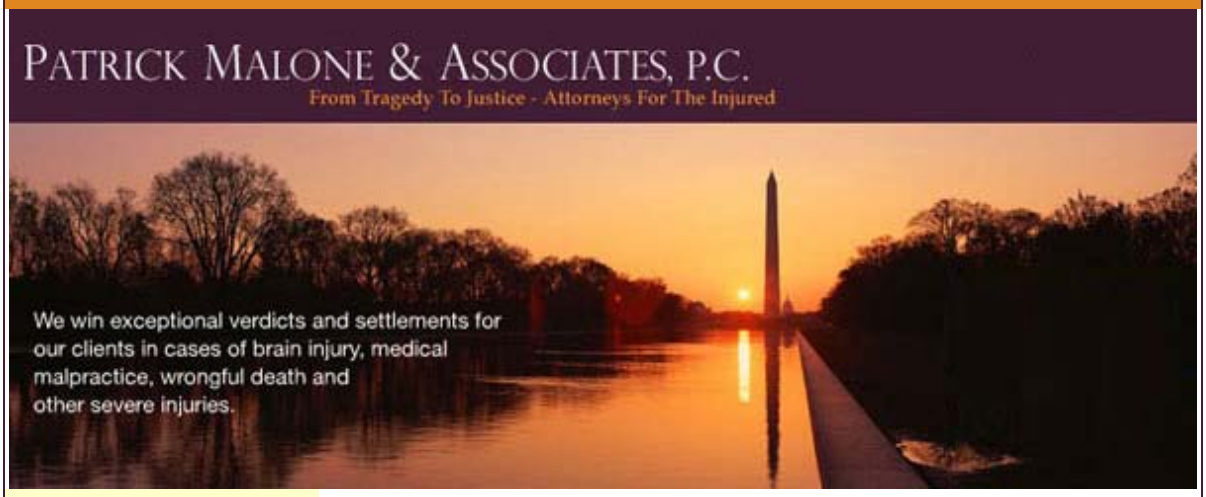
Getting the Best Medical Care: a Newsletter from Patrick Malone



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Read an excerpt from Patrick Malone's book: ***The Life You Save: Nine Steps to Finding the Best Medical Care -- and Avoiding the Worst***

Learning Your Own DNA Sequence: the Promise and Peril of Genetic Testing

Dear Patrick,

The promise of DNA testing is pretty stunning, but the peril is very real too. If we crack the code of the 3 billion letters that make up each of our unique individual DNA blueprints, shouldn't that help our own health care? In theory, we can anticipate and address medical problems with customized treatments. Better outcomes, fewer side effects -- that's the idea. But there's a downside, and it's called TMI: Too Much Information.

This month's newsletter focuses on genetic testing: Should you get your whole genome sequenced? What about more limited genetic testing for specific diseases? Read on for the low-down.

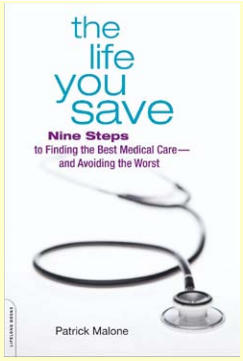
So What Exactly Is DNA?

Think of your genetic blueprint as a book, written in a DNA language that has only four letters, but the book is 3 billion letters long. That's your genome.

DNA stands for deoxyribonucleic acid. The structure of DNA was discovered by Watson and Crick in the 1950s. DNA is shaped like a spiral staircase, and each step on the stairs has a pair of chemicals that begin with the letters A, C, G and T. A always pairs with T, and C always pairs with G, so if you know the right side of the spiral staircase, you know the left side too. All of life is encoded by the repeating pattern of A, C, G and T along each individual's DNA.

Some fun facts about DNA : (Click the link for even more fun facts.)

- Each cell of the human body (except for red blood cells) has a complete set of that person's DNA, all 3 billion letters long. (Egg and sperm cells have only half a set each, which becomes a whole set when egg and sperm combine into a new life.)
- If uncoiled and laid end to end, the strands of DNA in one cell would stretch almost six feet long but would be only 50 trillionths of an inch wide.
- Human DNA is organized into about 20,000 to 25,000 individual



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genes, which contain the instructions for the proteins that make the building blocks of all human tissue, from brain cells to fingernails. Each of these genes is about 10,000 to 15,000 letters long. (Remember, it's a four-letter alphabet: A with T and C with G.)

