

Should Anesthesiologists be Equipped as Genetic Counselors?

THE ever-expanding role of anesthesiologists may soon include genetic counseling. Like other medical specialties, since the completion of the Human Genome Project, anesthesiologists have placed much research and commercial interest in the development of pharmacogenomics. The promise of personalized medicine tailored to each patient's genetics has encouraged the exploration of various genes related to the practice of anesthesiology, with far-reaching implications.¹⁻³

Despite the concerted effort, review of the current pharmacogenomics literature of pain management, whether in the acute or chronic setting, reveals promising but inconsistent data.^{4,5} Furthermore, no study has yet shown genetic testing to be beneficial to pain management, and its theoretical benefits remain controversial.

The problem, however, is that the lack of beneficial evidence or controversy surrounding such tests does not always translate to lack of patients' interest in receiving it. A similar comparison can be made of the dietary supplement industry. The use of cranberry juice or echinacea in the management of urinary tract infections or the common cold remains a controversial yet widely popular practice.^{6,7} The dietary supplement industry, represented largely by medically unproven pills, is a multibillion dollar global industry. Demand for a product sometimes depends more on the word of mouth or a placebo effect than on reproducible scientific evidence.

Until recently, public access to medical genetic testing other than paternity tests was limited, largely because of availability and cost. Either a physician or genetic counselor directed the need for such tests or the test itself was too costly. Direct-to-consumer (DTC) genetic testing, however, is revolutionizing the public's access to medical genetic testing. DTC testing, also known by other terms, such as direct-access testing and patient-initiated testing, is a controversial service of the genomic industry. In essence, it is a medical laboratory test that is directly marketed to and purchased by the consumer, without the consent or involvement of a physician or a third party administering or explaining the test and its results.⁸ By mail, a patient receives an "at home" genetic test kit that includes a cheek swab. Within 2-3

weeks, the patient will have online access to his or her genetic profile.

James Watson, Ph.D. (1962 Nobel laureate in Physiology or Medicine, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York) famously predicted that a revolution in understanding human genetic variation would take place once reading each person's genome "gets down to the cost of a Chevrolet." In 2007, it cost approximately \$2 million to privately sequence James Watson's genome.⁹ Today, Complete Genomics, Inc. (Mountain View, CA) can sequence your entire genome for \$5,000; whereas 23andMe Inc. (Mountain View, CA) can read more than a half-million single-nucleotide polymorphisms for \$499.^{*10}

With unprecedented access to genetic testing, the question is, "Are people buying them?" Although private market reports of the DTC genetic testing industry exist, they are proprietary, and little is publicly known about consumer awareness and interest.⁸ A population-based survey across three states in 2006 found that awareness of nutrigenomic tests, a form of DTC genetic test, ranged from 24.4% in Michigan to 7.6% in Oregon, and less than 1% of respondents in each state had used health-related DTC genetic tests.¹¹

Because of the dynamic nature of Internet-based genetic testing companies, however, 4-yr-old data may not provide an accurate picture of awareness and interest today. Some Internet-based genetic testing companies have appeared and closed within a year, and novel means of marketing has made defining a "health-related DTC genetic test" a more complicated task, further demonstrating DTC genetic testing to be a difficult industry to follow.⁸ There are efforts by companies such as 23andMe, Inc., to make personal genetic information part of an Internet-based social networking site.* Like Facebook, Inc. (Palo Alto, CA), personal genetic information is fast becoming a part of the online popular culture. As of May 2009, there were 39 DTC genetic testing companies recognized by the Johns Hopkins Genetics and Public Policy Center.¹²

With DTC genetic testing becoming so widely available, anesthesiologists should prepare to counsel patients on the results of their genetic testing. Of the many genes related to anesthesiology, perhaps the genes of most interest are related to pain. In examination of the DTC genetic testing companies, pain-related genes were some of the most popular among the list of advertised genes.

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* <http://www.23andme.com>. Accessed May 6, 2010.

