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Liquid-based CGP is critical for matching cancer patients to therapies

Illumina collaborated on a study presented at ASCO 2025 showing that circulating tumor DNA provides actionable data for clinical trials

IN 2015, THE NATIONAL CANCER INSTITUTE (NCI), part of the National Institutes of Health, kicked off the Molecular Analysis for Therapy Choice clinical trial, or NCI-MATCH, which aimed to determine whether treating cancer based on genetic alterations in a patient's tumor was effective, regardless of cancer type.

Over eight years, NCI-MATCH screened approximately 6000 patients, making it the largest NCI-supported precision oncology clinical trial. In turn, the NCI received funding and oversight from the Frederick National Laboratory for Cancer Research, the NCI's federally funded research and development center.

Phase 2 of the trial established 38 "arms," or sub-studies, that matched a particular genomic alteration to a therapy under evaluation. Then it used molecular testing to screen each participant's biopsy and determine whether their tumor had one of these alterations. About 1600 patients qualified to enroll in a treatment arm.

Beginning in 2019, Illumina collaborated with researchers at Frederick's Molecular Characterization (MoCha) Laboratory to retrospectively study banked blood samples from the patients who had been screened for NCI-MATCH. For the project, they leveraged comprehensive genomic profiling (CGP),[1] a next-generation sequencing approach that uses a single assay to assess hundreds of genes, including cancer biomarkers that are prognostic or predictive, are relevant in clinical trials, or have been cited in recent clinical studies.

With only a plasma sample, researchers can sequence and analyze fragments of tumor DNA that have shed into the bloodstream. This is known as circulating tumor DNA, or ctDNA, and MoCha researchers have long sought solutions for analyzing and testing it. After careful evaluation of the available options, the study authors used the CGP assay Illumina TruSight Oncology 500 ctDNA v2.[2] Their abstract, "Comprehensive genomic profiling of matched ctDNA and tissue from patients with less common cancers enrolled in but not eligible for a treatment arm of the NCI-MATCH trial," was accepted for oral presentation by first author Bishu Das of MoCha at the annual American Society of Clinical Oncology meeting in Chicago this week.[3]

1. illumina.com/areas-of-interest/cancer/ngs-in-oncology/cgp.html
2. illumina.com/products/by-type/clinical-research-products/trusight-oncology-500-ctdna.html
3. asco.org/annual-meeting

A surprising 60% of NCI-MATCH participants had cancers that were rare or less common—cancers other than breast, colon, rectal, prostate, or non-small-cell lung—and 2194 of these patients with rare cancers had plasma available for liquid biopsy testing. The researchers wanted to know if a liquid biopsy, or simple blood sample collection, could also qualify these patients for therapy. In this cohort of patient specimens, they found that 85.5% of the cancer-causing mutations observed with tissue sequencing tests were also identified by ctDNA-based CGP.

Across the rare cancer types, they saw a high correlation between tumor variants found in tissue and those found in plasma. Overall, for oncogenic mutations, they observed a 98.1% correlation among the small cell lung cancer specimens, 96% correlation in esophageal carcinoma patients, and 94.6% for cholangiocarcinoma. Further, some markers of interest were identified *only* with ctDNA—for example, within the cholangiocarcinoma cohort, seven patient specimens had high microsatellite instability, and eight specimens revealed *FGFR2* fusions. These biomarkers were not detectable via the original tissue sequencing test.

"The ctDNA assay was successful, yielding usable sequencing results in 96% of the specimens, which is very important given the breadth of cancer types and variable ctDNA yield across samples," says Traci Pawlowski, vice president and head of Clinical Solutions at Illumina, and a coauthor of the study. "These patients had sufficient ctDNA and a high-enough tumor fraction in their plasma to be evaluated for a clinical trial by liquid biopsy."

Excising tumor tissue can be very difficult and invasive, and often the pathologist still doesn't end up with a lot of it. Pawlowski says that liquid biopsy is a much more accessible and reliable option: "All oncologists know that tissue can be a limitation. The saying goes, 'Tissue is the issue.' Still, they hesitate with liquid biopsy—they are concerned they will miss an important marker because it's not the actual tumor they're testing. This study shows that a ctDNA assay performed from a minimally invasive blood collection can provide enough information to enroll patients in a precision medicine clinical trial."

Plus, she believes that studies like this will give physicians greater confidence in using ctDNA to evaluate their metastatic patients. "These studies also help with drug discovery and development—our pharma partners all collect liquid biopsy samples, because tissue is scarce and often not adequate for testing."

MoCha researchers concluded that CGP using ctDNA should be considered as a reasonable screening option for future NCI-sponsored clinical trials.

Beyond NCI trials, Pawlowski says that ctDNA is the future for oncology patients, and demonstrating its utility is key to its adoption and implementation in the clinic. Liquid biopsy can benefit metastatic patients by matching them with therapies; it's central for molecular residual disease testing, and it increases overall patient access to precision medicine. ◆

ASCO accepted nine total abstracts authored or coauthored by Illumina experts. They ranged in topic from health care resource use and costs for advanced lung cancer patients to immune gene expression patterns in endometrial carcinomas.

To read about why so many cancer patients miss opportunities for clinical trials, follow this link: illumina.com/company/news-center/feature-articles/missed-opportunities-for-cancer-patients.html