- In between the genes are long DNA sequences that scientists used to think were "junk" but now know to contain important information that turns genes on and off.
- The genes are organized into big clumps called chromosomes. Every normal person has 23 pairs of chromosomes, half inherited from the mother, half from the father.
- My DNA and your DNA are 99 percent identical. It's the one percent difference that makes each of us unique.
- The Human Genome Project first uncoded the entire 3-billion-letter DNA sequence of a few representative individuals in 2003. That's about 3 gigabytes of data for each person.

What DNA Testing Is Currently Possible

Yes, you can get your entire genome sequenced, all 3 billion letters. But then what? For most of us, genomic sequencing is not yet ready for prime time. A few facts explain why.

Each of us has 20,000-plus genes scattered in those 3 billion letters. The genes are responsible for providing the coding that lets cells manufacture proteins. (By the way, a fruit fly has more genes than a human being. So does a roundworm.)

All of life consists of proteins, so if you uncode all the genes for all the proteins, that's all you need to know, right? Wrong. Here's a humbling fact: The genes make up less than TWO PERCENT of our genomes; more than 98 percent of the 3 billion letters consists of long chains of DNA that scientists are only beginning to understand. One important piece of it is the switching mechanisms that tell cells in the brain, for instance, to manufacture brain proteins but cells in the bone marrow to manufacture blood cells. Another important function of these non-gene pieces of our genome is in repairing the copying errors (mutations) that can happen every time a cell divides.

Plenty of genetic testing is done today that does not involve sequencing the entire genome. For example, identity testing for criminal forensics or fatherhood hones in on just a few DNA sequences.

Prenatal tests for some genetic abnormalities look at whether entire chromosomes have too many copies. Down Syndrome, for example, results from an extra copy of chromosome 21. (We recently blogged about the heartbreak of a chromosomal disorder known as trisomy 13 and 18 , whose numbers refer to the pairs of chromosomes involved.)

A few types of cancer also are linked to specific defects in a gene.

The BRCA gene , for instance, if it has too many copies or a specific mutation, can hugely increase a woman's risk for breast and ovarian cancer.

But most of the rest of genomic sequencing is something that we don't yet know how to use. Which also means it's fraught with opportunities for misuse.

The Pharmacogenomic Promise

It's always better to treat illness with a scalpel than a chainsaw. So individualizing our use of medications according to the unique ways our bodies break down drugs makes a lot of sense. The fancy term is pharmacogenomics.

A recent story on NPR highlighted this for a patient with a household name in the DNA world: James Watson, who shared a Nobel prize for discovering the spiral staircase (double-helix) structure of DNA, and who later headed the Human Genome Project in its early years.

Watson had high blood pressure treated with beta blockers. The medicine, he said, "put me to sleep." The sequencing of Watson's own DNA showed why: Watson's genes made him more sensitive than most people to the drugs. He revised his medication schedule, and now controls his blood pressure better because he knows more about his genome.

One day we will know enough about individual variation in the genetic levers controlling how the liver processes drugs that it will make sense to get your genome sequenced. But not yet.

The TMI Problem with DNA Testing

The frontiers of genetic testing show the problem of TMI: Too Much Information.

Too much information about one's DNA can cause not only unnecessary expense and worry, but sometimes genetic testing yields painful results for which there is no treatment or cure.

One example as reported recently on KaiserHealthNews.org concerned Alzheimer's disease , which can't be prevented or cured. A survey last year found that about 2 in 3 people would want to know if Alzheimer's was in their future. There is no test that determines this likelihood.

Most of the 5 million people with Alzheimer's developed it after age 60, probably because of a combination of genetic, lifestyle and environmental factors. About 5 in 100 Alzheimer's patients have inherited an early-onset form probably linked to a chromosomal mutation.

