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Study shows ability to do next-generation sequencing for patients with advanced cancers

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A pilot study led by the Translational Genomics Research Institute (TGen) and the Virginia G. Piper Cancer Center at Scottsdale Healthcare shows that, even for patients with advanced and rapidly transforming cancer, researchers can find potential therapeutic targets using the latest advances in genomic sequencing.

Sequencing spells out, or decodes, the billions of letters of DNA and other genomic data so that clinicians can discover what genetic changes might lead to cancer.

Better optics and faster computers, which are the hallmarks of today's Next Generation Sequencing (NGS), are leading to genomic analysis that enables development of new drugs that target specific genetic mutations. However, because patients' tumors often contain multiple abnormalities, their cancer often progresses beyond initial targeted therapies.

Researches showed that the most cutting-edge NGS—whole genome sequencing (WGS), and even more advanced whole transcriptome sequencing (WTS)—can reveal larger numbers of targets in an individual's tumor, and that these "could be addressed using specific therapeutic agents, and perhaps reduce the chance of progression," according to the pilot study published today in the scientific journal *PLOS ONE*.

The study—A Pilot Study Using Next Generation Sequencing in Advanced Cancers: Feasibility and Challenges—reported results on nine patients evaluated at the Virginia G. Piper Cancer Center Clinical Trials at Scottsdale Healthcare, a partnership of Scottsdale Healthcare and TGen.

"Patients with advanced cancer often exhaust treatment options. Targeting a single abnormality is not sufficient to prevent progression," said Dr. Glen Weiss, an Associate Professor in TGen's Cancer and Cell Biology Division and the study's lead author.

"We demonstrate the feasibility of using NGS in advanced cancer patients so that treatments for patients with progressing tumors may be improved," said Dr. Weiss, who previously was affiliated with Scottsdale Healthcare, and now is affiliated with Cancer Treatment Centers of America Western Regional Medical Center in Arizona.

For all nine patients, WGS was used to compare their germline DNA from white blood cells (the DNA an individual is born with) to the DNA from their tumor cells. For six of these patients, researchers also used WTS to sequence their total RNA isolated from the tumor, and compare that to total RNA from non-patient controls.

"Based on our findings, we found it was feasible to perform these advanced NGS technologies for patients in a clinical trial situation," said Dr. Daniel Von Hoff, TGen Distinguished Professor and Physician In Chief; Chief Scientific Officer for the Virginia G. Piper Cancer Center Clinical Trials; and one of the senior authors of the study.

In addition to identifying as many genomic changes as possible, a secondary objective of this pilot study was to develop a workflow process from tumor biopsy to treatment.

"This process must occur in a short enough timeframe in order for patient to benefit from this additional information in developing a treatment plan," the study said.

Some of the challenges include: NGS reporting delays, communication of results to out-of-state participants and their treating oncologists, and chain of custody handling from fresh biopsy samples for CLIA (Clinical Laboratory Improvement Amendments) target validation.

The study also showed that WGS and WTS both have advantages, and that newer technological strategies may capture the best of both.

"With improved efficiencies that decrease the time to get NGS results and at reasonable costs, we can envision how NGS might be applied more globally to advanced cancer patients," said Dr. John Carpten, TGen Deputy Director and also a senior author of the study. "Even during the relatively short time that this study was enrolling, we observed significant improvements in sequencing analyses and lower costs."

The study was funded by the National Foundation for Cancer Research (NFCR).

"We must be able to identify all causes of cancer. Working with TGen, we are pursuing this goal at a level that is unmatched," said NFCR President Franklin C. Salisbury Jr. "The world needs to know that, through the use of 21st Century medicine, we are on our way to conquering cancer."

More information: dx.plos.org/10.1371/journal.pone.0076438

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