Bloomberg Businessweek

Technology

http://www.businessweek.com/articles/2014-01-15/illuminas-new-low-cost-genome-machine-will-change-health-care-forever

Illumina's New Low-Cost Genome Machine Will Change Health Care Forever

By Ashlee Vance January 15, 2014

Dr. Bradley Patay, who is tanned and handsome, with a constant smile that pushes the limits of cheek physics, has an office at the Scripps Clinic, next to the Torrey Pines Golf Course and the Pacific Ocean. An internal medicine specialist, he also happens to be very well versed in genetics. If, like me, you've had your entire genome sequenced, Dr. Patay can tell you what the results mean. He'll pull your data up on a computer and show you how to explore your own genetic makeup. Having this genome decoding skill makes him a rarity for the moment. "I want to be prepared when people come in with their data and explain it to them in a competent manner," he says. Soon, your doctor may work this way, too.

Quietly and dramatically, genetics-based medicine has taken off in just the last couple of years. For about a decade, biotech companies had been haunted by their own hype. The promise of sequencing technology was that the mysterious triggers of disease would be uncovered and cataloged. The cures for cancer, Alzheimer's disease, and strokes would then follow. Instead, extracting information from DNA proved more costly, time consuming, and difficult than backers of the science either believed or let on from the outset.

Now children with rare diseases that previously went undiagnosed routinely get answers about the causes of their conditions—and sometimes therapies that ease their pain. Inexpensive consumer DNA tests offer insight into resistance to certain medicines. Two companies—Foundation Medicine (FMI) and Genomic Health (GHDX)—have changed the way cancer gets treated for adults. Instead of viewing all colon cancers as uniform things, for example, Foundation sequences a patient's tumor and compares its properties with a database of past specimens. The company then helps pinpoint a treatment that's proven to be effective against that particular type of tumor.

Scientists and entrepreneurs encouraged by these results have turned giddy once again: A long-awaited breakthrough in sequencing—an affordable test—is at hand. As of last year, the going rate to get your genome sequenced was about $10,000. Now it will be closer to $1,000. At the center of the excitement is Illumina (ILMN), a publicly traded biotech company based in San Diego with a market capitalization of $15 billion. Founded in 1998, the company invented and acquired its way to the top of the gene-sequencing-machine market. It's estimated that about 90 percent of all human genomes ever sequenced have been done on Illumina's machines. This year the company should report sales of more than $1.6 billion, according to Wall Street forecasts compiled by Bloomberg.


Bryan Sheffield for Bloomberg BusinessweekIllumina HiSeq X at the company's headquarters

On Jan. 14, Illumina reduced the cost of sequencing by a factor of 10 when it unveiled the HiSeq X (pronounced "high seek ten"). The machine, about the size of a large photocopier, is basically the first DNA-crunching supercomputer. It can knock out 20,000 human genomes per year. Assuming it's running at full capacity and including all costs—the purchase price, plus labor and materials (the reagents and other chemicals)—the machine can sequence an entire genome for $1,000.

HiSeq Xs, which cost $1 million each and must be purchased 10 at a time, are designed to meet the growing ambitions of hospitals, medical research centers, and entire countries. England, for example, plans to sequence 100,000 people and thousands of cancer tumors over the next couple of years in a bid to make genomic data part of the mainstream health service. Illumina also just released the NextSeq 500: a much smaller machine that costs about $250,000 and can fit on a lab bench. Where the HiSeq X is designed for research centers that need to crunch hundreds of whole genomes simultaneously, the NextSeq 500, which handles one genome at a time, is meant to be cheap enough for a hospital or other commercial customer.

The $1,000 genome has long been considered a milestone—the price at which sequencing can finally go mainstream. Researchers can sequence thousands of people, creating much richer data sets that can in turn be used to pinpoint the causes of illness. Children with rare diseases can expect to be analyzed and treated much more quickly, and adults with cancer can afford to have their tumors analyzed. Unlike other companies that declared victory in the $1,000 genome race only to stumble, Illumina has its product in customers' hands. "This isn't hocus-pocus," says Jay Flatley, the company's silver-haired, longtime chief executive officer. "We are shipping the machine."

The first human genome required $3 billion and 13 years to sequence. Ten years later, with the HiSeq X, that time has fallen to about 24 hours. It's now possible to take a blood test and meet with your doctor a week or two later to go over your inherited strengths and weaknesses on an iPad. With the flick of a finger across the screen, you might learn, as I did, of a resistance to the drug Warfarin, which is used to prevent blood clots. The process can be nerve-racking, particularly as your doctor hunts for genes that can indicate a susceptibility to breast and colon cancer. "Well, you're clear," Dr. Patay tells me. "I probably shouldn't have saved that for the end of our hour, because we might have been having a very different and more difficult conversation." He's still learning, too.