Some brains scans may show signs of Alzheimer's decades before symptoms appear via the presence of a protein found posthumously in the brains of people who had the disease. And changes in proteins in the blood or cerebrospinal fluid may also be associated with the disease.

But tests to measure these changes are available only in a research setting, and insurance typically doesn't cover them. Insurance generally does not cover genetic testing, either. And about half of people who get late-onset Alzheimer's did not demonstrate the presence of a certain chromosomal variant it signals when they underwent genetic testing.

If you have such tests, you can face insurance discrimination: Long-term care insurers can use the results to deny you a policy. So if your result even hints at the possibility of Alzheimer's but you can't do anything about it, isn't that information more harmful than helpful?

As KaiserHealthNews notes, the Genetic Information Nondiscrimination Act prohibits health insurers and employers from discriminating against people based on their genetic information, but life and long-term care insurers are not covered by the law.

As George Perry, editor-in-chief of the Journal of Alzheimer's Disease told KaiserHealthNews, "The things we know that really impact the disease are related to lifestyle. Be mentally and physically active, eat a diet rich in fruit and vegetables. These reduce the risk of developing the disease by at least half."

You don't need a test to be able to do that.

Apart from reproductive decisions, the authors of a recent study about prenatal testing foresee whole genome prenatal sequencing having a negative impact on child rearing, according to The Hastings Center, a nonpartisan research institute for bioethics. (See our blog post about mapping fetal DNA .) If parents were able to get genetic information suggesting that their child's predicted IQ may be low, the authors surmise, they might not strongly encourage and support the child's efforts in school.

A discussion on The Conversation, a web forum on recent scientific research, suggested that widespread genetic testing will swell the ranks of the so-called "worried well"- people who are not ill, but who believe they are, or are at risk for becoming ill.

These medical consumers help to increase the cost of medical care by overusing resources. They're also more likely to buy into a phenomenon called "disease mongering ," which we've discussed on our patient safety blog.

As noted on The Conversation, only about 3,500 of the 23,000 genes in the genome have been associated with a particular disease. The genetic foundation for common illnesses such as cancer, heart disease and diabetes remain largely unknown. So, "If we are not careful, we may let the benefits of a sick label outweigh the benefits associated with being healthy. In this new millennium of advancing technologies, there's cause for concern when the race is no longer toward who can be described as healthy, but who can be classified as ill or diseased."

The Bottom Line: Advice for Sensible DNA Testing

Discuss with your doctor whether your medical history warrants the

potentially more thorough analysis of your health status that only genetic testing can provide. It might be reasonable if you're not responding to treatment, if close members of your family have diseases or disorders with a strong genetic component and/or you're considering having children and you might pass on genes that could affect the health of a fetus or child.

Remember that test results become a part of your medical file; your insurers and employers (if you are covered by insurance provided through work) will know their results, and although they may not deny you coverage, the results could be an issue of privacy or become a factor if you change plans in the future.

Consider as well how you might live life differently if you knew your chances of contracting a terminal disease were increased.

If you decide to undergo testing, make sure your life and long-term care insurance policies are in effect before you have the tests.

Arrange for testing through your doctor; although several companies, such as 23andMe and Navigenics, offer direct-to-consumer testing usually for less than what you would otherwise pay, results usually aren't accompanied by genetic counseling. Anyone undergoing a genetic test should have counseling because although some people are comforted knowing their genetic risk factors, others are distressed and emotionally vulnerable.

Getting your whole genome sequenced is something you can do, but right now it's strictly for vanity and curiosity.

Recent Health Care Blog Posts

Here are some recent posts on our patient safety blog that might interest you.

- Another screening test for cancer -- ovarian cancer -- turns out not to measure up. It's too bad, because cancer of the ovary can be so deadly.
- A compilation of the objective facts and statistics about medical malpractice lawsuits shows the real problem is we don't have enough accountability for medical errors that hurt patients, which still are happening at epidemic rates.
- ProPublica, the investigative journalism group, has more resources for patient safety .

Past issues of this newsletter:

Here is a quick index of past issues of our Better Health Care newsletter , most recent first.

To your continued health!

Sincerely,

Patrick Malone
Patrick Malone & Associates