcomed by the physician. Appropriate management and potential intervention, screening, or prophylaxis can be practiced by the physician for the patient with a deleterious mutation in, for example Factor V Leiden or *BRCA1*. (It's only been a year since the Genetic Information Non-discrimination Act was signed into law; thus, it seems reasonable to assume that while instances of a patient bringing such information to the physician, as opposed to the usual paradigm of the physician ordering the test and informing the patient, are on the increase, this is anecdotal and speculative on our part.) The patient may thus act as their own health advocate by independently seeking genetic health information that can further aid the physician. It seems obvious, yet important, to add that the lay "consumer" of genetic testing results must share the information and its source with his/her physician. The physician retains his/her position as the pivotal gatekeeper of health management and so in that sense, information obtained via DTC genomic testing challenges the physician to assimilate and use the information correctly. One wonders, however, how busy primary care physicians are themselves able to assess the quality of genetic lab testing and the nuances of interpreting results.

DTC as Genetic Fortune Telling

As scientists, we know that some diseases arise from a clearly associated mutation, but most diseases do not have such a direct cause-and-effect relationship. Multiple factors including diet, exercise, smoking, weight, environment, and ethnicity affect whether or not an individual will progress to disease. Still, some companies make unrealistic claims about their ability to predict future disease risk from genetic information obtained from a patient's buccal swab. Some claims border on scientific fraud. State, federal, and professional regulatory bodies are right to work to protect the public. It is the nature of regulation, however, that it has difficulty "splitting hairs;" there are labs out there that produce quality results and labs that do not.

Lab test results, genetic or otherwise, should only be provided if generated using a U.S. Food and Drug Administration approved/cleared test or developed and validated appropriately as a Laboratory Developed Test performed

in a Clinical Laboratory Improvement Amendments-certified laboratory. In part, this means test results must be provided in the context of clinical validity. "Labs" that fly under this regulatory radar (and we use quotes because that's all they are, not true, *bona fide* clinical labs) do not call what they do 'testing,' and instead use euphemisms to avoid appropriate regulation. Because the companies cannot make diagnoses, the final report focuses on questionable statistics and recommends changes in lifestyles, eating habits, etc—the same kind of generic advice freely doled out by family members, neighbors, and friends. This sort of commercial opportunism is at best problematic, at worst, malpractice—and has the potential to reflect badly on what *bona fide* molecular geneticists and pathologists practice professionally. The public may not be equipped to differentiate good labs from bad or good information from bad; regulators may be "handcuffed" from differentiating labs when they apply new regulations.

Disclaimer forms that must be completed before DTC genetic testing should send a very strong warning to consumers who may be spending hundreds or thousands of dollars for information that may or may not be correct, may or may not be interpreted appropriately or in context, and may or may not be applicable, or even necessary. On the other hand, there are many fine "DTC labs" in the marketplace that provide interesting information to those who choose to afford it, thus satisfying individual curiosity. In actuality, genetic understanding may stimulate reading about and interest in genomics and its promise. Knowledge also helps patients cope, moves clinical trials forward, spurs fundraising, and leads to conversation. As long as individuals eventually bring their physicians into the discussion, then harm is averted and care is enhanced.

Final Thoughts

Direct-to-consumer genomic testing is here. With advances in technology, the completion of the sequencing of the human genome, and the pressures of capitalism, its arrival was inevitable. With the Genetic Information Non-discrimination Act as the "law of the land," we should be freer than ever before to seek out genetic information about ourselves. Are there some snake oil salesmen out there? Maybe. Are there also responsible, professional enterprises providing well-intentioned, appropriately communicated information to consumers? Certainly. Is the information of value, and is it worth the asking price? The marketplace will settle this question long before we diagnosticians reach a consensus or regulators define jurisdiction. In the meantime, it is the consumer's responsibility to exercise caution to avoid becoming a victim of marketing ploys that prey on humanity's innate curiosity and fears.

The French philosopher Voltaire long ago made a point highly relevant to this debate. He famously wrote, "I disapprove of what you say, but I will defend to the death your right to say it." As molecular diagnosticians and physicians,⁵ we may (or may not) agree with the dissemination of genomic information directly to consumers without physicians as middlemen, but we will betray our convictions if we

hinder the consumer's right to acquire it. Indeed, we advance our own standing and reputation if we both assist the marketplace by providing guidelines and educate the public in the proper use of genomic information. As clinicians and diagnosticians, we have a responsibility to exercise our influence for the enhancement of patient health.

References

1. Goldstein DB: Common genetic variation and human traits. *N Engl J Med* 2009, 360:1696–1698
2. Hirschhorn JN: Genomewide association studies — illuminating biologic pathways. *N Engl J Med* 2009, 360:1699–1701
3. Kraft P, Hunter DJ: Genetic risk prediction — are we there yet? *N Engl J Med* 2009, 360:1701–1703
4. Sabel MS, Strecher VJ, Schwartz JL, Wang TS, Karimipour DJ, Orringer JS, Johnson T, Bichakjian CK: Patterns of internet use and impact on patients with melanoma. *J Am Acad Dermatol* 2005, 52:779–785
5. Hunter DJ, Khoury MJ, Drazen JM: Letting the genome out of the bottle — will we get our wish? *N Engl J Med* 2008, 358:105–107

Daniel H. Farkas

*Sequenom Center for Molecular Medicine and
Michigan State University College of Human Medicine*

Carol A. Holland

Beckman Coulter, Inc.