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DNA sequencer raises doctors' hopes for personalized medicine

The device could accelerate the use of genetic information in everyday medical care, physicians hope, improving diagnoses and treatments.

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Among the many stents, surgical clamps, pumps and other medical devices that have recently come before the Food and Drug Administration for clearance, none has excited the widespread hopes of physicians and researchers like a machine called the Illumina MiSeqDx.

This compact DNA sequencer has the potential to change the way doctors care for patients by making personalized medicine a reality, experts say.

"It's about time," said Michael Snyder, director of the Stanford Center for Genomics and Personalized Medicine.

Physicians who rely on genetic tests to guide their patients' treatment have had to order scans that reveal only small parts of a patient's genome, as if peeking through a keyhole, Snyder said: "Why would you study just a few genes when you can see the whole thing?"

Back in 2000, when the Human Genome Project completed its first draft of the 3 billion base pairs that make up a person's DNA, the effort took a full decade and cost close to $100 million. The Illumina MiSeqDx can pull off the same feat in about a day for less than $5,000 — and the results will be more accurate, two of the nation's top physicians gushed in the New England Journal of Medicine.

That confluence of "faster, cheaper and better" is likely to accelerate the use of genetic information in everyday medical care, Dr. Francis Collins, director of the National Institutes of Health, and Dr. Margaret Hamburg, commissioner of the FDA, wrote last month. DNA sequencing should guide physicians in choosing the best drug to treat a specific patient for a specific disease while risking the fewest side effects.

The Illumina MiSeqDx platform works by breaking down, rebuilding and recording the entire sequence of a person's DNA in a massively parallel fashion, completing the job in a matter of hours. The company intends to market the machine to diagnostic labs, medical centers and private practices, at a price slightly more than $125,000.

Now that MiSeqDx has been approved, several other whole-genome sequencers are likely to seek the FDA's blessing in the coming months, agency officials say.

Right away, the technology is poised to improve the diagnosis and treatment of cystic fibrosis. Two new assays for the chronic lung condition — both developed by Illumina for use on the MiSeqDx — were approved in November by the FDA. Instead of checking for the six mutations most commonly linked to the disease, the new tests are able to discern a total of 139 genetic variations that give rise to cystic fibrosis. They will also tell doctors whether a patient is among the 4% who has a mutation that's targeted by a specific, costly drug.

Whole-genome sequencing has begun to reshape the way physicians diagnose and treat cancer as well. For a growing number of patients, treatment is guided by a DNA scan that reveals which mutation gave rise to the malignancy, not the organ in which the cancer manifests itself.

Having a fuller, clearer picture of patients' complete genomes will also allow biomedical researchers to expand their understanding of how DNA variants work together to influence disease risk, said Dr. Robert Green, a medical geneticist at Harvard Medical School and Brigham and Women's Hospital in Boston.

In current practice, physicians use genetic tests to look for known mutations that show up in the "exome" — the 1.5% of the genome that dictates the composition and timing of how proteins are produced. When inherited in identifiable patterns, these mutations give rise to conditions like Huntington's disease and certain kinds of hearing loss.

But with machines such as MiSeqDx, researchers will be able to look for subtle variations and disease-causing patterns anywhere in DNA, including the long stretches that until recently were regarded as "junk." What they learn will enable doctors to warn their patients of their genetic vulnerabilities, allowing patients, in turn, to take steps to reduce their risk.

It may take a while for physicians to become proficient in conveying such information, and for patients to grasp its meaning, Green said.

"We know that people get state-of-the-art genetic counseling and still walk out of that office confused," he said.

Scientists promised that the age of personalized medicine had arrived when the Human Genome Project published our DNA blueprint. In the years since, that promise has proved elusive.

It was all very well to imagine that a single genetic scan would alert a patient to disease risks and — should he or she become ill — identify which treatments would work best.

In reality, the painstaking process of sequencing every patient's entire genome was a distant dream. Each expensive scan would take months to complete, making it a poor guide to treatment. Results were unreliable. And large stretches of the genome came out fuzzy, yielding a picture of a person's genetic makeup

too uncertain to base medical decisions on.

And then there was the question of what it all meant. Where in the genome's 3 billion base pairs should doctors look for clues to a patient's future illness? Which genetic variations should prompt immediate action and which could be safely ignored? How should all of these genetic risks and their inherent uncertainties be explained to a patient?

Lawmakers and bioethicists began to lay the groundwork for this new world, wrestling with issues such as whether companies could refuse to hire someone or health insurers could deny them coverage on the basis of their DNA. The Genetic Information Nondiscrimination Act made these actions illegal in 2008.

Last month, the Presidential Committee for the Study of Bioethical Issues urged doctors to come up with guidelines for dealing with the incidental findings that are bound to come up when a patient's genome receives such thorough scrutiny. Physicians ordering such tests — and the patients receiving their results — should decide in advance how much of that incidental information they want to know, the panel recommended.

In approving the MiSeqDx, the FDA declared that it would regulate the complex and fast-evolving industry of genomic sequencing services. The agency has already flexed its muscles by ordering 23andMe — a high-profile Silicon Valley company that encourages consumers to examine their own DNA by sending in vials of saliva — to stop marketing its $99 tests to the public until it had demonstrated to the FDA that its findings were accurate and reliable.

Elizabeth Mansfield, who directs the personalized-medicine office in the FDA's Center for Devices and Radiological Health, acknowledged the skepticism about the agency's ability to regulate this emerging industry. But standards have been developed and conveyed to companies, she said.

"We certainly hope to see more" devices like MiSeqDx in the coming year, Mansfield said. "Bring it on."

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