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Whole genome sequencing s routine treatment of bl Washington U. stu

Michele Munz
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Watch now: Genome sequencing to be used in fight against cancer

ST. LOUIS — Washington University researchers are among the first to sho that whole genome sequencing, which used to be time-consuming and expensive, can be used routinely in patient care.

A study by university doctors found that sequencing the genome of people v blood cancers is often better and even quicker than conventional tests and c about the same. The study was published Wednesday in the New England Journal of Medicine, one of the most prestigious peer-reviewed medical journals.

“What we showed is that genome sequencing has reached a point that it is r practical, fast, economical, clinically feasible and accessible for the routine testing of patients,” said Dr. David Spencer, medical director of Washingtor University’s McDonnell Genome Institute Clinical Sequencing Lab.

Whole genome sequencing has evolved at lightning speed. It took scientists working all over the world more than 10 years and about $1 billion to seque the 6 billion bases of DNA that make up the human genome. That process v declared officially complete in 2003.

Just over a decade later, ultra-fast sequencing machines sold in groups of 1 could sequence 18,000 human genomes in one year at $1,000 to $1,500 pe genome. The latest machines can double that.

There’s a saying, though, in the genome world that captures the barriers to the newfound capability in practice, said Spencer:

"It's the $1,000 genome, but a million dollar analysis."

He continued, "So you sequence the entire genome and it doesn't cost very much, but it's really complicated, and it takes forever to understand the information that it contains. That has been a perceived barrier to using this technology to a certain extent. You can sequence it, but what do you do with next?"

Spencer and his team found that as whole genome sequencing costs less an less, the analysis can be easier and faster in instances where scientists know where on the genome they need to look for abnormalities.

A genome leader

The Genome Institute at Washington University **has long been a key pla** in the field of genomics. The institute ultimately contributed 25% of the blueprint to sequence the first human genome. That was thanks partly to quadrupling the speed of sequencing by developing a way to identify the fou bases that make up DNA with fluorescent dye and lasers.

In 2008, the institute was the first to sequence the cancer genome of a leuk patient, which revolutionized the understanding of cancer and how it can b treated.

In the recent study of blood cancers, researchers took blood samples from 2 patients, sequenced their entire genome and compared the results with traditional genetic tests. The patients were treated at Siteman Cancer Cente Barnes-Jewish Hospital in St. Louis.

For nearly three decades, treatments for blood cancers such as acute myelo leukemia and myelodysplastic syndrome have hinged on how chromosome look under a microscope. Recently, doctors have also incorporated genetic sequencings of a limited number of genes to identify changes important in guiding treatment.

Both cancers are often deadly, but patients can be treated effectively if they receive proper therapy. Based on their test results, patients are divided into three risk categories. The highest risk patients immediately require the mos intensive treatment — usually chemotherapy and a stem cell transplant.

The researchers found that whole genome sequencing identified all of the s abnormalities and, importantly, identified additional abnormalities in 17% cases. Among 117 newly diagnosed patients, additional abnormalities were found in 25% of cases.

The new information changed the risk category for 19 patients, likely alteri their treatment.

In addition, genome sequencing does not require living cells, as does testin that involves looking at chromosomes under a microscope — called karyoty Often, samples don't contain enough living cells to determine the risk categ for blood cancer patients.

The entire cost for sequencing in the study was about $1,900 per patient, compared to conventional genetic testing which costs $1,000 to $2,000. Re were returned in an average of five days.

“Our study emphasizes that the time it takes, the cost and the type of information that you get out of whole genome sequencing — that can all be distilled into an accessible laboratory test,” Spencer said, “I think that is the major breakthrough here.”

“The time for this sort of thing is here, or it’s coming very shortly,” he said “That’s the major result.”

Researchers will continue to evaluate whole genome sequencing for acute myeloid leukemia and myelodysplastic syndrome patients at BJC HealthCa hospitals, which are staffed by Washington University physicians. BJC HealthCare will cover the costs, Spencer said.

They hope to extend the method soon to other cancers.

“If there are cancers where you need to identify these chromosomal-level changes and gene mutations, and it’s hard to capture all those with current testing methods, then this approach should be useful,” Spencer said, “and t are many solid tumors that are like that.”

‘Game-changer’

Dr. Robert C. Green, a medical geneticist and professor of medicine at Harv Medical School, said there has been tremendous enthusiasm around the no of analyzing the DNA of a cancer in order to better treat it, but the hype has quite stood up to the promise.

This study is a start, Green said. “So all of you doctors out there who are tre these type of cancers, pay attention and consider using sequencing now, be you can do this faster and more accurately than the techniques you were al using, and I think that is why this is a potential game-changer.”

The steps involved in conventional genetic testing can even be more labor intensive and complicated to execute, Spencer said, and results can take eve longer to obtain.

“The thing about whole genome sequencing is it’s really a fairly simple laboratory approach … the laboratory steps are actually, I would say, simple than these more targeted tests,” he said. “It’s easier and faster to just seque the whole thing, and look at the parts that you care about.”

Dr. Peter Campbell, who leads cancer genome sequencing studies at the Wellcome Sanger Institute in Cambridge, U.K., said genomic sequencing ha reached a point where scientists can identify every relevant genetic change patient’s cancer. They know what neighborhoods they need to look at on a massive genome map.

"This fascinating study demonstrates, first, that this technology can be implemented in real-world clinical practice, and second, that we can make accurate choices of treatments for patients with blood cancers," Campbell s "Our task is now to take this blueprint for blood cancers and apply it to all cancers."

Dr. David Spencer poses for a portrait in the sequencing lab at the McDonnell Genome Institute in St. L Wednesday, March 10, 2021. Spencer is the lead author on a study being published in the New Englanc Journal of Medicine. Spencer and his team at Washington University say that gene sequencing can fina put into practice by helping determine the best course of treatment for patients with blood cancers. Th among the first studies to show that whole genome sequencing can be used in routine clinical practice that was, until recently, cost prohibitive. Photo by Colter Peterson, **cpeterson@post-dispatch.com**

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