Last November, Illumina took over the Estancia La Jolla Hotel and Spa, an elegant Mexican-villa-style resort just north of San Diego, to run one of a series of events it calls Understand Your Genome, or UYG. About 60 people paid $5,000 each to have their genome sequenced. The attendees, a mix of doctors, scientists, genetic counselors, and the curious, gathered for two days of lectures and personal DNA exploration. They got white gift bags that contained an iPad tied with a gold bow, a framed glass slide of their DNA sample, a

hard drive holding their entire DNA sequence, and a binder with a clinical report disclosing which markers are tied to which conditions. In my case, there were no direct genetic links to anything scary. I am, however, a carrier for five rare diseases—none of which my children have, fortunately—plus there's the resistance to Warfarin.

If the public knows anything about DNA tests, it's likely through companies such as 23andMe, which will analyze a saliva sample by mail for $99. Such inexpensive consumer tests examine only about half a million points of your DNA sequence, leaving billions more in the shadows. (A 23andMe spokeswoman says the company looks at a "small subset of locations in the DNA.") In the blood-based UYG test, Illumina investigates all 3 billion base pairs, or As, Ts, Cs, and Gs, that make up a human's genome. Something like Canavan disease, of which I am a carrier, is associated with 10 or so gene mutations, but the consumer tests typically examine only the one or two most common. Illumina looks at them all. It does not provide the glossy information found in some consumer-friendly tests, such as guesses about where your ancestors might have come from and the likely hair color of your offspring. Instead, the company zeroes in on about 1,600 genes that have well-researched and proven links to 1,200 conditions. "This is about clinical implications," Dr. Patay says.

Before attending a UYG event, participants must agree to sit down for two sessions with their doctor, one before they get their genes sequenced and one after. The first session is a discussion of costs and benefits of sequencing. Not everyone wants to know they're headed for heart disease or Alzheimer's. The second session is a "good news, bad news" chat about the test results.

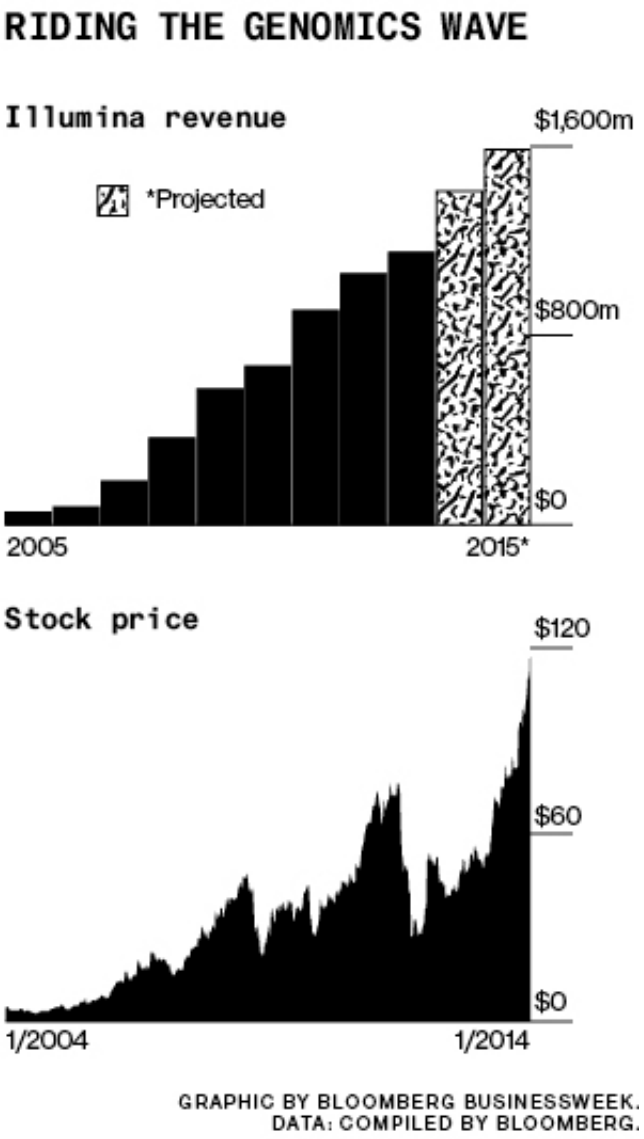
Illumina plans to hold dozens of UYG events in 2014. The company wants people such as Dr. Patay to go through its course and then conduct their own UYGs for other doctors and medical professionals. "The whole goal is to build up a network of physicians that have been commonly trained in this," says Matt Posard, a senior vice president at Illumina. "Just like a French fry tastes the same at every McDonald's, we want everyone to have that same kind of experience that you had with Dr. Patay."