In particular, the cytochrome P450 2D6 (CYP2D6) enzyme involved in the metabolism of opioids and the catechol-O-methyl transferase (COMT) gene involved in pain sensitivity stand out among advertised genes of interest. *CYP2D6* is a gene located on chromosome 22q13.1, and patients who possess certain allelic variants can be classified into poor, intermediate, extensive, or ultraextensive opiate metabolizers.¹³ Many different internet-based DTC genetic testing companies, such as DNA-direct, Inc. (San Francisco, CA) or Genelex, Inc. (Seattle, WA), specifically advertise genetic testing of *CYP2D6* and imply that knowledge of your genetic variation can help find the right dose of pain medications. For example, DNA-direct advertises “Test results can help your doctor find the right drug—at the right dose—for you.”†

COMT is a gene located on chromosome 22q18.31–18.34 the enzyme from which degrades catecholamine neurotransmitters such as norepinephrine and dopamine. Initial studies demonstrated COMT mutations to be associated with varying levels of pain sensitivity, and patients who possess certain allelic variants were classified as having low, average, or high pain sensitivity.^{14,15} However, review of other studies has shown conflicting results, which may be due to nongenetic factors, including study design and environmental factors.⁴

Adding further complexity to the anesthesiologist’s role as genetic counselors are functional genomic studies that aim to understand the relationship between the patient’s individual genome and his/her phenotype as it relates to perioperative outcomes. For example, studies have shown that variations in the chromosome 4q25 region are independently associated with postoperative atrial fibrillation after coronary artery bypass graft surgery.¹⁶ Other studies are daring to question the perioperative use of β -adrenergic receptor blockers for hemodynamic stability and improving outcome. Recent data show that, depending on β -adrenergic receptor genotype, not everyone may benefit from the use of β -adrenergic receptor blockers after acute coronary syndrome.¹⁷ Although not yet part of standard of perioperative care, such studies are reminders that the promises of pharmacogenomics are slowly becoming reality and may influence future clinical practice.

Unlike pharmaceutical companies, DTC genetic testing companies are not under the stringent regulation of the U.S. Food and Drug Administration. The current Food and Drug Administration marketing guidelines allow for the growing list of pain genes to be advertised for their potential benefit to the consumer without the need for rigorous scientific data.⁸ It is also unclear how online genetic profiles for the purpose of social networking will be regulated, if at all. In short, with very little legislation concerning DTC genetic testing, com-

panies have a *de facto* carte blanche on how they may advertise and provide personal genetic information.

As anesthesiologists, an important part of our patient care concentrates on creating rapport and relieving anxiety and pain. If a preoperative patient is anxiously waiting for the anesthesiologist to share a printout of her online genetic profile that reports she is more sensitive to pain, a faster metabolizer of opioids, and at an increased risk for atrial fibrillation, will the anesthesiologist be ready to counsel and relieve her concerns? Is our current knowledge and training in the genetics of anesthesiology enough?

Today, the cost of a new Chevrolet is well over \$11,000.‡ No one, including James Watson, can predict how the revolution of genetic information will change medical practice. In a recent ruling, New York Federal District Court Judge Robert W. Sweet invalidated seven patents related to the genes *BRCA1* and *BRCA2*, mutations in which have been linked to increased risk of breast and ovarian cancer. His argument that genes do not constitute patentable subject matter may greatly affect patents covering thousands of human genes and the commercial future of DTC testing.¹⁸

Dismissing the potential of pharmacogenomics of anesthesiology because of lack of clinical evidence or for not yet being a standard of care may not be the practical approach. Studies are starting to show that personal genome information can be incorporated to yield clinically relevant information.¹⁹ For the sake of our patients, perhaps we should take a more active interest in educating ourselves on the current genetic research in anesthesiology and should begin preparing for the uncertain future of DTC genetic testing.

Frank H. Lee, M.D., Srinavasa N. Raja, M.D., Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Medical Institutions, Baltimore, Maryland. leefh9@gmail.com

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