One of the first speakers at the November UYG event is Dr. Eric Topol, a cardiologist and geneticist, who describes a "womb to tomb" list of genetics-services companies. Couples looking to have a baby, for example, can turn to Counsyl or GenePeeks to screen for heritable diseases. Expectant couples can go to Verinata Health (owned by Illumina), Natera, and Ariosa Diagnostics for prenatal tests on a wide variety of conditions. This is a huge advance over amniocentesis, the common—and risky—test for fetal chromosomal abnormalities that involves sticking a needle into the mother's uterus. "The end of amniocentesis is near," Topol says.

By sequencing children and their parents, doctors are treating unusual diseases more quickly and effectively. "If we can decode the genome for these diseases, we can find the root cause," says Dr. Stephen Kingsmore, the director of the Center for Pediatric Genomic Medicine at the Children's Mercy Hospital in Kansas City, Mo. Dr. Kingsmore says he's already seeing much swifter diagnosis of such conditions as muscular dystrophy, cystic fibrosis, and kidney disease. "We want to provide a diagnosis within a month for every kid," he says. "For babies, we want to be able to provide it within a day."

Knowing in advance that they're predisposed to a condition will let patients take preventive steps long before the condition appears. Illumina's Flatley found out he's more vulnerable than most to dying under anesthesia, which changes his risk-benefit calculation of getting knocked out for surgery. Macular degeneration is among the devastating conditions that can be flagged. "That is actionable information," Topol says. "Wouldn't you want to know that early in life? And then be very careful about things like avoiding sun exposure to the eyes."

In late 2011, Dr. Franz Humer, the colorful chairman of Roche (ROG:VX), reached out to Flatley and Illumina Chairman William Rastetter. Humer was visiting San Diego and wanted to have a chat. Rastetter invited everyone to his beach house, and the three shared 20 minutes of small talk and some coffee. “Then Franz said, ‘We will acquire Illumina,’ ” Flatley recalls. “It was so matter-of-fact. That is the part that set me back. The meeting lasted about eight minutes after that.”



Over the next couple of weeks, as Illumina’s board discussed a possible acquisition, Humer moved forward with a hostile takeover plan. Roche first offered $44.50 a share, an 18 percent premium at the time. Illumina said no; Roche came back with $51 per share, or $6.2 billion total. Roche wanted to round out its pharmaceutical and diagnostic products with the leading gene-sequencing machines, but Illumina’s board thought the company had plenty of room to grow and saw even the sweetened offer as too low. It took a couple of months, but Flatley fended off the deal.

Illumina is used to fighting these sorts of challenges. Startup after startup has appeared and promised to make its machines irrelevant. Some companies have technologies that are better at reading super-repetitive plant DNA or speeding through a sequence. Last year, China’s genomics research and clinical services superpower BGI acquired Complete Genomics, another California-based sequencing company. The deal, which thrust China into the sequencing-machine business for the first time, has created a deep-pocketed rival for Illumina. Life Technologies also sells sequencers and a wide range of products, from stem cell therapies to forensics

technology to genetic engineering. “The breadth of Life’s products creates a whole different animal that someone like Illumina has to compete with,” says Ron Andrews, president of genetic and medical sciences at Life.

Illumina, however, continues to dominate the market for general-purpose machines. “It will be a while until the existing Illumina machines are threatened,” says Jimmy Lin, a cancer researcher and founder of the Rare Genomics Institute.

Investors seem to agree with Lin: Illumina’s stock closed at $121.51 a share—an all-time high—on Jan. 14, the day the HiSeq X was announced. Flatley says the company has been able to keep producing faster, cheaper machines mainly by improving the chemicals needed to perform the sequencing work. The company’s scientists work on building enzymes that can travel along DNA more quickly and creating brighter fluorescent dyes that help illuminate the As, Ts, Cs, and Gs. At the same time, Illumina is diversifying beyond hardware into software and services. It bought the prenatal test maker Verinata for $350 million one year ago; more recently it acquired NextBio, which is building a database of links between diseases and specific genes.

Flatley says Illumina is working on some promising technologies in-house, too. Some may find uses outside medicine, such as a handheld sequencer that could be used by a policeman to identify a suspect on the spot. The cheaper sequencing gets, the larger the impact will be. “In the next couple of years, we will blow open the cancer market,” Flatley says. “That’s the next huge breakthrough.”

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